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STUDENT GRANTS FOR UNIVERSITY EDUCATION

THE report of the committee appointed in June 1958 under the chairmanship of Sir Colin Anderson "to consider the present system of awards from public funds to students attending first degree courses at universities and comparable courses at other institutions and to make recommendations" was published on June 2*. Eleven out of its sixteen members reported in favour of abolishing any means test for parents; but its key proposal is that all those ordinarily resident in Great Britain and admitted for the first time to first-degree courses in receipt of grants from the University Grants Committee should receive awards from public funds, provided, for universities in England and Wales, they had two passes at Advanced level in General Certificate of Education examinations or the equivalent; for Scottish universities they should have the statutory minimum entry qualification, that is, the 'attestation of fitness' of the Scottish Universities Entrance Board.

On July 28, the Minister of Education, Sir David Eccles, announced that, after consultation with the universities, local authorities and others concerned, the Secretary of State for Scotland and he accepted this recommendation. It was also their intention that the local authorities should continue to participate in the administration, but in view of the wide divergencies of view expressed by the public in regard to some of the Committee's recommendations, the Government needed more time to consider them. The Committee had specifically recommended that Parliament should make the Minister of Education and the Secretary of State for Scotland responsible for settling the detailed requirements, after rejecting proposals to simplify the present system either by making the universities, colleges and other institutions of higher education responsible for administering grants to students as agents of the Government, or by entrusting the award of all grants to an *ad hoc* national grants board, financed by public funds and enjoying some autonomy. The Anderson Committee recommended indeed that a Standing Advisory Committee should be appointed to advise the Ministers on decisions of policy and on problems arising in the day-to-day administration of the awards system; but while the Committee discusses in this report in some detail the advantages and drawbacks of local authorities as award-making bodies, it gives no clear lead as to the course to be followed. If the Ministry of Education and the Scottish Education Department do not assume entirely the detailed executive functions of award-making, it is suggested that these functions should be discharged by the two Departments but with the local authorities acting as their agents for some functions, or alternatively, by the local authorities, under rules drawn up by the two Ministers, subject to the students having a right of appeal to one or other of the Ministers.

From Sir David Eccles's statement it would appear that the Government intends to adopt something on the lines of the second of these three courses, possibly because it offers the best prospect of securing agreement in a field where opinions differ widely and are frequently strongly held. The Committee itself comments on the contrast between the community of interest and purpose among its witnesses and the wide diversity of their answers to the Committee's key questions. It was surprised to find how wide a difference of opinion existed, even within some well-defined groups, about the steps which should be taken to improve the present system and, except in minor matters, it was unable to detect any consensus of professional or public opinion on how to solve any of the main problems.

This is reflected to some extent in the report itself, though not, happily, in an admirable second chapter, which sets forth some general principles which should form the foundation of any system of granting awards from public funds. For this chapter alone and for the key recommendation already noted, as well as for useful but subsidiary proposals for simplification, the report is an important and valuable step which may yet lead to an agreement on major points of policy still at issue. It is a useful contribution to lucid thinking about a problem that has far-reaching implications, and not its least important feature is the way in which the reasons responsible for divergence of views among its own members on the question of the parental contribution are detailed.

First, the Committee is convinced that, while Britain urgently needs the greatest possible number of highly educated men and women, it should not depart from the ancient and sound tradition that young men and women go to a university to become all-round citizens and not merely to learn a special skill. Likewise, the Committee believes that no distinction should be drawn between men and women students: in the national interest all potential talent should be given its chance to develop. Full-time paid employment is not the only means of enriching the national life, and a sustained increase in the number of highly educated mothers, as well as fathers, would benefit the nation to an extent that is not yet generally appreciated.

The Committee recognizes that its proposals can scarcely avoid having an effect on both schools and universities, though this is not intended; and it thinks that the greater responsibility should properly rest on the universities and colleges. Nevertheless, it

* Ministry of Education: Scottish Education Department. Grants to Students: Report of the Committee Appointed by the Minister of Education and the Secretary of State for Scotland in June 1958. Pp xii+135. (Cmnd. 1051.) (London: H.M. Stationery Office, 1960.) 6*s*. 6*d* net.

is impressed with the need for uniformity in the treatment of applicants for awards, and the Standing Advisory Committee it proposes is intended to assist here and to deal with the practical and human problems that will inevitably present themselves. No feature of the report is more impressive than the way in which the Committee recognizes these human problems and seeks to dispel the anxiety which many students at present inevitably experience while waiting to hear whether they will receive the grant on which their ability to take up a university place depends. This is very notable in the comparatively minor recommendations contained in the final chapter of the report, which discusses various practical matters of importance to students and their parents.

Nor is this human interest one-sided. In commenting on the importance of interviews, the Committee expresses the hope that universities, in addition to making more uniform the present procedures and conditions of admission, will extend so far as possible the practice of interviewing candidates before acceptance. Quite apart from the function of interviews in helping to determine the choice between one border-line candidate and another, it believes that the influence of a properly conducted interview on the student himself is important. As the Committee rightly remarks, the student will in effect be applying for a grant of a large sum of public money, and it is unquestionably right that a positive effort should be made, in an interview, to remind the applicant that he or she is seeking the privilege of being backed by the community. Recognition that a university place is a privilege—although it has been earned—is too often overlooked, and if it were more generally remembered, as well as its implications, the criticism that many graduates look on a post as something which the community owes them, rather than as an opportunity to serve the community, might be less frequently heard.

This could be the more important if universities became in effect free for all as a result of the adoption of the majority recommendation to abolish the parental contribution. The Committee's observation, moreover, gains strength from the obvious liberality of the views of its members and their sympathetic understanding of the point of view of the student. The Committee is emphatic that students throughout Great Britain should have the freedom of choice of institution. Much of the value of higher education, it points out, lies in the contacts the student makes and the life he leads within the student community and outside the lecture room and the laboratory; and to get the full benefit, it is important that the student body should not be drawn from too narrow a field—it will gain richness from a wider field. Again, the Committee believes that it is important that students should be able to rely on a grant for the full normal period of the course on which they have embarked, and it specifically recommends that all awards should be so made, subject only to satisfactory progress and conduct and to appropriate measures to deal with arbitrary changes of courses by indifferent students while taking care of reasonable changes, particularly at the end of the first year.

Of the selection for awards no more need be added than that the Committee is emphatic that the universities themselves are best fitted to select those who should receive a university education. It thinks that since effective selection by local education authorities is mainly confined to border-line candidates, the return, in terms of improved selection and of public money saved, is small, and the present arrangements impose an undue burden on the schools and their pupils. It also concludes that no second process of academic selection should be required for the main stream of entrants to first-degree and comparable courses.

The major issues on which the Committee was agreed may be briefly reviewed. It recommends in the first place that the method of expressing the maximum grant in terms of "payment of fees plus a standard sum for maintenance" should apply throughout Great Britain, and each standard figure should include the same amount for books, clothes and incidental expenses. It rejects firmly the suggestion that the grant for books should be in kind. The student should be treated as a responsible person and left free to spend the money granted according to his own circumstances and his judgment of his own needs. Further, it thinks it important that the student and his university teachers should be aware how much has been allowed in his grant for the purchase of books, and accordingly publication of this amount is recommended. It also recommends that a fixed sum for travelling expenses should be included in the standard figure of maintenance, and it endorses the principle of grouping universities and of including in the standard figure of maintenance for each group an amount for the maintenance of students living in colleges or halls of residence or in lodgings. Holders of awards should be covered for the payment of national insurance.

In all this detailed assessment of the needs of holders of awards, the Committee treats the student as a responsible person, and if its sensible recommendations are adopted, it is only reasonable to expect that this will be generally recognized by students themselves. The recommendations for grants for vacations and vacation courses are no less sensible, and are generous although clearly recognizing the public interest. They are based on five principles: that award-holders should receive standard grants for maintenance throughout the vacations; this grant should be calculated at the same rate as that for 'keep at home' during term-time; the grants should be paid before the vacations for which they are given; deductions from subsequent grants should be made for any vacation periods in which the holder has been in paid employment; the standard vacation grant for the final long vacation should be calculated to cover four weeks only, and should not be subject to any declaration about paid employment.

The miscellaneous recommendations stress the importance of dealing with all applications for awards

as quickly as possible. A pamphlet should be printed to provide a general guide to the awards system, and if university and comparable awards remain the responsibility of local authorities, it is essential that full information about the local arrangements is widely available in each area. When the student is notified of the amount of his grant, he should also be told the conditions attached to the award and given a statement of the way in which it will be administered. If parental contributions are retained, the parent should be notified both of the amount of the grant to the student and of the amount of the parent's contribution. The recommendations regarding payment of awards are also sensible and would eliminate the practice of withholding payments until a certificate of attendance has been obtained from the university or college authorities. Instead, subject to the agrement of the university or college authorities, cheques for ordinary grant payments should be made available to award-holders through the university or college office, on the lines now followed by the Ministry of Education for State scholars. In addition, the Committee recommends that all award-holders should be able, on application, to draw an advance payment of up to £30 before the start of their first term.

Collectively, these minor recommendations should not only simplify the present system and establish some uniformity of practice, but also remove some of the anomalies and grievances which have been a source of complaint and even hardship to students. Nor is the cost excessive. With the abolition of parental contributions, the net cost of which in 1958–59 is estimated at £5·5 million, the total increased cost arising from the proposals of the report is about £8·2 million, compared with £7·1 million if the modified parental contributions suggested as alternative are adopted. For a university population of 135,000, assuming the students from the United Kingdom following first-degree courses continue to form roughly the same proportion as in 1958–59, the cost to public funds is estimated at £22·9 million under the present system, £32·3 million with modified parental contribution and £33·8 million if the parents' contributions are abolished.

Financial considerations should thus not be of decisive importance in determining the abolition or retention of the parents' contribution, particularly in view of the general agreement that some modification is required; and the difference in opinion between the advocates of a more generous system and those who would abolish the parents' contribution does not turn on cost. The evidence submitted to the Committee indicated that, while none of the bodies giving evidence was entirely satisfied with the present system, the reforms suggested differed widely. Out of seventy organizations, forty recommended complete abolition of the parents' contribution and fifteen its abolition for approved fees while retaining it for maintenance. Moreover, it was apparent that differences of opinion existed within the organizations themselves, and the division of opinion on the Anderson Committee itself thus reflects that existing in Britain generally.

Nevertheless, it is important to note that there was a considerable measure of agreement on the Anderson Committee. It was agreed, for example, that none of the half-measures suggested offers a satisfactory solution, and that a straight choice has to be made between relieving parents altogether or maintaining a system of assessment of parental income for awards purposes. Again, the Committee agreed that the abolition of parental contributions would be a fundamental change, and that an assessment of its probable effects is a matter of judgment. In the Committee, the difference of opinion lies in the assessment of those effects. The majority is firmly convinced that they would be beneficial, and the argument is cogently and convincingly presented. The minority sees a strong possibility of harm, and does not regard the difficulties of the present system as serious enough to warrant running the risks involved in abolition; but that case is far less convincingly argued. None the less, all are agreed that the demand for parental contribution must deter some well-qualified boys and girls from entering universities, that the present system imposes too heavy a burden on many parents and students, and that if parental contributions are retained they must be substantially reduced. There is also agreement that the level of contributions proposed in the report, which would, for example, relieve a married couple with one child from any contribution if their gross income is less than about £1,000, would largely remove the hardship on the middle-income parent on whom the present scale bears most heavily.

Having gone so far, the majority of the Committee would complete the process by abolishing the parental contribution altogether; believing that the higher the income below which no contribution is expected, the greater the number of families who get complete exemption and the smaller the actual yield both absolutely and in proportion to the cost and the administrative effort involved in collection. Secondly, and even more important, the smaller the number of families who are still required to make a contribution, the less the exaction of that contribution can be justified on grounds of general equity and the greater its resemblance to a discriminatory tax on a limited section of the community. If the level of contributions recommended in the report is adopted, about 60 per cent of all the present university and comparable awards would not be subject to parental contribution, and there is logic in the Committee's contention that a system of university awards should not superimpose what is in effect a second taxation system on some parents.

Whether or not the argument that abolition of the parents' contribution would provide a great stimulus to higher education is sound, the elimination of administrative complexities is undoubtedly an advantage, and it is clearly unjust and illogical to allow an awards system to penalize a small class of parents; not does the minority advance any convincing social or practical reasons for its retention. Prof. Brinley

Thomas, who also considers that the Committee does less than justice to the role of the State scholarship in the educational system of Britain in recommending that all types of State scholarship should be discontinued and suggesting that the State scholarship should be retained in a new form, with possibly a new name, dissents from his colleagues who wish to retain the parents' contribution in advocating at the same time the introduction of substantial sixth-form bursaries in the maintained schools. He regards public expenditure on ensuring that gifted boys and girls in the public sector are able to stay at school until the age for entry into the university as a first priority, and holds that to remove or reduce drastically the cost of university education for middle-class families while doing nothing to stop the leakage of talent among children at the age of fifteen in the lower-income groups would be an unwise and unjust use of public funds.

Prof. Brinley Thomas's note of reservation is much more cogently and convincingly argued than his colleagues' case for retaining the parental contribution; but nevertheless, he does not meet the real objection, namely, that to retain that contribution under present conditions is tantamount to differential taxation. It should be remembered, moreover, that the report proposes that parents should no longer be able to deduct child allowances from their taxable incomes in respect of children receiving grants. While it is perhaps understandable that the report should be somewhat hesitant in dealing with the financial aspect of the administration of grants as between the Government and the local authorities, the Committee leaves the Government in no doubt as to where the weaknesses of local authority administration lie and the need for some central direction in order to secure uniformity. That question must be settled by the Government before effect can be given to the rest of the report, and it is to be hoped that there will be no undue delay in reaching a firm decision and giving effect to some such simpler and fairer system of awards as the report outlines and removing injustices which were recognized as such by all its members.

UNIVERSITIES OF THE COMMONWEALTH

Commonwealth Universities Yearbook, 1960

Edited by J. F. Foster, assisted by T. Craig. Thirty-seventh edition. Pp. xxxi + 1509. (London: Association of Universities of the British Commonwealth, 1960.) 84*s*.; 13 dollars.

THE bulky appearance of this well-established Year-Book is an effective reminder of the extent of higher education in the Commonwealth. It was first launched in 1914, and, because of stable conditions in its first year of life, did not need revising each year.

Since then thirty-seven volumes have appeared, and, because of rapid changes, now needs to be reissued in new dress each year.

When the Year-Book edition of twenty years ago was published, it included references to eighty separate university institutions and recorded a (full-time) population of less than a quarter of a million students. In the present volume 135 institutions are encompassed with a total student population of 1,115,000.

The 1960 Year-Book follows a year of remarkable progress in Commonwealth educational development made noteworthy by the Commonwealth Education Conference held at Oxford in July, 1959. One of the recommendations of the Conference was the launching of a scheme to award a thousand scholarships, mainly at the postgraduate level, tenable in the 'sponsoring' countries by students from the rest of the Commonwealth. A special appendix describes the working of the scheme.

Five new universities are included for the first time. These are Monash University in Australia, and Gorakhpur, Jabalpur, Marathwada and Vikram Universities in India; their inclusion is itself tribute to the way the Commonwealth countries are developing their professional man-power. One small item which will give much pleasure in Britain is that "the youngest member of the university family is the University College of Sussex at Brighton which was formally constituted in 1959 . . . . It is hoped that enough progress will have been made with academic buildings and the recruitment of staff for 200 students to be admitted in October, 1962".

The format of the book follows the pattern of earlier years, universities being grouped in countries, and each group is introduced by an essay describing in general terms the university system of the country and its general provision for higher education. For the first time the British section includes a table showing at which colleges of the University of London courses for a first degree are provided in fifty different subjects of study. This supplements a similar table for the universities of the United Kingdom as a whole which was warmly approved when it was introduced two years ago; it re-appears in the present edition.

One feature of the book which should bring legitimate pride to graduates from universities of the 'Mother Country' is that there are few faculties of universities in member countries which do not include some members of staff with British degrees. Before becoming overwhelmed with self-gratification, however, British graduates should study the interesting faculty developments in other Commonwealth universities and reflect whether or not development in Britain is still too hide-bound by tradition.

The value of this tremendous compilation is well brought out in Appendix 1. Without introduction or explanation it includes details of the Universities of the Republic of Ireland; it is encouraging to find a way of seeing that our Irish friends are not left out.

Other appendixes deal with university admission requirements, particulars of students from other countries who are not at present in British universities; details of British academic institutions abroad and of the Association of Universities of the British Commonwealth whose book this is. Could they now be persuaded to ask a research student to investigate the entrance examinations to all Commonwealth universities, the patterns (and costs) of administration, student admissions, rejections and achievements, and to issue a report? The overall view would be received with interest.

FIRST CENTURY ROMAN ARCHITECTURE

Roman Construction in Italy from Tiberius through the Flavians

By Marion Elizabeth Blake. Carnegie Institution of Washington. Publication No. 616. Pp. xvii+195+13 plates. (Washington, D.C.: Carnegie Institution of Washington, 1959) Paper 8.25 dollars; cloth 9 dollars.

IN 1957, Dr. Marion Blake published her "Ancient Roman Construction in Italy from the Prehistoric Period to Augustus", a chronological study of the methods and materials employed by the earliest Roman builders which has proved of great value to scholars. Now she continues her researches through the first century A.D. to the end of the Flavian period, incorporating into them, as before, many of the copious notes and photographs left by the late Dr. Esther Van Deman for a work of this kind. The extensive bibliography shows, however, how these have been supplemented by the work of other scholars, while the illustrations include excellent photographs by Prof. Lugli and Dr. Ernest Nash.

About half the length of its predecessor, the new volume begins with a brief introduction describing the building materials in use during the time of Augustus and the types of evidence valuable for chronology. After this the detailed examination of the evidence begins in Chapter 2, covering the Julio-Claudian Epoch from Tiberius's accession in A.D. 14 to Nero's death in A.D. 68. Tiberius seems to have adopted no innovations, apart from an increased use of brick-faced concrete, and Claudius built comparatively little in Rome. But Nero was anxious to beautify and enliven his city, and in the early years of his reign new baths and an amphitheatre arose as well as a palace, the Domus Transitoria. The great fire of A.D. 64 gave him an opportunity for town-planning which he used wisely, replacing the narrow, crooked lanes with wider streets and open spaces. Less timber was used for building and the employment of Gabine stone and peperino was encouraged as these materials were believed to be more resistant to fire. Plans were made for the great Domus Aurea which replaced the Domus Transitoria, but the new palace was never completed, and many interesting constructional details are revealed by its unfinished state. The walls show the first use of concrete faced with the triangular bricks made by cutting square tiles diagonally in half, and several new developments in vaulting are also noted. Roman private houses and tombs of this period are also briefly described, and some consideration is given to building in other parts of Italy, notably at Ostia and at Pompeii, where the earthquake of A.D. 62 made extensive reconstruction necessary.

The third chapter takes us from the Civil War of A.D. 69 to Domitian's death in A.D. 96. Vespasian, the first of the Flavian emperors, continued Nero's policy of reconstruction. He also initiated the building of the Colosseum, work which was carried on by his sons, Titus and Domitian. Dr. Blake's account of it is full of details of human as well as of structural interest; for example, the use of awnings to shade the spectators from the sun, and the various barriers and other measures needed to protect them from the wild beasts. Titus's brief reign is chiefly noteworthy for another disastrous fire in A.D. 80. As a result of it his successor, Domitian, was faced with problems similar to those which confronted Nero and he also seized the chance to add, enlarge or elaborate. Temples, baths and fora, as well as the great palace on the Palatine hill, were all under construction during his reign. The chapter concludes with an interesting description of buildings on the imperial estates, various engineering works and public monuments in other parts of Italy, and the latest developments at Pompeii and Herculaneum prior to Vesuvius's eruption.

The final summary includes a brief résumé of building methods, and shows us how the development of a nearly perfect concrete left architects free to experiment with ground-plans of increasing elaboration. Not all the problems of weight and stress, however, had yet been solved, and consequently much of Domitian's vaulting was to need reinforcement in Hadrianic times. This carries us beyond the limits of the present book, and we look forward to the next volume in the series which, Dr. Blake promises us, will carry her researches to the time of Constantine.

JOAN LIVERSIDGE

THE MECHANISM OF ADAPTIVE BEHAVIOUR

Design for a Brain

The Origin of Adaptive Behaviour. By W. Ross Ashby. Second edition, revised. Pp. ix+286. (London: Chapman and Hall, Ltd., 1960.) 42s. net.

AT one time it was not generally thought that learning could be regarded as a mechanical process. The view that it could is now widely held. This is due partly, if not largely, to Dr. Ashby's writings over the past twenty years. A major work of his, "Design for a Brain", now appears in its second edition. This is virtually a new book. Its object is to analyse the character of the activity of the brain, and learning in particular, in mechanistic terms. To drive home this approach an analogue computing device, the homeostat, has been so constructed as to exhibit purposeful, adaptive behaviour. The description and discussion of this device remains one of the central features of the book.

In broader terms, "Design for a Brain" is devoted to the consideration of goal-seeking mechanisms that change continuously. Mechanisms using discrete-step operations are easier to analyse, but continuously changing mechanisms are more readily comparable with organisms. Dr. Ashby is a creative thinker and a rigorous one. He defines precisely all the terms he uses. He deals with dynamic systems, that is, with sets of variables selected from vast numbers of variables that constitute machines. The systems considered are those that are stable and that show purposeful behaviour. The stability in a system, brought about by feedback, characterizes only certain combinations of the parts of the system. It is contended that adaptive behaviour of a system, or learning, is mediated by two feedback loops, one forming a close link between sensory and motor channels and another "working intermittently and at a much slower order of speed". Such a system is called ultra-stable, and the behaviour of the homeostat exhibits ultra-stability.

The action of the brain appears to be in principle like that of an ultra-stable system, but, of course, it is much more refined than anything so far designed.

Chapters 1–9 of the book are concerned with the basic problem of the mechanism of goal-seeking, adaptive behaviour, while Chapters 10–18 give consideration to the refinements of such a mechanism. One of them is a method for coping in an efficient manner with recurrent disturbances in the environment. Again, the homeostat is so constructed that every unit interacts with every other unit. It is shown that this makes for slowness of adaptation. It is known that in the brain not all units are interconnected. The book considers designs in which units are not fully joined, and where success at learning that is partial is not disregarded. This brings us a little nearer to biological reality which the machine design attempts to meet. Another step towards this end that is being considered is poly-stability; a poly-stable system "is any system whose parts have many equilibria and that has been formed by taking parts at random and joining them at random".

Dr. Ashby is knowledgeable in many fields. The reader cannot fail to be impressed by the precision of his exposition. Even so, many will retain a sense of doubt. Put briefly, the doubt is as to whether the approach represented by "Design for a Brain" is the right one towards a better understanding of the functioning of the brain. In striving towards this aim there is, of course, no substitute for experimental studies in physiology and psychology. The cybernetic approach is likely, however, to be of some help to many of those who are engaged in experimental work.

W. SLUCKIN

SURVIVAL IN THE COLD

Recent Research in Freezing and Drying

Edited by Dr. A. S. Parkes and Dr. Audrey U. Smith. Pp. vii+320. (Oxford: Blackwell Scientific Publications; Springfield, Ill.: Charles C. Thomas, 1960.) 63*s*. net.

IN 1951 the first international symposium on freezing and drying created a great deal of interest and the Institute of Biology, which organized it, decided that so many advances had been made that a second symposium was justified in 1958. Unfortunately, it has taken two years for publication of the papers presented so that the volume is already out of date in many of the subjects with which it deals. At the first symposium Fry had shown that the addition of glucose decreased the lethal effect of freeze-drying for micro-organisms, and many of the papers read in 1958 described work or theories to explain the role of adjuvants such as glucose, sucrose and glutamate. The effects varied with the method of freeze-drying used; Greaves showed that a mixture of 5 per cent dextran and 5 per cent sodium glutamate was excellent for bacteria that were pre-frozen but was not suitable for the spin-freeze method of drying; for this method a mixture of 5 per cent bovine albumin and 5 per cent sodium glutamate was satisfactory. Obayashi reported that for *BCG* vaccine glutamic acid alone gave better survival-rates than glutamic acid plus sugar. On the other hand, Muggleton used a mixture of dextran, sucrose and glutamate for his *BCG* vaccine. W. J. Scott believed that certain essential metabolites of living cells may be toxic to dried cells. This hypothesis is controversial, but Scott's finding that survival depends on the water activity of the dried product will find more general acceptance. G. R. Scott and Rampton sought guidance on the influence of size of batches in the preparation of virus vaccine. Their experiments suggested that the difference in antigenicity between different batches was much less than Daubney had postulated in 1951, and asked if they had misinterpreted their results.

An important part of the symposium, and so of the book, dealt with the freezing and drying of tissues, and here the greater advances were recorded. The use of glycerol to prevent ice crystal formation has done much to make the freezing of cells a safe procedure but, of course, glycerinated material cannot be dried. Bone, skin, arteries and corneas have all been freeze-dried; but, as Parkes says, the tissue cells seldom survive, and the material only forms a scaffolding on which new tissue can form. In the cornea freeze-drying modifies the protein constituents, and the antigenicity of the material is so reduced that it is possible to use tissue from another animal species.

Several papers dealt with the theoretical aspects of freezing and drying and these have a special interest for the biophysicist. In general, the papers are printed as they were delivered, and, as few make attractive reading, it is a pity that the editing was not more strict.

S. T. COWAN

MATHEMATICAL METHODS IN ECONOMICS

Studies in Linear and Non-Linear Programming

By Prof. Kenneth J. Arrow, Prof. L. Hurwicz and Hirofumi Uzawa. With contributions by Hollis B. Chenery, Selmer M. Johnson, Samuel Karlin, Thomas Marschak and Robert M. Solow. (Stanford Mathematical Studies in the Social Sciences, Vol. 2.) Pp. ix+230. (Stanford, Calif.: Stanford University Press; London: Oxford University Press, 1958.) 60*s*. net.

THIS book is the second in the series, Stanford Mathematical Studies in the Social Sciences. It is a collection of research papers, and most of the results were obtained during 1955–58. It is divided into three parts, after an introductory chapter which explains and summarizes the contents of the various papers.

The first part is purely mathematical and deals with existence theorems, including the Kuhn–Tucker theorem on concave programming. There is a paper by Hurwicz on programming in linear spaces, and this includes an account of linear topological spaces and their properties. This account is of an introductory nature and will help considerably the reader who is not already familiar with the field.

The second part is concerned with the gradient method, so called because the gradient of a certain vector figures prominently in it. The idea is to solve a certain set of differential equations by using the finite difference approximations. The gradient method is available for non-linear programming problems, but for a linear problem it is not suitable since it gives rise to an oscillatory rather than a convergent path.

The third part deals with methods for solving certain particular problems, linear or non-linear. One problem concerns price speculation, where an individual may buy or sell a commodity, but is not allowed to borrow. If the costs are those for holding a stock

of the commodity the problem is linear; but if the costs are brokerage fees proportional to the amount bought or sold the problem is non-linear. Optimal operating policies are determined in each case. Another problem deals with the allocation of n tasks to m machines, where the machines are ordered in terms of increasing capability and the tasks in order of increasing difficulty. A third problem—directly in the field of inter-industry economics—is solved by a method which was originally applied to the problem of resource allocation in under-developed countries.

Mathematics has by now invaded in force the social sciences. The vigour with which various classes of problems in economics, for example, are being attacked mathematically is quite surprising. This situation implies an increasing divergence between what one might call the verbal or linguistic economist and the econometrician, who deals, so far as possible, with measurable concepts. The book under review is certainly meant for the latter—in fact it will probably only be understood by the mathematician interested in economics rather than the economist who would like to understand the workings of mathematics within his subject. L. S. GODDARD

MANAGEMENT IN THE UNITED STATES AND THE U.S.S.R.

The Red Executive

A Study of the Organization Man in Russian Industry. By Dr. David Granick. Pp. 334. (London: Macmillan and Co., Ltd., 1960.) 21*s*. net.

AN amalgam of wide reading, many personal discussions and actual visits to a variety of industries inside the U.S.S.R. and the United States has enabled Dr. D. Granick of the University of Wisconsin to provide a great deal of comparative information about Russian and American management which hitherto has been subject to little more than speculation.

During his investigations Granick set out to determine the educational background of the managers, the pressures and incentives which govern their lives, the tasks before them and how the factories and social environment of the U.S.S.R. differ from those in the United States. For the British student, at least, the book is most satisfying and worthy of recommendation to many readers. The most striking of the findings are those which show that the similarities between the Russian and American management greatly outnumber the differences and, indeed, link them more closely than American and British managers.

The main differences stem from the nature of each country's economy. In the U.S.S.R. the marketing manager does not exist; everything produced can be sold. Salesmanship, advertising and product design to meet competition and make last year's model obsolete, which are major American pastimes, do not exist in the U.S.S.R. Their problem is the getting and allocation of raw material, and the American purchasing officer is replaced by a procurement official.

A major difference might appear to be the place of the trade unions. Whereas in the United States the unions are reputed for their ability to drive hard bargains and, sometimes, disrupt production, in the U.S.S.R. the trade unions are imagined to be apostles of productivity and essential props for management. This may well be, but those familiar with the politically backed works commune would support Granick's statement that the American manager has little cause for grumbling compared with the Russian. A surprising difference is that the Russian manager is much more prepared to try out new ideas than his American counterpart. Granick believes that this may spring from the much more "theoretic" nature of the Russian training.

Among the many similarities of the Russian and American managers, the most striking (and from the British point of view the most challenging) lies in their educational backgrounds. In the U.S.S.R. the majority of managers get full-time education up to university level; in the United States little more than half are college-trained. In the U.S.S.R. the majority have engineering degrees; in the United States almost half the college-trained managers have general arts degrees. The American preoccupation for the "rounded" man is bound up with the fact that students are free to choose courses for themselves. This is also true of the U.S.S.R., but the courses made available are circumscribed by the needs of the economy.

The American graduate business training schools are largely missing in the U.S.S.R., which professedly believes in the value of manual work in introducing graduates to industry. The differences are not so great, however, because the Russian engineering graduates take a postgraduate diploma which necessitates involvement in an industrial organization. Another point of similarity is that, although the position is hardening in the United States, in both countries the way to the top is still wide open to the boy of ability and application.

Many other matters emerge to make this book of absorbing interest. Russian academic authorities, for example, appear to be as hazy about Russian management practice as most American university lecturers are about what goes on in their business training schools. The echo from Britain would also resound to complaints from research workers from both sides of the Iron Curtain about the difficulties they meet in obtaining permission to study factory administration in any kind of depth.

In both countries students are encouraged to work in industry as part of their educational (*sic*) development. One large American university has about one-seventh of its better-off full-time students doing forty-hour-a-week-jobs. In the U.S.S.R., as in Britain, the student is expected to study full-time during university term. Before graduating to the managerial level, however, the Russian spends a considerable period as foreman or assistant. The attitude of some British university teachers to vacation work for students may need reconsideration.

Granick also deals with the size of industry in both countries, the inverse operation of Parkinson's Law in the U.S.S.R. over the past twenty years (this supports those who believe it to be based on false premises), the lack of definition of the foreman's job in the United States, U.S.S.R., and Britain, and enough related matters to make his book worth a place in libraries in many countries. He should now perform a service to British management by preparing a second volume describing the observations he has made during his year as a Fulbright Fellow in Great Britain. T. H. HAWKINS

The Road to Man

By Herbert Wendt. Translated by Helen Sebba. Pp. 253+31 plates. (London: Lutterworth Press, 1960.) 30*s*. net.

IN his preface the author of this work confesses "'The Road to Man' is therefore not just a sober, factual account of the animal world, but a kind of novel of the animal world, a novel with many chapters—which are only superficially disjointed". Depending on one's estimate of superficiality, this is an acceptable description of the book. In the course of twenty-nine brief chapters reference is made to virtually the whole of the animal kingdom. It follows that scant justice is accorded to most aspects of the subject, and the general reader, for whom the book is intended, will close it with some dissatisfaction at having been brought to innumerable doorways and then led hastily away in order to complete his tour before closing time. Mr. Wendt's objective has been to demonstrate man as one among many animals, and not, as many would like to think him, the central figure about which the rest of Nature revolves. It cannot be said that he has successfully achieved this admirable end, although certainly he has demonstrated an enormous diversity of natural phenomena. But the pattern inherent in his sub-title, "An Informal History of Evolution", is sacrificed to a disjointed series of examinations of individual threads in the weave.

Inevitably, with so much ground to cover, the author has taken many short cuts to what he believes to be the truth, and many of these are tolerable approximations to probability. But it is impossible to pass unchallenged such statements as "Protoplasm which has the same chemical structure as that of the sea at the time when life is believed to have evolved" (p. 22), or "A lot still had to be accomplished before the lampreys became real vertebrates" (p. 64). Nor can one accept the assumption that "the mature eel being totally oriented to seaweed and deep sea . . ." is thereby constrained to migrate to the Sargasso Sea in order to breed; while the description of the actively carnivorous habits of sea urchins can only be ascribed to the author's aforementioned fictional approach to his subject. The book is embellished with a number of excellent photographs, rather more randomly selected than is the text. A word must be added in praise of the translation, the style of which is excellent. L. A. HARVEY

Studies on Agar Gel Electrophoresis

Techniques—Applications. By R. J. Wieme. (University of Ghent: Department of Internal Medicine.) Pp. 531. (Brussels: Arscia Uitgaven, N.V., 1959.) 680 Belgian francs.

THE beautiful technique of immuno electrophoresis introduced by Grabar and his associates gave great encouragement to the choice of agar gel as a supporting medium in zone electrophoresis. It has a number of advantageous features such as good resolving power for proteins, adaptability for very small scale work, and its ability to be converted to a thin transparent film after electrophoresis and staining makes it suitable for photometric scanning. These and other features are discussed in much detail by Dr. Wieme in his monograph. The author describes his various modifications of carrying out the electrophoretic run on microscope slides coated with agar, and of interest is an ultra-microprocedure whereby as little as 0·03 μl. of serum or 2 mgm. of tissue may be analysed. Applications, mainly of one particular micro technique to studies of constituents of normal human sera and of animal tissue enzymes, are described, and thereafter clinical studies of sera in some fields of wide interest, namely, plasmocytoma and primary macroglobulinæmia, modification of γ-globulin in disease and examination of lactate dehydrogenase in disease. All the sections include a thorough survey of the work of others and a good coverage of the literature on the various subjects discussed.

This monograph gives a highly detailed exposition of practical and theoretical aspects and is therefore of value to those interested in agar-gel electrophoresis. Unfortunately, it is written as a thesis and therefore not entirely suitable for general reading. It could form the basis of a very useful book of wide appeal if the subject-matter were better arranged, unnecessary details cut out and the English improved. (Some of the phrases, being literal translations of Flemish idiomatic expressions, are very quaint, and would delight the heart of Paul Jennings.) There is a great deal of useful information in this work, and so it would be a pity to leave it in its present form and not attempt to make it more presentable and more reasonably priced. R. CONSDEN

The Indian Ephemeris and Nautical Almanac for the Year 1961

Pp. xxvi+448. (Delhi: Manager of Publications, 1960.) Rs. 12.50 nP.; 19*s*. 6*d*.

THIS volume, the fourth annual issue of the "Indian Ephemeris", plays an important part in the development of modern astronomy in India. It is a worthy tribute to the enthusiasm and persistence of the late Prof. M. N. Saha, to whom the original proposal and a large part of the preliminary organization and planning were due.

The initial impetus for the introduction of a separate "Ephemeris" arose from the necessity to reform and unify the many different calendarial systems in use in India. It is therefore not surprising that no fewer than 48 pages are devoted to the Indian Calendar, giving full details of the Reformed Calendar of India.

In other respects the ephemeris follows very closely the models adopted by the other national ephemerides. The fundamental calculations have for long been shared between the ephemeris offices of France, Germany, Spain, the United Kingdom, the United States, and the U.S.S.R.; and these have been made readily available for the preparation of this volume The work of preparation has thus largely been concerned with compilation, presentation and printing: these have been done excellently under the competent guidance and supervision of Sri N. C. Lahiri. But the ephemeris of the Moon at ephemeris transit, and the special tables of sunrise, sunset, moonrise, and moonset for India have been calculated specially.

The low standard of practical astronomical knowledge in India, coupled with the prevalence of astrology, was one of the main reasons for the inauguration of a new national ephemeris at the time when, in other countries, there was a strong tendency towards unification. The introduction of the "Indian Ephemeris" has already started to inspire serious astronomical work in India; in general competence and in attention to detail, of both content and presentation, no better standard for that work could have been set up. D. H. SADLER

WORLD FOOD AND POPULATION

IN recent years the British Association for the Advancement of Science has become increasingly aware of the necessity to re-align its activities to meet modern needs. Gone are the days when its annual meeting provided a forum for discoveries, great and small and made within the preceding twelve months, to be disclosed to an expectant world: radio, television and the scientific and technical press are only too anxious to publicize at once whatever discoveries are deemed to have 'news value'. But not only is the lay public bewildered by this bombardment; scientists themselves also find it increasingly difficult to assess the meaning and implications of work other than that in their own, often narrow, specialisms. The annual meetings of the Association have always provided a welcome opportunity for scientists in the many branches to meet one another and to make contact with an interested public. Now the Association is making a determined effort to present a balanced view of scientific progress to a wider audience—through its work with young people, its programmes of lectures at local centres, the new and attractive format of its bi-monthly journal, *The Advancement of Science*, and in other ways. At the Cardiff meeting a bold new experiment was tried. Coincident with the inauguration on July 1 of the five-year Freedom from Hunger campaign of the Food and Agriculture Organization of the United Nations, the Association chose as a central theme, to be emphasized by as many sections as wished, the numerous aspects of population pressure on land resources. A complete innovation was the suspension of all sectional programmes for one whole day—Monday, September 5—in favour of two plenary sessions of the entire Association in the Sophia Gardens Pavilion, devoted to a symposium on "World Food and Population".

Some 2,000 members assembled to hear the president, Sir George Thomson, open the proceedings. He reminded the audience that it was the success of medical science that necessitated a falling birth-rate to match the falling death-rate. It was not right that scientists should pass the problem to the politicians who, in any event, had to deal with the toughest and most resistant material in the world, human nature.

Dr. Norman C. Wright, deputy-director general of the Food and Agriculture Organization, presented the facts of the world food situation as they are known to that Organization. He drew a distinction between under-nutrition and malnutrition, and gave reasons for using calorie intake as a measure of under-nourishment. What proportion of the world's people can be described as under-nourished clearly depends on the standard taken. While British conditions suggest that 2,800 calories a day are necessary for the development of full health and vigour, requirements for the peoples of tropical climates, with lower average body-weights and stature, are clearly less. But 60 per cent of the world's population appear to have an intake of less than 2,200 calories, of which nearly half have less than 2,000 calories a day. With a poor harvest, under-nutrition passes very easily into semi-starvation and loss of mental alertness, and even moral standards. Malnutrition accompanies under-nutrition, but is also found when the intake, though adequate in amount, is derived from an insufficiently varied diet—especially a shortage of protein from an all-cereal diet. Such malnutrition is reflected in the presence of several deficiency diseases—notably kwashiorkor—liable to affect children after weaning, that is, when they are transferred from a milk to a cereal diet. Dr. Wright urged that neither distribution of food surpluses from countries such as the United States nor a world-wide adoption of vegetarian diets could solve the problem—only the widespread and rapid application of recent scientific and technical advances.

Sir Alexander Fleck took up the latter point in the afternoon. Apart from advances in all kinds of techniques constantly being made, there is an adequate body of knowledge, and has been for many years, to secure sufficient food, indeed abundant food, for all mankind if only that knowledge is applied. There are six ways of producing more food: by extending the area under cultivation, substituting more suitable crops or varieties and animals or breeds, providing more water, more nutrients, adopting better techniques, and increasing efficiency of crop or animal use. A comparison of present-day yields, for example, between Japan and India in rice shows at once the enormous possibilities to be achieved by providing crops with adequate nutrients and water.

Both Sir Alexander and Prof. H. D. Kay—obviously through his extensive practical experience in recent years in many countries—stressed the human aspects of the problem: how to get right to the peasant cultivator to help him to help himself. The missionary spirit and the sense of dedication to a cause is nothing new to the British: both are badly needed to-day. Equally vital is the need to convert governments and administrations to the necessity for constructive agricultural policies. Too often agriculture is a Cinderella among government departments.

Prof. David Glass, speaking on the present trends of world population, stressed the double importance of focusing attention on the remainder of the present century, since by 2000 A.D. world population is most likely to increase to more than 6,000,000,000. Because of the present age-composition of the population in the less-developed countries, even such sharp reductions in fertility as might result from a rapid spread of birth control would not prevent very considerable increase in numbers by the end of the century. Even with a 50 per cent fall in live births in India during 1956–81, the population would still increase by more than 200 million by 1986. At present the evidence does not justify an assumption of a general fall in fertility: it is more realistic to plan for an increase of world population at the rate of at least 1·6 per cent per annum. Prof. Glass considered that we must be prepared for a very massive underpinning of planned economic and social development. Although he included emigration among the measures to be included, he noted that the present increase in world population in one year is about equal to the

net oversea migration from Europe in the 150 years 1800–1950. He noted, however, the symbolic value of emigration in promoting also economic and social change. In view of the relative ease of increasing food output in Western lands in mid-latitudes, the planned disposal of food surpluses in the West may be no less essential than the raising of agricultural productivity in less-developed regions.

Prof. Arthur Lewis, recently elected to the office of principal of the University College of the West Indies, discussed economic conditions for greater output under the four main headings of incentives, knowledge, capital and organization. He placed expanding demand first among incentives: rising standards of living in the towns demanding more food and more expensive foods. Provided the fruits of the farmer's labours accrue to him and not to the middle man or landlord, he doubted the importance of price stability, preferring freedom of prices to rise. Prof. Lewis was insistent on the enormous capital requirements needed in farming, but some of his assertions regarding organization can be questioned. In his own summary he asserted, "in most of Asia, where labour is abundant, mechanization contributes only where it brings under the plough land which could not otherwise be cultivated, or makes possible more crops in a year. Mechanization has more to contribute to the under-populated parts of Africa". He advocated subdivision of large properties, especially in Latin America, and considered that compulsion should be used when farmers are too ignorant and conservative to use better seeds or improved cultural practices, and advocated collectivization where necessary. As a West Indian who has a wide experience in many lands, it is interesting that Prof. Lewis more than any other speaker should advocate such forceful methods.

Prof. Dudley Stamp, speaking on land use and food production, stressed the contrast between a population not only increasing at an unprecedented rate—in excess of 45,000,000 a year—but also with rising standards of living, which meant both more and more varied food, more spacious layout of homes, facilities for recreation and movement and other extensive demands on land, with the known, fixed and broadly inextensible extent of the Earth's land surface which had to satisfy those many demands. While any part of the Earth's surface may have an economic importance through the occurrence of minerals, or for other reasons, the ecumene or habitable surface of the Earth having sufficient heat, moisture and soil to produce crops to support human life, is of limited extent. A fifth of the surface is too cold, a fifth too arid, a fifth too mountainous and a tenth soil-less, so that only 30 per cent is potentially cultivable even if the many hazards of soil management in the tropics are overcome: at present each of the world's 2,900,000,000 inhabitants has a share of about 12·5 acres, or 4 acres 'potentially cultivable'. Of this, 1·1 or 1·2 acre is cultivated. Equating non-food crops with the contribution in food from the great open grasslands, it takes the produce of rather more than 1 acre to feed one human being. Against this world yardstick, extreme contrasts can be seen between one country and another—ranging, for example, from Canada with 140 acres a head, 21·5 officially classed as cultivable, with 3·5 used, or the United States (12·5, about 6, 3·0) to England and Wales (0·8, 0·6, 0·55) and Japan, where the food has to be wrested from a cultivated acreage of 0·17 acre a head. In some countries it is clear that concentration on high-calorie foodstuffs and intensive cultivation is a national first priority; in most countries comprehensive land planning is the only sensible approach to the problem. Such planning must be based on objective surveys and mapping of existing land use (hence the importance of the world-wide scheme of the World Land Use Survey of the International Geographical Union) with an attempt to understand the reason for the present position and trends.

Prof. Stamp advocated further attempts to rate land of different types according to potential productivity and compared actual production by using a Standard Nutrition Unit of 1,000,000 calories farm production per annum (equivalent to a food intake of 2,460 per day) pointing out that 'carrying capacity of land' varies in even leading countries from less than 0·3 to 7 such units an acre. He appealed especially for fresh thinking in many directions, and by the many different sciences which have contributions to make. In particular he pointed out the fallacy of discussing 'over-population' unrelated to standards of farming technique—Britain has been over-populated at least since Norman times. A maximum population which could be supported is very different from the small body of experts which might most effectively produce the food. In erosion and flood control more emphasis should be placed on trapping and distributing eroded material where it could provide useful land. While it is desirable to preserve naturally good agricultural land and provide conditions where the microfauna and microflora can do their work without cost, why should not modern earth-moving machinery over large areas mix sterile sands and intractable clays to the right texture to receive the chemist's nutrients?

In the afternoon, after Sir Alexander Fleck and Prof. Kay had spoken, eight or nine speakers who had previously given in their names took part in a general discussion before Prof. P. M. S. Blackett wound up. Ritchie Calder remarked on the historic significance of the occasion—perhaps the first time in 129 years that the Association as a whole had got together to debate a problem of world-wide importance. Science had provided a vast super-market of knowledge: the user must have a thought-out shopping list. The common tacit assumption of the economists that efficiency in farming is to be equated with large-scale monoculture was voiced by Colin Clark, and brought vigorous headshaking from Dr. Kay; further, he doubted whether protein deficiency is widespread and whether many of the policies of the Food and Agriculture Organization are right—especially any encouragement of small-scale intensive mixed farming. Mr. James Callaghan, M.P., sharply reminded the Conference that a 5 per cent increase on prices paid for the agricultural raw materials of the 'under-developed' lands more than equalled all 'aid': guarantee their prices and forget 'aid'. Sir Charles Darwin felt that only part of the problem is being considered: man is an animal and behaves as such. With plenty of space there has been unparalleled expansion for two hundred years—the struggle for existence must come. Birth control may stave off the evil day, but is it not possible, he asked, that those who have believed in birth control would be the ones to go under? Prof. Sargant Florence, however, held that we do not want just to keep alive, but at a proper standard: we must increase production, but decrease reproduction.

In his summing-up, Prof. Blackett stressed four points: first, nothing we can do, short of nuclear warfare, can alter the fact that a great increase in population is inevitable in the near future; secondly, the technical 'know-how' exists; thirdly, there must be initiative and 'crash-action; fourthly, the educational aspect is vital and we should open the doors of our universities and technical colleges, however difficult it may be, more widely to overseas students. Finally, he felt that the day's useful discussions had ended on a note of restrained but robust optimism.

L. DUDLEY STAMP

AFFORESTATION OF INDUSTRIAL WASTE

THE sight of derelict land is all too familiar in the industrial areas of Great Britain, and the purpose of the session which was held in Sub-section K* (Forestry) of the British Association on September 2 in Cardiff was to explore the possibilities of afforestation as a land-use tool to improve the amenities of such areas. The three speakers looked at the problem from different points of view: that of a Forestry Commission officer, a planning officer of a county council, and a land agent to an owner of substantial areas of ironstone workings. It was refreshing to find that there was a large measure of agreement between all three as to where and in what circumstances afforestation could be usefully employed.

The symposium was opened by J. Q. Williamson of the Forestry Commission with a review of the evidence which has been built up over the past fifty years on the planting of trees on colliery spoil heaps. In his opinion the earlier doubts as to the success of such planting because of the probable lack of fertility of such apparently sterile sites has proved groundless. A large range of tree species can be planted successfully on tips so long as certain precautions are observed. The choice of planting species must first be governed by local conditions, particularly by the smoke pollution factor, which may rule out all conifers. Exposure is of great importance in tree growth generally, and the miniature mountains created by many spoil heaps could lead to severe exposure, especially if the heap happened to be already in an exposed position.

In areas where there is atmospheric pollution, birch, alder, sycamore, and in more fertile sheltered areas, ash and poplar, were recommended by Mr. Williamson as the most likely to succeed. Where tips are situated in more rural areas, over which the atmosphere is purer, conifers can also be grown, and this is much more attractive from the economic point of view. Of the conifers, Corsican and Austrian pine are usually to be preferred, but Japanese larch and Scots pine can also do well. His experience has shown that there is no special difficulty in establishing such species by normal forestry methods, but the trees must be looked after. Grazing animals must be rigorously excluded from the young plantations and, most important of all, the local population must be taught to cherish the young trees. Most failures in the past have been due to vandalism, and it is almost a waste of time to embark on a planting scheme unless there is a determined effort to guard the trees from damage during their early years. He recommended strongly that a programme of forestry education for the local population should accompany the planting of any colliery spoil heap, and if possible the local school children should be encouraged to take part in the actual planting and to look on the resulting woods as their own.

Mr. Williamson then gave details of the experimental afforestation of an open-cast coal site in Coed Morgannwg. He pointed out that by applying a restoration specification, which did not entail levelling and restoration of the top soil, a great deal of money can be saved. The result of this work had been most encouraging, and of the species used Corsican pine, Lawson cypress and Japanese larch among the conifers and common alder, grey alder and false acacia among the hardwoods had grown well. The trees on the more porous slopes had grown better than on the level ground where the passage of heavy machines had led to compaction of the soil

After this technical appraisal of the problem, it was encouraging to learn from Mr. J. Casson, of the Planning Department of the Lancashire County Council, that the extensive work of afforestation carried out by his Department over the past nine years has led him to the same conclusions. He considers that there are thousands of acres in Lancashire alone which could be afforested with comparative ease and at not much, if any, greater expense than that incurred in establishing forest crops on normal sites. It is unfortunate that not many planning authorities in England and Wales have yet made use of Section 89 of the National Parks and Access to the Countryside Act of 1949 to undertake planting work aimed at enhancing the countryside. He considers that while the main objective of such a planting programme is the improvement of amenities, this work could obviously, to a greater or lesser degree, make a contribution to the economy of any area where forestry operations could be successfully carried out. The effect of enhanced amenities in checking emigration and attracting new industry could well be valuable in arresting economic decline; the converse is undoubtedly true—ugliness leads to emigration and discourages new industrial development. He looked on the work done in Lancashire up to the present as being mainly a fact-finding exercise to see how far forestry operations are practicable under various conditions of difficulty (climate, soil, pollution, etc.). They have located their siting in significant localities as experiments, not only in forestry, but also in the use of forestry as an instrument of land-use policy in the overall physical and economic rehabilitation of depressed and damaged regions. His Council's policy has been to acquire or plant under agreement without resort to compulsory purchase. While there is a wide choice of sites which might be planted in Lancashire, it is significant that land acquisition rather than technical difficulties has been the greatest problem in planning a forward programme. For every 100 acres planted, investigations and negotiations have been opened for 200–300 acres which have had to be

abandoned for one reason or another. Shifts in the value of waste materials and land, the presence of 'admitted' claims, conflict in the opencast coal-mining programmes, changes in legislation affecting land values and acquisition procedures, and the psychological factor that as soon as a public authority takes an interest in derelict land its 'value' often rises sharply, have all helped to hinder progress. In spite of this, he thought that it would not be justifiable to use the compulsory powers of the Act in the absence of any overall plan for rural afforestation and with such a wide choice of sites. The same arguments would not be so applicable in urban areas where town plans are well advanced.

More than 300 acres has been planted in Lancashire since 1951 under this scheme, and a great variety of sites has been tackled, varying from colliery spoil heaps, hæmatite waste and Gritstone quarries to degenerate woodland and bare land and moorland. The excellent slides shown by Mr. Casson and his forester assistant, Mr. L. A. King, illustrated very well the progress of the work and, although they had had their failures, it was obvious that, taken as a whole, this well-thought-out planting scheme has been most successful. Fourteen men are now employed on the work and a small nursery has been established to provide the necessary plants. With the development of 'know-how', they are increasingly able to introduce an element of landscape design into the work and they feel that they are now more successfully harmonizing economic, ecological and amenity aspects within a 'forestry' approach.

In spite of the very encouraging picture that was emerging, Mr. Casson admitted that there is a great deal still to be learned, and he made a strong plea that more scientific research should be done on the biological and technical problems posed by land dereliction, mineral working and the tipping of waste. He thought that such work would be of value not only to programmes of reclamation but also in the greater and increasing field of the planning control of the extractive industries. He realized that it is asking a great deal of local authorities to expect that they should embark on forestry schemes without the technical skills or documented data necessary to bring about a transformation in their derelict areas by using forestry; nevertheless, a great deal more could be done than was being done at present.

It was perhaps appropriate that Mr. Casson's inspiring talk on the tremendous possibilities of extending afforestation on industrial waste should be followed by a very factual account of the successful afforestation of ironstone workings in Northamptonshire on a really large scale. Mr. J. W. Houldsworth, land agent for the owners, Stewarts and Lloyds Minerals, Ltd., quoted chapter and verse of how more than 1,000 acres of land left derelict on 'hill and dale' after the ironstone had been extracted is now carrying flourishing plantations. This woodland area provides considerable amenity value to the nearby industrial town of Corby, as some of the earlier plantations are now 25–30 years of age and looking most attractive. Experience has shown that on the lighter soils a mixture of 40 per cent European larch with 40 per cent sycamore and 20 per cent Scots or Corsican pine is most suitable for the site, and the present intention is to leave the sycamore as a final crop after the gradual removal of the conifers. On the heavier boulder clay, common alder and occasionally oak have been planted, but this latter species has been very slow growing.

A permanent staff of 20 men is maintained under a head forester and two foremen. The biggest problem facing the Company is not the establishment of plantations but the extraction of produce from them, especially as the size of pole increases as the plantations mature. Up to date there has been no difficulty in disposing of the produce, because a small estate sawmill is maintained for converting it into fencing material for use on the estate and quarries; a large quantity of the second-grade material goes into the steel work for loading strips.

Mr. J. W. Houldsworth was emphatic that, apart from the difficulty of extraction, the establishment and maintenance of plantations on this very unpromising waste present no particular problems; in fact there are certain advantages over normal forestry, as no weeding or cleaning is necessary on these bare 'soils'. His conclusion was that afforestation is the most economic solution to the problem of treating some of this worked ironstone land, and that it would prove a good long-term investment.

In the discussion which followed the papers, it was generally agreed that much more use could be made of afforestation in reclaiming industrial waste than had been done in the past. One of the main problems which perhaps makes public authorities a little reluctant to embark on ambitious schemes is the difficulty of making more than intelligent guesses as to what will grow successfully on any particular site. As each site usually varies so greatly within itself, the cost of extensive soil analyses is scarcely justified, and the general opinion of the meeting was that although more research should be undertaken on the constitution and plantability of the various types of industrial waste, there is now sufficient evidence to convince the most doubting authority that at least the easier sites could be planted with a fair degree of confidence.

The most controversial point discussed was the future treatment of plantations on waste land, once they were approaching maturity. Mr. Williamson thought that it would be of no use ever to consider clear felling and replanting, and advocated the introduction of some form of uneven-aged selection system in order that the soil was never bared and the amenity was maintained; but several others felt that there was no reason why such areas should not be clear-felled on maturity and then replanted, so long as attention was paid to shelter belts being left where necessary.

On the extraction problem in the plantations on the ironstone workings, the simple solution of using horses was suggested for at least the small- and medium-sized produce.

The growth of different species was discussed, sycamore and birch in particular, and it was agreed that both these species are difficult to establish; this accords with normal field experience.

This symposium did not minimize the difficulties which are present in the planting of industrial waste, where every site and every part of a site has to be considered separately; but there seems to be no doubt that enough knowledge is now available to encourage public authorities to embark on more ambitious planting schemes than they have ventured on up to date. The inspiring example of Lancashire will, it is hoped, lead to a more vigorous approach being made to this problem in many other parts of Britain.

J. Q. WILLIAMSON

INVESTIGATION OF THE UNIVERSE BY RADIO ASTRONOMY*

By Prof. A. C. B. LOVELL, O.B.E., F.R.S.
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ALTHOUGH nearly all the major advances in radio astronomy have taken place during the past fifteen years, the basic discoveries were made thirty years ago. At that time Jansky realized that the residual noise in his receiving equipment had a daily sidereal variation and must be the result of radio waves reaching the Earth from outer space, and Appleton in the United Kingdom with Breit and Tuve in the United States, through their studies of the ionosphere, laid the foundation of the radio-echo techniques of radio astronomy. The radio emission from outer space can be received on Earth in the wave-length range from a few millimetres to 10–20 metres. The short-wave end is limited by absorption in the atmosphere and the long-wave end by the ionosphere, and this upper limit tends to vary in sympathy with ionospheric conditions throughout the sunspot cycle These hindrances will soon be overcome when suitable equipment can be carried in Earth satellites; then it should be possible to determine the true wave-length range of these extra-terrestrial emissions.

Here we are concerned with some of the significant advances made by the application of these techniques to the study of the solar system and the universe, with points of interest from the immediate environment of the Earth to the deepest penetration of the universe.

Some of the earliest successes with the new techniques arose from the study of the transient echoes which are obtained when a radio beam is directed into space. It was shown that these echoes originated from the scattering of the radio waves by the ionized trails of meteoric particles which were evaporating in the height-range of 80–120 km. above the Earth's surface. Methods were developed for the measurement of the velocities of these meteors and later for the determination of the orbits of individual meteor particles. A long-standing controversy was settled when it was shown that the sporadic meteors were members of the solar system and not visitors from interstellar space. New meteor showers active in the day-time sky were discovered and progress has been made in the basic problem of the genesis of this meteoric dust which pervades the solar system.

The extension of these radio echo techniques to the investigation of the Moon and the planets is a more recent activity which required the development of large radio telescopes and powerful transmitters. The lunar work has had two unexpected outcomes which arose from an analysis of the fading of the lunar radio echoes. One has been the discovery that the radio waves are effectively scattered from a rather small portion of the forward hemisphere of the lunar surface; and this led to the demonstration of the possibility of using the Moon as a reflector for round-the-world communication. The other was the proof that a component of the fading arose from Faraday rotation in the ionosphere which has led to an important method for measuring the total electron content along the line of sight from the Earth to the Moon. The attainment of planetary echoes is still a difficult technical problem, and so far only limited success has been achieved in the case of Venus. The future of this work is full of promise since it may involve refinement of the value of the solar parallax, the determination of the rotation period of Venus and preliminary information about the nature of the planetary surface and atmosphere.

The emission from the Moon and many of the planets has now been measured in the radio-frequency range, and this has made possible a comparison of the black-body temperatures in the radio and visual regions. The measurements on Jupiter have been of particular interest for two reasons. First, it appears that the effective size of the disk depends on the wave-length, which indicates that the planet may be surrounded by radiation belts. Secondly, the planet exhibits a strong non-thermal and sporadic type of emission on frequencies below 30 Mc./s. The origin of this emission is unknown although it is believed that it may arise from a relatively few places on the planetary surface.

The Sun has been the most exhaustively studied single object in radio astronomy. Various types of emission in the radio-frequency range have now been delineated. The thermal component originates in the solar corona with an extension which depends on the wave-length. In the centimetric range the effective radius is similar to that of the solar disk with pronounced limb brightening. As the wave-length of observation is increased the effective size of the solar disk increases, until at wave-lengths of several metres the coronal radiation can be detected out to many solar radii. Various types of powerful sporadic emission are associated with sunspots and flares, and the mechanism of emission and the relation to the ejection of particles from the Sun remains an active subject of investigation. The recent results obtained by Simpson of Chicago in the American space probe *Pioneer V* have been of outstanding interest. In this work the cosmic rays from the Galaxy have exhibited a sudden decrease in intensity coincident with solar eruptions, radio emissions and geomagnetic disturbances, when measured at distances of several million kilometres from Earth.

The radio emission from the Milky Way has various origins, the study of which forms a major feature of contemporary research in radio astronomy. The most striking general feature is the resemblance of the intensity isophotes to the concentration of common stars. It has long been realized, however, that the common stars (even if they emit at all) do not contribute significantly to this radiation. The following classes of emission are now recognized:

(*a*) There are a number of localized, discrete sources of emission (radio stars) concentrated near the galactic plane. A few of these have been clearly associated with galactic nebulosities characterized

* Substance of a Royal Society Tercentenary Lecture, delivered on July 23

by a filamentary gaseous structure with violent internal motion. These include the three known cases of supernovæ (the Crab Nebula, and the supernovæ observed by Kepler and Tycho Brahe), and the most intense radio source in the sky in Cassiopeia. It seems likely that the Cassiopeia source and the other radio nebulosities may also be supernova remnants the initial outburst of which has not been recorded.

(*b*) There is a generally distributed emission observable over a wide range of wave-lengths the isophotes of which are similar to the stellar distribution. At short wave-lengths this emission has thermal characteristics and probably originates in free-free transitions from the movement of electrons in the field of the interstellar protons. At long wave-lengths the intensity and spectrum of the radiation are incompatible with such an origin, and this emission is believed to be synchrotron radiation arising from the relativistic motion of the electrons in the galactic magnetic field.

(*c*) Radio emission is observable from regions far beyond the galactic disk of visible stars. This halo or corona of emission is thought to originate in the same way as the long-wave radiation in the Galaxy, that is, from the relativistic motion of electrons in the galactic magnetic field.

(*d*) In 1951 observers in Leyden, Harvard and Sydney almost simultaneously established the existence of line emission from the neutral hydrogen clouds in the Galaxy on a frequency of 1420 Mc./s. This emission is associated with the transition between two levels in the hyperfine structure of the ground-state of the hydrogen atom. The two levels correspond with the two possible orientations of the electron spin in the magnetic field of the proton. The original suggestion was made in 1945 by van de Hulst, and since the practical demonstration of the existence of this line remarkable progress has been made, particularly by the Leyden school, in observations of the Doppler frequency shift and the derivation of the motion of the galactic hydrogen clouds. This work has given the first detailed insight into the spiral structure of the Galaxy, and is now in process of extension to determine the hydrogen content of extragalactic nebulæ.

An important outcome of the existence of the observable hydrogen line emission is the possibility of measuring the galactic magnetic field by observing the Zeeman effect. The magnetic field should split the line into three components with an extreme frequency difference of 2·8 Mc./s. per gauss. Since the interstellar field is not expected to be more than 10^{-5} gauss the maximum observable shift is likely to be of the order of 30 c.p.s. Experiments are in progress on this problem at Jodrell Bank, and so far an upper limit of 4×10^{-6} gauss has been set for the interstellar magnetic field.

Even a cursory inspection of the intensity plot of a high-resolution radio survey of the sky shows that there are prominent features which are not explicable in terms of the emission from the Milky Way. The most striking feature is the existence of large numbers of localized sources (radio stars) which seem to have a nearly isotropic distribution. A small number of these (two or three dozen) can be associated with the nearer normal types of extragalactic nebulæ. The Andromeda nebula (*M* 31) has been studied in some detail, and as a radio emitter it is found to be essentially similar to the Milky Way, including the existence of an extensive corona around the Galaxy. Studies of the other spiral nebulæ within the range of present-day radio telescopes are still in progress, but the existing evidence is that they also conform to this general pattern.

The problem of the majority of these isotropically distributed sources which are not associated with normal extragalactic nebulæ is believed to be one of the most significant issues in astronomy to-day. It is thought possible that the failure to associate these with visible objects may be because they lie at very great distances in the cosmos. The direct evidence for this arises from a few cases where colliding or interacting nebulæ at great distances have been associated with rather strong radio sources. The most outstanding case is that of the galactic collision in Cygnus at a distance of 700 million light years which is related to the second strongest radio source in the sky. The disparity between the visual and radio luminosity of this source is such that a similar event at ten times the distance could only be observed optically with great difficulty but would still be easily recorded as a radio source. Recently one of these radio sources, the apparent angular diameter of which is about 8 sec. of arc, has been related to a rich cluster of nebulæ at a distance of 6,000 million light years with a recessional velocity amounting to 46 per cent of the velocity of light. The lecture concluded with a reference to the cosmological issues involved in this work, and to the experiments now in progress which are believed to be giving information about the condition of the cosmos at distances of many thousands of millions of light years.

A NEW THEORY OF THE ANGIOSPERM FLOWER

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THE interpretation of the Angiosperm flower as a structure built up from modified leaves bearing either ovules or microsporangia dates back to Goethe's essay on the metamorphosis of plants[1]. Most attention and much controversy has been focused on the structure of the ovary, which in its simplest state was supposed to have been produced by the infolding of a leaf bearing ovules on its margin to form a box-like structure similar to the pod of a pea. The carpel theory does account for many of the facts of floral structure; but numerous incongruities are glossed over or avoided by its proponents. Alternative theories have been put forward from time to time, one of the more recent being Saunders's theory of carpel polymorphism[2]. This was shown to be untenable by Eames[3], in a paper in which he expounded the modern form of the carpel theory, that assumes the primitive carpel to have been a palmate leaf

bearing the ovules on its lateral lobes. Even in the comparatively primitive flowers of the Ranunculaceae this theory requires the fusion of vascular tracts in the ovary, which presupposes a long and intricate evolution. Contrary to this, the Angiosperms spring into prominence in the Cretaceous, apparently after a sudden and rapid burst of evolution.

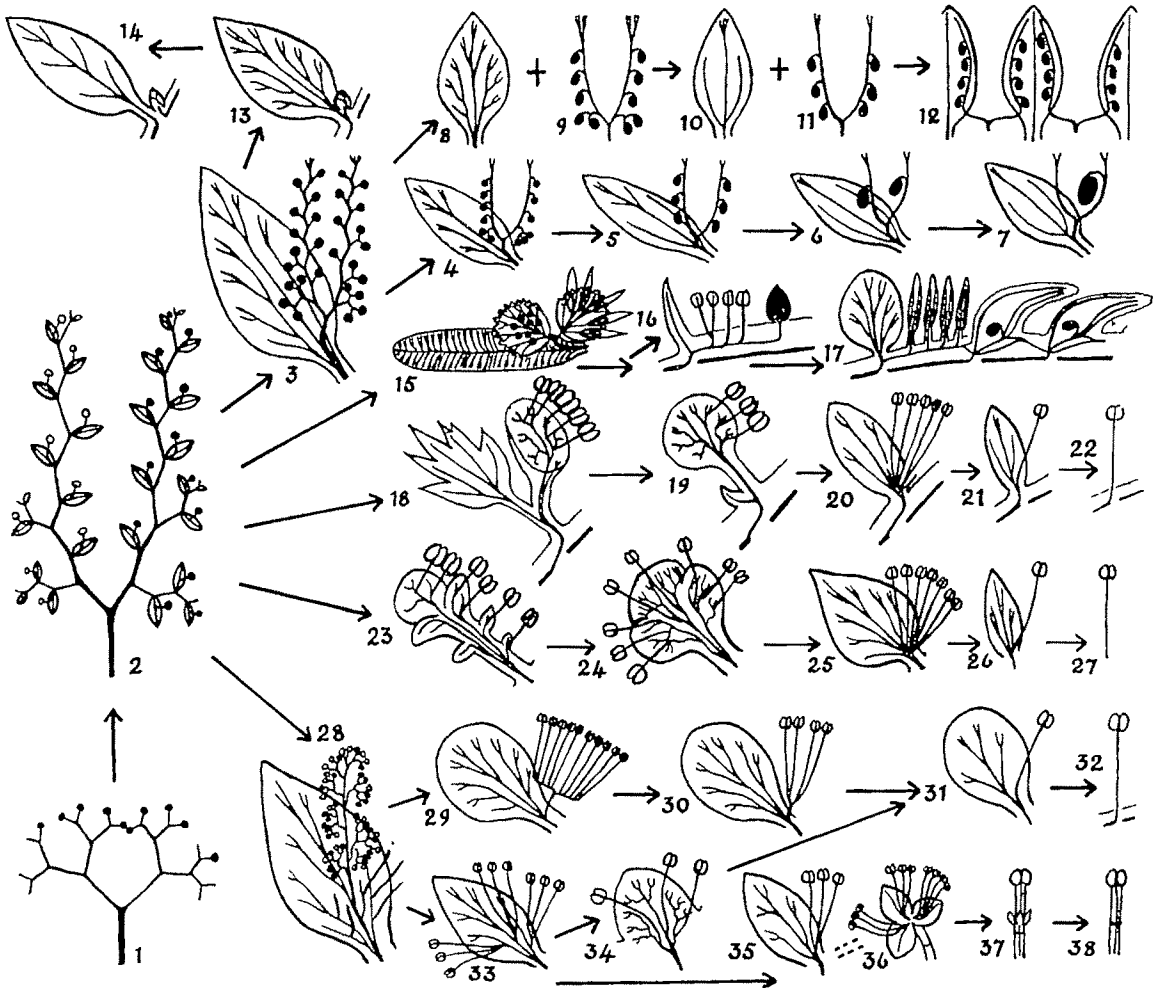
No fossil plants are known with carpels of either the pinnate or the palmate type. Only *Cycas* among recent Cycadales has a megasporophyll with the open pinnate carpel structure; but its microsporophylls bear no relationship to the Angiosperm stamen, and numerous anatomical differences distinguish it and other cycads from the Angiosperms. Although pinnate microsporophylls occurred in flower-like structures in the Bennettitales, the female organs associated with them differed so markedly from the Angiosperm gynæcium that this group, also, cannot be on the Angiosperm line of descent. The failure to find fossil precursors of the Angiosperms is commonly blamed on the paucity of the palæobotanical record. Nevertheless, it is inconceivable that the most successful group of modern plants can have left no trace of its ancestors in the rocks. Darrah[4] believes "that we have most if not all of the clues to Angiosperm origin, but botanists have not been able to put them into a logical story". It is unlikely that they could do so if the carpel theory were based upon false premises.

Starting with the one assumption—that the carpel theory might be wrong—a re-investigation of the vascular structure of the flowers of a range of Angiosperm families has been made. Bleaching and clearing techniques have been used for obtaining preparations in which the complete vascular system could be examined as a three-dimensional object and the exact relationship of its parts determined. Out of this work arose the conviction that the basic structure of the Angiosperm ovary was a leaf bearing on its midrib or petiole a dichotomous fertile branch. From this structure, or its simple derivatives, the gynæcia of all modern flowering plants could be easily formed. The basic structure of the male organs was similar, but, not being restricted by the function of enclosing ovules, more primitive stages in the evolutionary sequence have survived in the andræcium than in the gynæcium. To obviate confusion, it is proposed to avoid the term 'carpel' and to call the basic structure a 'gonophyll'. The male, female and bisexual analogues may then be called 'androphylls, 'gynophylls' and 'androgynophylls'. The theory may be called the 'gonophyll theory'.

For brevity it will be convenient here to present the theory as a 'logical story', leaving the detailed evidence for separate papers on the gynæcium and andræcium to be published elsewhere. The Psilophytales of Silurian to Devonian age may be taken as the starting point. In the simpler members of this group such as *Rhynia* and *Horneophyton*, the plant body was a leafless dichotomous branch system bearing terminal sporangia (Fig. 1). Zimmermann[5] derives all megaphyllous leaves from dichopodia of the Psilophytalean type, by overtopping, planation and fusion. Some of the early stages in these very generalized processes are to be found in the Psilophytales and in the Coenopterid ferns of the Devonian and Carboniferous, while later stages survive in modern ferns and Angiosperms. The development of the megaphyllous leaf used up one of the branchings of each dichotomy, so that, instead of a diffuse branch system, there was a tendency to produce a single main stem bearing a succession of leaves. The main stem dichotomized only occasionally as in *Lyginopteris oldhamia*[6], a habit which has been retained in living cycads and palms. Other plants of the Carboniferous period developed another kind of branching, which proved to be of great significance for the evolution of the higher plants. Early examples occur among Coenopterid ferns, where, as in *Ankyropteris grayi*[6], the petiole trace rounds off to give rise to a stem-like structure shortly after its departure from the stele of the main stem. It then forks, the abaxial part supplying the leaf and the adaxial forming a branch. Thus arose the leaf–branch combination, which formed the repetitive unit in this new kind of branch system.

It is likely that the epiphyllous branch first arose as a reproductive structure, though little fossil evidence on this point has come to light. Excluding adventitious shoots, the only epiphyllous shoots surviving in modern Angiosperms are reproductive in function. An incomplete list of genera in which they are found is given by Velenovsky[7]. The fertile branch may be reduced to a single flower bearing the same relationship to the leaf as the branch of *Ankyropteris*. Examples are to be found in several genera of Epacridaceae, where, as in *Andersonia*, the terminal leaves are fertile and those immediately below have epiphyllous buds in the corresponding position. Here, and in the Chailletiaceae studied by De Candolle[8], the axillary bud appears to have evolved by the sterilization of an epiphyllous inflorescence (Figs. 13, 14). Theoretically, axillary buds could have arisen also by the condensation of compound branch systems composed of the primitive leaf–branch units, but evidence for this alternative is lacking.

The first and sometimes some of the later branchings of the epiphyllous inflorescence in the Chailletiaceae are dichotomous. The main peduncle may be relatively long, or the primary dichotomy may be sessile or sub-sessile on the petiole. The peduncle, also, may vary in position even in a single species, so that at times it may take up a truly axillary position. If the peduncle is then reduced until the dichotomy is sessile, a pair of fertile branches in a single leaf axil results. Both epiphyllous and axillary inflorescences occur in *Dichapetalum pedunculatum* (Aubl.) Baill. and pedunculate and paired axillary inflorescences in *D. timoriense* (DC.) Boerl. and other species. The anatomy of these epiphyllous inflorescences indicates that they are not due to adnation, but that leaf and inflorescence stalk fuse into a single structure, which repeats, in all essentials, the condition in *Ankyropteris*. Further evidence for the view that the Chailletiaceae have retained a primitive form of attachment of the inflorescence is provided by other fossils. Whereas the primitive epiphyllous branch is found in *Ankyropteris grayi* of Lower Carboniferous age, paired axillary branches occur in the later *A. glabra* of Upper Middle Pennsylvanian age[9]. Parallel evolution of simple and paired axillary branches took place in the Cordaitales, where the simple branch is usual, but paired branches occur in *Mesoxylon birame* Baxter[10]. Other groups may have followed a similar path. Rather specialized epiphyllous inflorescences have recently been described by Plumstead[11,12] for the Glossopteridales. There is positive evidence, therefore, for the existence at the end of the Carboniferous or early Permian of plants with epiphyllous, simple axillary and paired axillary



Figs. 1–38 Evolution of the components of the gynæcium and andræcium of the Angiosperm flower. 1, Dichopodium with terminal sporangia, Psilophytalean phase; 2, Condensation to branch system with sporangia epiphyllous on leaflets, 3, Primitive gynophyll, a leaf with complex epiphyllous ovuliferous branch, 4–7, Reduction series giving follicles, legumes and achenes by enfolding, 8–11, Separation of the ovuliferous branch from its blade and reduction, 12, Enclosure of branchlets of ovuliferous branches by alternate whorl of sterile blades or tegophylls, 13, Epiphyllous vegetative bud, Epacridaceous type, 14, Axillary vegetative bud, usual Dicotyledon type, 15, *Glossopteris* (*Scutum*), an androgynophyll with foliaceous male and female branches; 16, *Gnetum*, an androgynous branch adnate to the inflorescence axis, 17, *Magnolia*, androphylls and gynophylls with adnate branches, 18, Catkin scale of *Populus*, an androphyll with cupular fertile branch, 19, *Homalanthus*, cupular fertile branch with reduced bract; 20, *Salix pentandra*, elimination of bract and reduced number of stamens with staminodes, 21–22, Theoretical reduction to single aphyllous stamen, 23–27, Reduction of pinnate androphyll, 23, *Juglans*; 24, *Corylus*; 25, *Carpinus*, 28, Primitive androphyll with many complex branches (one shown), *Ricinus* type, 28–32, Reduction to aphyllous stamen; 29, Tiliaceae (*Sparmannia*), 30, Malvaceae (*Hoheria*), 31, Rhamnaceous type, 32, Ranunculaceous type, 28, 33, 35–38, Euphorbiaceae; 35, *Mercurialis* androphyll, 36, *Mercurialis*, male flower; 37–38, *Euphorbia* spp, male flowers, 34, Rosaceous type androphyll-sepaloid. The examples cited indicate evolutionary stages—not lineages To avoid confusion, the full complement of stamens is not shown in Figs. 18, 19, 23, 28

inflorescences. The elements necessary for condensation into modern flowers were already present.

In the primitive form of the gonophyll, the leaf–branch unit was repeated many times (Fig. 2). The structure could be condensed in a variety of ways. The male and female organs could be confined to separate parts of the branch system of one gonophyll, or separated completely on different gonophylls. The foliar part of the dual combination could be suppressed in the secondary gonophylls of the fertile part, giving rise to an epiphyllous ovuliferous branch on the primary gonophyll blade (Fig. 3). The same processes, carried further, would produce axillary ovuliferous branches and then ebracteate ovuliferous branches (Fig. 9), which in turn could become associated with sterilized gonophylls in alternating whorls (Fig. 12). Thus could the elements of the modern Angiosperm ovary come into being.

The simplest kind of ovary was formed by folding the blade of the gonophyll around the ovuliferous branch system, which usually dichotomized somewhere near the base. The legumes of the Papilionaceae and the achenes of *Thalictrum* and *Ranunculus* (Ranunculaceae) have this structure, the number of ovules varying from many to one. Fusion of a number of such units gave rise to a multilocular ovary, as in *Oxalis* (Oxalidaceae) and *Triglochin* (Juncaginaceae). In a number of families, the ovary has been formed from sterilized gonophylls, which may be called 'tegophylls', alternating with bifurcated ebracteate ovuliferous branches. With this arrangement, a tegophyll encloses one of the branches of each of the adjacent ovuliferous branch systems (Fig. 12). If the ovuliferous branch bifurcates near the base, the ovary may be a collection of follicles, as in *Caltha* and *Helleborus* (Helleboraceae), or the follicles may be

more or less fused, as in *Butomus* (Butomaceae). When the ovuliferous branch bifurcates at a higher level, the undivided part may take up an axial position and the components of the ovary are clamped together by the enfolding of the adjacent branches in the upper part, as in *Buxus* (Buxaceae). Simple unilocular ovaries with parietal placentation are formed from alternating components by the overlapping of the margins of the tegophylls and the application of the ovuliferous branches to the wall so formed, as in *Berberidopsis* (Flacourtiaceae). Another class of ovary may be formed by simple apposition of the margins of fertile gonophylls. *Koelreuteria* (Sapindaceae) has this structure, false septa between the axial ovuliferous branches and the midribs of the gonophylls helping to hold the components together. A number of modifications of these basic types of structure are to be found in particular families. Similar principles apply to inferior ovaries, with the added complication of adnation and fusion of vascular strands of the ovary with those of the enclosing sepals and petals. This aspect of inferior ovaries is not in dispute and has been described and illustrated by Eames[3].

It is necessary now to return to the primitive androphyll and follow its evolution into modern types of andræcium. Starting with the 'gonophyll of gonophylls' (Fig. 2), a primary gonophyll blade may be retained and the secondary gonophylls with their blades condensed into another expanded leaf-like structure bearing the terminal fertile organs on branches arising directly from its surface and attached to its dichotomous vascular system. This structure is found in the individual male flower of *Populus* (Salicaceae) (Fig. 18), where the vascular system of the 'perianth' branches off from that of the bract, which represents the primary androphyll blade. Essentially the same structure occurs in *Homalanthus* (Euphorbiaceae) where the bract is much reduced (Fig. 19). The bract is eliminated in *Salix* (Salicaceae) (Fig. 20), where the catkin scale represents the secondary blade or the 'perianth' of *Populus*. In *Salix* the number of fertile stamens varies from twelve to two in different species. The nectaries of *S. pentandra* L. are staminodal stumps retaining vestiges of their vascular system, which, by their mode of attachment to that of the bract, indicate their derivation. Further reduction in this series would lead to an androphyll with one stamen (the *Rhamnus* stage—see below) and then to a simple aphyllous stamen (Figs. 21, 22).

If the original compound gonophyll were bisexual, the condensation could take the form of a leaf bearing a pair of leaf-like structures, one male, the other female. These would be opposed on the primary dichotomy of the epiphyllous branch and their ovules and micro-sporangia would be attached to the opposing surfaces. This structure is exactly that of the *Glossopteris* fructifications (Fig. 15) of Lower Permian age recently described by Plumstead[11,12]. Although palæobotanists have not unreservedly accepted her interpretation, the continued existence of similar unisexual structures is in its favour. Moreover, the presence of a once bifurcated branch arising in the opposed position on the adaxial side of the vascular system of the 'perianth' in the staminate flower of *Populus canescens* L. (Fig. 18) is in the position it would need to be if it were derived from a sterilized female branch. Thus the possible origin of the male flower of *Populus* from a primitive bisexual structure of the *Glossopteris* type is an open question. The present evidence suggests that *Glossopteris* must have been very close to the pro-angiosperm stock at that level of evolution.

The bisexual condition is found also in the androgynous inflorescences which often occur on male plants of *Gnetum*[13]. They probably represent the primitive condition in the Gnetales. Here, there is a fertile branch attached to the vascular trace of the bract, but it is adnate to the inflorescence axis (Fig. 16). Allowing for the modifications due to adnation, this arrangement is similar in essentials to that found in the Glossopteridales and suggests a relationship with that group. Adnation of the fertile branch to the main axis is found again in the flower of *Magnolia* (Fig. 17). The sepal of *Magnolia* is an androphyll bearing stamens in a manner similar to *Gnetum*, but the tip of the fertile branch trace continues upwards and fuses with a small branch arising from the ovuliferous branch of the follicle above. The latter is produced by the enfolding of a gonophyll of the type shown in Fig. 6. After the anastomosis, the branch trace continues upwards and fuses with the corresponding branch of the follicle next above. In this way, the main stele of the floral axis is enclosed in a network of vascular traces resembling a dictyostele, through the meshes of which the follicles protrude. The similarity of the staminate part of the *Magnolia* flower to that of male *Gnetum* in the essentials of its vascular structure suggests that the Gnetales and the Magnoliales are divergent offshoots of a common stock. Thus, there is at last evidence to link the Dicotyledons with the Gymnosperms through their reproductive organs.

Another type of condensation of the primitive system could lead, by overtopping and planation, to a pinnate leaf-like structure bearing fertile branchlets on the leaflets. Reduction of the fertile branchlets to single stamens would then lead to the condition found in the individual catkin scales of *Juglans* (Juglandaceae) (Fig. 23). Further reduction of this to the three-lobed condition would give the catkin scale of *Corylus* (Corylaceae), in which two stamens are borne, one each on the two main branches of the vascular system of the terminal lobe and three on each of the lateral lobes (Fig. 24). There is no aggregation here into a flower-like structure, but *Alnus* (Betulaceae) is more advanced in this respect. In it, the subtending scale bears three flower-like structures consisting of four scales, each with a single epiphyllous stamen. Further condensation in the Corylaceae leads to the fusion of the three lobes of the catkin scale into one in *Carpinus* (Fig. 25) with relegation of the stamens to the basal portion of the vascular system. The logical end-points of this sequence, again, would be an androphyll with a single stamen and then an aphyllous stamen (Figs. 26, 27).

Yet another type of condensation of the original compound gonophyll would lead to a flat blade with several fertile branches of one sex attached to it. Such is the condition of the perianth lobes of the male flowers of *Ricinus* (Euphorbiaceae) (Fig. 28). The complex staminal branches are dichotomous systems in which the terminal branchlets bear a pair of anther sacs on either side of a minute leafy blade, here interpreted as the ultimate androphyll with a pair of microsporangia. Numerous stages in the reduction of this complex androphyll occur in the Euphorbiaceae, leading to androphylls (perianth lobes) with three or four stamens in *Mercurialis*

(Figs. 35, 36) and three, two or one in *Dalechampia*. These male flowers have an abscis layer below the perianth. They are borne in complex inflorescences capable of a second cycle of reduction, which may lead from a flower of the *Mercurialis* type to one with three perianth lobes and one stamen (Fig. 37) and thence to the unistaminate male flower of *Euphorbia* (Fig. 38) with no perianth, but an abscis layer in the middle of its stalk[14].

Reduction of an androphyll of the *Ricinus* type could take two other paths. In one, the compound branches would be reduced to single stamens, so producing a blade with a variable number of simple stamens distributed over its surface. A whorl of five of these relatively primitive structures fuse together to form the sepals and perigynous cup of the Rosaceae (Fig. 34). The petals in this family are sterile structures, probably evolved from androphylls of the same kind. The second type of reduction leads to an androphyll bearing in a median position on its surface a single dichotomous branch system, each branchlet terminated by a stamen. This condition occurs in the Tiliaceae (Fig. 29) and Malvaceae (Fig. 30), where the stamens are grouped in dichotomous systems attached to the petals, with filaments free in the one and adnate with those of adjacent petals into a column in the other. Either of these types of androphyll could lead by further reduction to a single epipetalous stamen, as in *Rhamnus* (Rhamnaceae) (Fig. 31) and finally to a single aphyllous stamen attached at a 'leaf-gap' to the floral axis, as in *Ranunculus* (Fig. 32).

The vascular structure of the flower provides evidence for a number of evolutionary lines within the Angiosperms. The primary diversification of the pre-angiosperm stock appears to have taken place during its gymnospermous phase in the late Carboniferous or early Permian. Many Angiosperm lineages must date back to this period as distinct lines of evolution, so that, in this sense, the Angiosperms are polyphyletic. Already the new theory is throwing much light on Angiosperm phylogeny. The great disparity between the floral vascular systems of Ranunculaceae and Magnoliaceae, indicating an origin from widely divergent modifications of the gonophyll structure, implies a very ancient separation of these stocks. A number of other lineages must be as old.

From its mode of origin it might be anticipated that derivatives of the gonophyll would be found in parts of the plant other than the gynæcium and andræcium. Reference has been made above to staminodal nectaries, but the nectarial flap of the *Ranunculus* petal is not obviously of this origin. It is often provided with a vascular trace[15], which is opposed to the petal trace, as it would be if it had originated from an epiphyllous branch. The petal of *R. gunnianus* Hook. has several nectarial flaps, which indicates the probable origin of the *Ranunculus* petal from an androphyll of the rosaceous type (Fig. 34). Other structures with opposed vascular systems are the coronas of the perianth of *Narcissus*[16] and of the sepals and petals of *Passiflora*[17]. In the latter, the vascular system of the corona is often elaborately dichotomous and apparently little altered from that of its gonophyll precursor.

The flower and inflorescence are both condensation products of the primitive gonophyll of gonophylls. As in the flower, condensation of the inflorescence has taken many paths. Sometimes evidence of the epiphyllous origin of the fertile branch is retained in the attachment of the flower to some part of the vascular system of its bract (Epacridaceae, Proteaceae). The compound female inflorescence of *Dobinea delavayi* Baill. (Anacardiaceae)[18] provides a striking example in which the individual flowers are attached to the centre of a rounded dentate bract reminiscent of the fertile scale of *Glossopteris* (*Scutum*). Allusion has been made already to the occurrence of epiphyllous inflorescences in a number of families. DeCandolle's study[8] of the Chailletiaceae indicated that the epiphyllous inflorescence of this family is not adnate to the leaf, but is part of it and that all stages in the detachment of the inflorescence from its leaf occur, leading to the axile position. Similar evidence is to be found in other families.

In this brief summary of the gonophyll theory it has been possible to cite comparatively few examples It is hoped, however, that enough has been said to illustrate the scope of the theory in explaining not only the gynæcium but also other parts of the flower and the inflorescence. Many facts that formerly appeared to be anomalous in the context of the carpel theory now fall naturally into place. For the first time it is possible to indicate a link between the reproductive structures of *Gnetum* and those of Angiosperms and to point out similarities between those of *Glossopteris* and the andræcium of certain Angiosperms.

In conclusion, it is my pleasure to acknowledge the help of my daughter, Mrs. F. A. Wrigley, in making preparations for the study of the gynæcium, and of my colleagues at the Royal Botanic Gardens, Kew, for many stimulating discussions and for directing my attention to relevant plants and literature.

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OBITUARIES

Dr. C. E. Kenneth Mees, F.R.S.

WITH the death of Dr. C. E. Kenneth Mees on August 16, at Honolulu, Hawaii, at the age of seventy-eight, the world has lost a major pioneer of industrial research. To-day industrial research is fashionable, and many good scientists are attracted to it. Things were very different in 1906 when Dr. Mees joined the small firm of Wratten and Wainwright, makers of photographic plates. He had just emerged from a brilliant university career with degrees of B.Sc. and D.Sc., both by thesis in collaboration with Samuel E. Sheppard under Sir William Ramsay of University College, London. Sheppard adopted the

more usual course and went to Germany to continue academic research, though he rejoined his old colleague later to continue an association which lasted throughout Sheppard's life. Mees turned to industry for reasons which he afterwards stated to be political. The son of a Wesleyan minister, he was a Fabian who realized that an equal sharing of wealth, while effectively depriving the rich, would do little to benefit the poor. What was needed was a general increase in the standard of living, and this he believed could be achieved only by the application of science to industry. An experience from the Wratten and Wainwright days can now be seen to epitomize what he considered should be the objectives of industrial research. Mr. Wratten had told him that plate prices were being cut, profits were diminishing and that he must devote his energies to reducing their manufacturing cost. Mees completely ignored these instructions. The blue-sensitive plates of the day were being bathed by the user in solutions of dyes to make them sensitive to longer wave-lengths. He found out how to incorporate this step during manufacture and proceeded to market outstandingly good panchromatic plates at a premium price with great benefit to the Company's profits. Throughout his subsequent career he was always aiming to open up new markets with new products; others could worry about holding existing markets. In another way these early years in industry set the pattern of what was to come, in that despite his many preoccupations with commercial problems, he found time to publish several scientific papers of importance.

He had made himself so indispensable to Wratten and Wainwright's that when, in 1912, George Eastman wanted his services in order to found a research laboratory, he had to purchase the Company. His subsequent career with the Eastman Kodak Co. continued until he retired in 1955, seeing him appointed a director in 1923 and vice-president in charge of research in 1934. He became internationally recognized as a pioneer in industrial research and a great exponent of it. The reputation of his laboratory in Rochester, New York, grew by his insistence on high standards and on the publication of the results of research. The decision whether to publish or not was based on the principle that results of value to science ought to be published. This was in line with his belief that industry should repay its debt to pure science, in accordance with which belief he undertook to supply special—and unprofitable—plates to astronomers and started the manufacture of Eastman organic chemicals when the United States was cut off from German supplies during the First World War—a service still valued by organic chemists everywhere. He established research laboratories in the Company's subsidiaries in England and in France and was a frequent visitor to Europe.

Mees's influence on the commercial success of the Company was equally great, and he was largely responsible for such outstanding contributions as the introduction of amateur cinematography and for the popularization of colour photography in all its forms. Of his personal work, apart from many scientific papers, must be mentioned one of the earliest books on the organization of industrial research, published in 1920, which was brought up to date much later by the publication in collaboration with John A. Leermakers of "The Organization of Industrial Scientific Research". His greatest contribution to scientific literature was the "Theory of the Photographic Process" (1954), which had its origins in the book published in collaboration with Sheppard based on their research theses in 1907 which became known simply as "Sheppard and Mees". Recognition of his work was made plain by his receiving from almost every scientific body connected with photography their highest awards, by his election to the fellowship of the Royal Society (1939) and to membership of the U.S. National Academy of Sciences on becoming an American citizen in 1950.

Perhaps Mees's outstanding characteristic was his insistence on the importance of facts and his ability to analyse their implications. It was for this reason that in debate he could be a devastating opponent, but if it could be shown that the facts were against him he cheerfully accepted, not defeat, but the new circumstances. Mees usually dominated any group in which he found himself, mainly by the clarity with which he saw any problem (and the solution to it) and the consequent forcefulness with which he could express himself. He once gave the advice to one of his men, who was writing a book: "If you don't know for certain, don't say it; if you must say it, be dogmatic!" He was widely read, an authority on many subjects, ranging from astronomy to the history of ancient Egypt, having as a central theme the growth of science and technology through the ages. This interest led to the publication in 1946 of "The Path of Science", written in conjunction with John R. Baker. He was a brilliant lecturer, as those who remember his Royal Institution Christmas lectures in 1935 will know, and a stimulating conversationalist. His views on the organization of industrial research were widely sought by other directors of research and by industrialists. They can well be summed up as insistence on the importance of the individual. He had no use for the idea that research had to become a team effort, and he believed that the youngest of men could do worth-while research if given the opportunity, as he had indeed proved in his own case. He surrounded himself by many brilliant individualists, gave them the freedom such men require, and regarded his job as the protection of these men from the direction of others rather than the direction of their work by himself. He asked the Company to judge by the end-results. It had no regrets.

Mees married in 1909 Alice Crisp (she died in 1954), by whom he had a son and a daughter.

E. R. Davies

Dr. R. C. Farmer, O.B.E.

The death of Dr. R. C. Farmer on July 30 at the age of eighty-two has removed one of the great pioneers from the world of military explosives. He was well known not only for his contributions to the defence of the State but also for his publications, which appeared over a number of years in scientific journals. It is remarkable that his last three papers were printed in the *Journal of the Chemical Society* when he was within a few weeks of eighty-two. He married, in 1908, Maud Mary, daughter of Mr. T. T. Sharpe, of Liverpool, and had two sons and one daughter, all of whom have taken up scientific work.

Robert Crosbie Farmer was born on November 30, 1877, in Liverpool, where he received his early education and later graduated with first-class honours at the University. With the aid of scholarships he studied at Wurzburg under Hantzsch and Röntgen, and was awarded the Ph.D. (*summa cum laude*) for

his work on the tautomerism of hydrazones and oximes. After a short spell as analyst in a paint works, he entered the University of Birmingham with a Priestley scholarship and worked on the use of liquid nitric peroxide as a solvent for organic compounds. He also developed a new way for measuring hydrolytic dissociation (partition method). Afterwards he was appointed lecturer and demonstrator and was awarded the degree of M.Sc. (Birmingham and Victoria).

In 1902 he became principal assistant to the late Dr. O. J. Silberrad at the Experimental Establishment of the War Office Explosives Committee (later Research Department, Woolwich), of which Lord Rayleigh was president and Sir William Crookes a member. His earliest work was on the mechanism of the decomposition of nitrocellulose and on cordite Mk. 1, which had ignited spontaneously in several magazines in India. This work was embodied in his thesis for a D.Sc. (Liverpool). When Dr. Silberrad left in 1906, the vacant post was offered to Dr. Farmer, but serious ill-health at that time prevented his acceptance and Dr. (later Sir) Robert Robertson was appointed. During the ensuing years he continued his work on the chemical stability of explosives and developed the vacuum stability test for high explosives, a test which is now regarded of first importance in considering their suitability for Service use. When War started in 1914, he devised a process for the manufacture of trinitrotoluene which was used on the largest scale in Government factories and by several private firms. Early in 1915 he was transferred to the Department of Explosives Supply and became chief chemical adviser to the director general, Lord Moulton. In this capacity he was responsible for guidance to manufacturers and safety of processes, several of which he improved. He had control of extra-mural research in this field at the universities and was a member of many committees, including those on Munitions Inventions and Nitrogen Products.

At the conclusion of the War in 1918 he was made O.B.E. and received a Russian decoration, the Order of St. Anne. He left the Government service, forfeiting all rights to pension, and became a director of W. J. Bush and Co., manufacturers of fine chemicals. In 1922 he accepted an invitation to return to the Research Department as deputy director of explosives research and later became chemical adviser. In these capacities he was largely responsible for organizing researches and dealing with a multitude of technical problems arising in the Fighting Services. He represented the Department on a number of committees, including those on Adhesives and Forest Products under the Department of Scientific and Industrial Research, and for some years was a member of the Council of the Institute of Chemistry. On retirement he continued research work at King's College, London, up to his last years.

Dr. Farmer was of a lovable disposition and sacrificed all considerations of self to duty. He had abundant wit and his speeches on lighter occasions were masterpieces. His recreation was walking. No one can be more indebted to him for his generously given help through strenuous years than myself.

GODFREY ROTTER

NEWS and VIEWS

Bacteriology at University College Hospital Medical School: Prof. Wilson Smith, F.R.S.

PROF. WILSON SMITH is retiring from the chair of bacteriology at University College Hospital Medical School, a position he has occupied since 1946. Prof. Smith is a Manchester graduate, having qualified in 1923. In 1927 he went to work at the National Institute for Medical Research at Hampstead and soon came to the fore as a contributor to knowledge about viruses, particularly vaccinia and herpes. In 1933, with P. P. Laidlaw and C. H. Andrewes, he demonstrated that influenza virus would infect ferrets, a discovery which opened the way to a laboratory investigation of the disease; and in the following years these three workers laid the foundations of present-day knowledge of influenza in its laboratory aspects; they soon found that the virus would infect mice, could be grown in fertile eggs and in tissue culture and could be studied by means of various serological tests. In 1939 Wilson Smith was appointed to the chair of bacteriology at the University of Sheffield, but returned to London in 1946 to the chair which he is now vacating. With various collaborators he has continued to work on influenza, particularly its serological aspects, and on poliomyelitis. His contributions have not only been to virology, however, but also to bacteriology. He was elected to the fellowship of the Royal Society in 1949 and has twice served on its council. He delivered the Society's Leeuwenhoek Lecture in 1957 on "Virus-host Cell Relationships".

Messrs. Macmillan announce that, as from January 1, 1961, the subscription price for *Nature* will be £8. 8*s*. per annum and *pro rata*. The price of single issues remains 2*s*. 6*d*.

Prof. G. Belyavin

PROF. WILSON SMITH is succeeded in the chair of bacteriology in University College Hospital Medical School by Dr. George Belyavin, who is at present senior lecturer in that department. Dr. Belyavin was educated at St. Paul's School and the Westminster Hospital, from which he graduated M.B., B.S. in 1943. He was awarded the M.D. in 1960. During 1944–46 he acted as resident pathologist to the Westminster Hospital, and from 1946 until 1949 he was a member of the Department of Biological Standards of the National Institute for Medical Research, Hampstead. Since 1949 he has been continuously at University College Hospital Medical School. Dr. Belyavin has had two main research interests—immunology and virology which, as his

published work shows, he has been able to combine successfully. He has been concerned with the mechanism of the antibody response, and in collaboration with Prof. Wilson Smith he has studied the kinetics of the formation of different types of antibody in response to infection with poliomyelitis and influenza viruses. Recently, he has investigated the immunological response in Hashimoto's disease in collaboration with Dr. W. R. Trotter, and has identified the antigen responsible for the positive complement fixation test in this disease. A major interest for some years has been the study of the antigenic characters of influenza viruses and factors in normal sera which combine with these viruses.

Atomic Energy Research Establishment: Solid State Physics Division

A SOLID State Physics Division has been formed at the Atomic Energy Research Establishment, Harwell. Its initial term of reference will be: to carry out basic research leading to greater knowledge and understanding of the structure and behaviour of solids. Dr. W. M. Lomer, at present head of the Theoretical Physics Division, has been appointed head of the new Division. Dr. W. C. Marshall, at present a group leader in the Theoretical Physics Division, is to succeed Dr. Lomer as head of the Division.

The formation of the new Solid State Physics Division reflects the importance which the Authority attaches to a better understanding of the structure and properties of solids. The nuclear reactors at Harwell, and particularly the research reactor *Bepo*, and the materials testing reactors *Dido*, *Pluto*, play a very important part in studies of the properties of materials. The programmes of work fall broadly into two parts. First, there are basic and applied studies of the effects of nuclear radiation on materials of decisive importance to reactor technology: this work will remain under the control of existing Harwell Divisions, particularly the Metallurgy Division. Secondly, there are more basic studies of the behaviour of solids in general, without reference to any particular application in reactor technology: this work will be the special concern of the new Division. It will include studies of the formation and nature of defects in crystals; other physical properties of metals, alloys and magnetic materials; and fundamental crystal physics using extracted beams of neutrons from the Harwell reactors.

The International Atomic Energy Agency

IN a statement issued in Vienna on the third anniversary of the establishment of the International Atomic Energy Agency, Mr. Sterling Cole, its director-general, said that the experience of three years had demonstrated that a balanced development of the peaceful uses of nuclear energy could be achieved only by international co-operation on the widest possible basis. It was now apparent that the development of reactors, and in particular power reactors, would take considerably longer than was originally expected, but progress in the use of radioisotopes and other radiation sources had been rapid and substantial, especially in industry and medicine. Early hopes that nuclear power would soon become an effective instrument for the rapid industrialization of under-developed countries had been somewhat hampered, and in assisting such States the Agency at this stage was more concerned with preparing the groundwork than with advanced projects. Technical assistance and training were now two of its most important programmes; the exchange and dissemination of information was another developing function; and its research problem was mainly concerned with problems of radiation protection.

The Russian Earth Satellite 1960λ

REFERENCE was made in *Nature* of September 3, p. 830, to the Earth satellite (1960λ) or *Sputnik* 5, on the basis of reports then available. This satellite was launched on August 19 at about 0845 hr. U.T., and consisted of the 'space capsule' itself, and the last stage of the launching rocket. The two objects were seen from the United Kingdom at about 2113 hr. U.T. on August 19 with apparent magnitudes of + 3 and + 6, the fainter object following the brighter in the same orbit, with a separation of about ½′—whether the brighter or the fainter object was the 'capsule' is not certain. Transmissions from the satellite on frequencies of 19·995, 39·990 and 59·985 Mc./s. were received by staff of the Radio Research Station, Slough, during transits occurring at about 1322 hr., 1510 hr., 1938 hr. and 2113 hr. U.T. on August 19. Signals from the satellite were also received at the Radio Research Substation, Singapore, at about 0800 hr. U.T. on August 20, but were not received at Slough later that day when the satellite was next due to be in the neighbourhood of Great Britain. This was explained by a *Tass* report of August 21, in which it was reported that the space capsule was brought out of orbit from a height of about 300 km. soon after 1200 hr. U.T. on August 20, having performed 18 revolutions.

Effects of Autonomy on Science and Technology

UNDER the somewhat misleading title "Local Self-Government", Political and Economic Planning has issued an admirable objective analysis of the experience of such regions of the United Kingdom as Wales, Scotland and Northern Ireland, and also the Isle of Man and of the Channel Islands (Vol. 26, No. 444 (12th September, 1960). Pp. 229–280. (London: Political and Economic Planning, 1960.) 5*s*.). That such an impartial account of the varying degrees of independence and interdependence of the governments of these territories and assessment of the present position scarcely touches on scientific matters as such in itself points to the spurious character of some of the claims for separate national scientific institutions or departments, and although the conclusions drawn touch only on the political and administrative aspects of autonomy, the broadsheet provides a reasoned and impartial appraisal of the arguments for and against autonomy, and of the difficulties and advantages that may well be of service to the scientist or technologist confronted with such claims. It is a real contribution both to the understanding of the present situation and to clear thinking about the real issues involved. The arrangements described are complicated, but it is clear that they are understood by interested and informed opinion in the territories concerned and that while the measure of autonomy enjoyed is varied, it is what it purports to be.

Survey of Information/Library Units in Industrial and Commercial Organizations

THE results of a survey of the information/library units of some 52 British industrial and commercial

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organizations made in 1956–58 by Dr. D. J. Campbell are analysed in a report by Mr. C. W. Hanson, now published by the Association of Special Libraries and Information Bureaux (Pp. vi+42+vi. London: Aslib, 1960. 12*s*. 6*d*.; Aslib members 10*s*.). The survey was undertaken to provide factual data on the size, scope, organization, methods and cost of such units in the United Kingdom and it is based on a 12 per cent sample. Two-thirds of the units surveyed were responsible to a head of research or to a director, the remainder mostly to a senior technical officer. In terms of employees or staff the smaller organizations had relatively larger units than the larger organizations; the number of people served per information/library worker averaged 54, ranging from less than 20 to 200. 58 per cent of the heads of units were either graduates or chartered librarians or both. There were more men than women heads, but more of the women were qualified, and among the supporting staff there were three women to one man. Salaries and wages of staff accounted for about three times as much as the purchase of documents. Accommodation averaged 200 sq. ft. per member of information/library staff, but two-thirds of the organizations outside of London exceeded this figure. Two-thirds of the organizations took between 100 and 300 periodicals, the median number being 210, and one in twelve was in a foreign language; 16 per cent were later bound and 25 per cent were kept indefinitely unbound. Data on books were insufficient to permit any deductions, and only 6 out of the 52 units were responsible for the present organization's technical correspondence files. About half the units scanned national or local newspapers; 37 per cent possessed a microfilm reader and 8 per cent a microcard reader. About half used the Universal Decimal Classification, the rest using their own schemes. The main catalogue of 35 units comprised a classified index on cards; only one used a punched card subject index. Documents borrowed from outside libraries for 27 of the units averaged 12 per cent of the number lent from their own stock. About half did little or no stocktaking, and 48 units employed 23 different methods for recording loans. Only one-third could report how many inquiries they handled, but 90 per cent issued some kind of serial publication, commonly lists of new books and selected literature references, with abstracts.

Kirkia: a New Herbarium Journal

THE aim of *Kirkia*, the new journal of the Federal Herbarium, Salisbury, Rhodesia and Nyasaland (editor, H. Wild. From the Government Printer, P.O. Box 8062, Causeway, Salisbury. £1 10*s*. per annum), is to provide botanists in these regions, and elsewhere, with a readily available source of taxonomic information on a floristic region of very considerable interest; and to afford a medium for relevant botanical publications. To quote: "With regard to the aims of the journal our intention is to confine ourselves to articles concerning African botany and to give priority to articles dealing with taxonomy, floristic studies, phytogeography and the history of botany and botanical exploration which have some bearing on the flora of the Federation. Ecological articles may be published but usually only if they are of a general nature. As space permits we will welcome articles on these subjects relating to other African territories and particularly those territories which are our near neighbours". The name chosen for the new journal commemorates the work of Sir John Kirk (1832–1922), who, as botanist, accompanied Livingstone to the Zambesi, Victoria Falls, Lake Nyasa, etc.

Museum of Comparative Zoology, Harvard

THE annual report for 1957–58 of the Director of the Museum of Comparative Zoology at Harvard College records progress in its usual activities of research, instruction to graduate students and curatorial routine (Pp. 28. Cambridge, Mass.: Museum of Comparative Zoology at Harvard College, 1960). The year was also marked by rather unusual activities such as expeditions by members of the staff to Asia, Australia and South America. Especially noteworthy of mention was a substantial grant from the National Science Foundation for the improvement of the collections and other facilities. The grant is to be spent over a five-year period and much of it will be used on scientific and technical assistance to bring the collections into good shape. Microscopes, other types of equipment and badly needed storage cases were also purchased. The report concludes with an impressive list of publications.

The National Museums of Southern Rhodesia

THE chief item of interest in the annual report for 1959 of the three museums which comprise the National Museums of Southern Rhodesia is an account of the handing over of the Umtali Museum. This was previously owned by the Umtali Museum Society, but is now administered by the Trustees of the National Museums of Southern Rhodesia. The Municipality of Umtali has allocated a one-acre site to house the material collected by the Society and also made a generous grant. The staff has been reorganized so that the Director of the Museums is now relieved of detailed administration of any one Museum and can devote his energies to overall planning.

New Electronic Teaching Apparatus

THE Griffin-ClarkeSmith electronic teaching apparatus 'Mechtronics' is a set of apparatus designed for easy assembly by pupils. A minimum amount of manual and technical skill is demanded of the user, since soldered joints are eliminated and the assemblies are screwed or clipped together on a peg-board layout. The complete set contains radio valves, transistors, a photoelectric device, and other electrical components. For qualitative experiments batteries only are required. For quantitative experiments external instruments are required together with suitable power supplies. The 'Mechtronics' set covers the requirements of the revised syllabus for the General Certificate of Education at Ordinary and Advanced Levels, and may be used by the enthusiast for a wide range of other electronics experiments. The apparatus is obtainable from Griffin and George, Ltd., Ealing Road, Alperton, Middlesex.

American Palms Illustrated

THE Chicago Field Museum of Natural History, which has issued many admirable volumes on the flora of Central and South America, including B. E. Dahlgren's "Index of American Palms" (14, Bot. Ser., pp. 438; 1936), has now produced a companion volume of palm illustrations (Dahlgren, B. E., 14, 412 plates; 1959. 10 dollars). These consist of

photographs of type specimens and of hitherto unpublished plates of Liebmann's elegant drawings, each with its appropriate references and annotations. This handsome volume should be of great value to workers in systematic botany remote from herbarium resources.

Geochemical Landscape

A 'GEOCHEMICAL landscape' is a term introduced by B. B. Polynov for a geochemical characterization of a given part of the Earth, as based on a joint influence of climate, relief, geological structure and vegetation, on the chemical processes occurring in this region and especially on the prevalent chemical elements and of their migration and accumulation. A. I. Perelman (*Priroda*, 3, 23; 1960) emphasizes that the main geochemical features of a geochemical landscape are determined by the biological cycle, although there are geochemical landscapes, like those of the polar or desert type, which are more or less abiogenic. For a brief characterization of a geochemical landscape, Perelman proposes a special geochemical formula, giving first the typomorphic elements and then, above the bar the element deficient and, below the bar the elements in excess of the average. The author emphasizes the importance of the study of geochemical landscapes for agriculture, the study of ore deposits and population health. A map in colour to the scale 250 km. = 1 cm. of the geochemical landscapes of the Soviet Union is given.

Medicinal Plants of the Arid Zones

UNDER this title a new investigation has recently been published under the auspices of Unesco ("Arid Zone Research." Pp. 13. H.M. Stationery Office, June 1960. 15*s*.). It will be noted that some twelve volumes in the Unesco Arid Zone Research Series have already been issued. These include digests of research on major topics such as plant ecology, hydrology, etc., and also monographs on particular subjects. In the present publication, which is of interest both to botanists and pharmacologists, indications are given of the directions in which research on medicinal plants is tending and of the economic possibilities which the utilization of such plants may afford. Dr. I. C. Chopra, of the Drug Research Laboratory, Jammu, India, has been primarily responsible for the botanical aspects, and Prof. R. Paris, of the Faculté de Pharmacie, Paris, for pharmacological aspects. The monograph contains a list of medicinal plants found in the arid zones. In the botanical section, following some general introductory matter, the genera and species of interest in pharmacy are set out alphabetically, briefly described, and their special properties and the relevant literature indicated. In the pharmacological section, the therapeutic or other commercial properties of the species are indicated, together with notes on local usage, artificial synthesis and the scope for further work on, and utilization of, the natural product. Some species possessing medicinal properties, on which no scientific work has yet been done, are mentioned. This section not only contains many items of considerable interest, but also affords a valuable brief survey of an extensive field of traditional and contemporary knowledge.

Eichhornia crassipes

H. R. J. DAVIES (*Nature*, 184, 1085; 1959) and N. W. Pirie (*Nature*, 185, 116; 1960) suggest that the danger of the presence of *Eichhornia crassipes* in the Nile is over-rated, that uses might be found for the plant, and that research should therefore be concentrated in that direction rather than merely on the problem of its eradication.

A meeting was organized by the Scientific Council for Africa South of the Sahara in Leopoldville in 1957 to consider problems related to the spreading of this weed. This meeting was attended by specialists from Belgium, France and the United Kingdom, and was presided over by Prof. J. Lebrun, secretary-general of the Institut National d'Etudes Agronomiques au Congo and vice-president of the Scientific Council for Africa South of the Sahara, who is well known for his work in the field of tropical botany. The agenda of this meeting covered the following topics: biology and ecology of *Eichhornia crassipes* in tropical Africa; its effect on natural plant communities and other organisms; results of direct control measures; means applied to achieve control; effects of treatment on natural vegetation and on riverine crops; treatment in relation to climatic or hydrological conditions; utilization of *Eichhornia crassipes*; measures to be taken to avoid invasion by other aquatic pests. The recommendations made by this meeting (*Eichhornia crassipes*, CCTA/CSA Publication No. 27; PMB 2359, Lagos, B.P. 949, Bukavu) have served as the basis of the action undertaken by the Member Governments of the Commission for Technical Co-operation in Africa South of the Sahara in this field. That referring to the possible utilization of *Eichhornia crassipes* states: "The Symposium, bearing in mind that considerable research work and a number of experiments have been carried out in all countries affected by this pest, considers that there is no need to pursue such experiments. It draws attention to the danger of the dissemination of seeds by cattle food and composts produced from *Eichhornia*".

Leaf-Shape in Hybrids

IN a metrical study of leaf-shape in some F_1 hybrids and their parents, R. Melville has examined the proposition that the leaves of hybrids tend to be intermediate between those of their parents (*Kew Bull.*, 14, No. 1, 88; 1960). Leaves from four genera, *Forsythia*, *Prunus*, *Rhododendron* and *Ribes*, were investigated, with the following results. No exact intermediates were found in which the hybrid interaction was uncomplicated with some other phenomenon. The simplest type of interaction was an intergrading of characters along the leaf-axis, one parent being partially dominant towards the leaf-base and the other towards the apex, as in *Prunus* × *fontanesiana*. The parental effects were equally balanced in the *Rhododendron* hybrid, but there was positive heterosis on the character of relative leaf-breadth. In the *Ribes* hybrid axial intergrading was complicated by negative heterosis on the lengths of the large basal lobes of the leaf and positive heterosis on the breadths of the subterminal lobes. The *Forsythia* hybrid was found to have a leaf-shape exactly intermediate between the leaves of the simple leaved parent and the terminal leaflets of the other parent which had both simple and trifoliolate leaves.

Experiments on Polarity in Flax Buds

H. F. GULLINE has investigated experimentally the polar development in adventitious buds of flax (*Linum usitatissimum*) and their associated vascular

system in hypocotyls (*Aust. J. Bot.*, 8, 1; 1960). Buds were induced on portions of epidermal tissue grafted in inverted positions on hypocotyls, and on hypocotyls subjected to reversal of the direction of gravity and electric polarity normally acting on them. The effects of experimental incisions into adventitious meristems, and in close proximity to them, were also studied. The basic pattern of development remained constant under all treatments. These experiments show that the epidermal and cortical cells from which the adventitious buds and their dependent vascular traces develop possess a very strong inherent polarity which could not be varied by extracellular changes of field.

Roosting Preferences of a Whiskered Bat

INVESTIGATIONS by Lord Cranbrook, and outlined in a recent issue of the *Transactions of the Suffolk Naturalists Society* (2, Part 4), have shown that a whiskered bat, given the opportunity of roosting in a vertical crevice, a horizontal crevice, a bare wall or hanging freely from the roof, showed a strong preference for the first. In a crevice of varying widths, it chose a place where the tips of the hairs on its back just touched the surface behind it, and it did not appear to mind whether it roosted in darkness or light; touch seemed to be the deciding factor.

Popular Culture and Personal Responsibility

THE National Union of Teachers is organizing a conference entitled "Popular Culture and Personal Responsibility", which is to be held at Church House, Westminster, London, S.W.1, during October 26–28. The conference has been divided into eight sessions, including such topics as the growth of communications in modern society, moral and cultural standards, the effects of mass media (with particular reference to young people), how the mass media are being used, the responsibility of the provider, the restrictions of working in the media, and the approach and attitude to the mass media. Further information can be obtained from the Public Relations Department, National Union of Teachers, Hamilton House, Mabledon Place, London, W.C.1.

University News: London

DR. J. S. ROWLINSON, senior lecturer in the University of Manchester, has been appointed to the University chair of chemical technology tenable at the Imperial College of Science and Technology.

Among those appointed to readerships are: Dr. R. J. Goldacre (cell physiology), tenable at the Institute of Cancer Research, Royal Cancer Hospital; Mr. M. J. Way, at present principal scientific officer at Rothamsted Experimental Station (applied entomology), tenable at the Imperial College of Science and Technology.

College of Aeronautics, Cranfield

AMONG the recent appointments to lectureships at the College of Aeronautics are Mr. A. Rothwell (aircraft design) and Dr. A. C. Smith (mathematics).

Announcements

MR. H. STANESBY has been appointed deputy director of research at the General Post Office. He is at present staff engineer in the Radio Planning and Provision Branch of the General Post Office Engineering Department. Mr. Stanesby has been closely connected with the work of the Institution of Electrical Engineers, and was chairman of the Radio and Telecommunications Section in 1955–56. In 1953 he was awarded the Insignia Award for Technology of the City and Guilds of London for his work in telecommunications.

DR. D. C. GARRATT has been elected chairman of the British Pharmaceutical Conference for 1960–61 and will preside at the meeting of the Conference to be held in Portsmouth during the week beginning September 18, 1961. Dr. Garratt is chief analyst to Boots Pure Drug Co., Ltd., Nottingham; he is also a vice-president of the council of the Society for Analytical Chemistry, and is chairman of its Analytical Methods Committee.

THE Palæontographical Society has appointed Messrs. Bailey Bros. and Swinfen as distributing agents for its publications; inquiries about these publications should be sent to Bailey Bros. and Swinfen, Ltd., Hyde House, West Central Street, London, W.C.1.

THE Department of Chemical Technology of the Bradford Institute of Technology is holding a special short course on "Recent Developments in Plastics and Polymer Chemistry" during October 28–29. Further information can be obtained from Dr. W. R. Moore, Department of Chemical Technology, Bradford Institute of Technology, Bradford, 7. The fee for the course is £2 5*s*. 0*d*.

THE American Association for the Advancement of Science will sponsor a symposium on the Sciences in Communist China during its annual meeting in New York City on December 26–27, under a grant from the National Science Foundation. Preliminary plans call for review papers delivered by eminent American and international specialists on Communist China. Publication of these papers as a monograph is contemplated for the spring of 1961.

PROF. A. R. UBBELOHDE (Imperial College of Science and Technology) will deliver the fifth Charles Tennant Memorial Lecture entitled "Melting and Freezing" in the Royal College of Science and Technology, George Street, Glasgow, on November 4. Further information can be obtained from the Society of Chemical Industry, 14 Belgrave Square, London, S.W.1.

THE sixth congress on Theoretical and Applied Mechanics and a symposium on High Speed Computation Methods and Machines are being organized by the Indian Society of Theoretical and Applied Mechanics at the University of Delhi during December 23–26. The symposium is being jointly sponsored with the IBM International. Persons wishing to be present at either or both functions should contact Dr. B. R. Seth, Indian Institute of Technology, Kharagpur, India, from whom further information can also be obtained.

ERRATA. In the article entitled "Evolution of Nuclear Power Plant Design", by Sir Christopher Hinton, in *Nature* of September 24, on p. 1065, col. 2, line 13, the size of uranium rods is wrongly given as 17 in. in diameter; this should be 1 in.; on p. 1067, col. 2, par. 3, line 5, for "reaction" read "reactor".

THE AGRICULTURAL RESEARCH COUNCIL

IN 1958–59 the Agricultural Research Council administered a grant in aid of more than £4 million. Most of this money has been used for established research programmes, since less than half a million pounds was allocated to capital expenditure such as new buildings and the purchase of special equipment. The large expansion programme, embarked on soon after the War, which resulted in the establishment of a number of new institutes as well as extensions to existing institutes, now appears to be nearing its end. There is still one major gap in the field to be covered, and this is referred to in the recent report*, namely, a meat research institute, for which there is a very urgent need. Meat in all its forms is the most valuable commodity coming off British farms, and evaluation of quality is still a very subjective process. We have no thoroughly reliable basis for meat-grading schemes, and there is no real definition of meat quality to provide standards for selection work. Performance and progeny testing of carcass animals is in urgent need of such standards. It is to be hoped that there will be no further delay in the setting up of this institute.

Altogether there are reports from more than forty institutes and research units which are wholly or partly financed by the Council. At one end of the scale there are the giants like Rothamsted with ninety names on the professional staff list, and at the other there are the research units, usually centred at a university, with as few as three or four people working under the direction of a member of the university whose initiative and academic ability have earned the reward of such assistance.

Such units have a continuity usually determined by the duration of the director's university appointment, but this does not generally apply to the special grants which the Council makes to universities, colleges and similar organizations. These are normally limited to three years. A perusal of the list of projects suggests that it is not feasible to organize and complete many of these research tasks in a period so short as three years. Naturally the Council has to safeguard its funds, but it is very important for it to remember that university research cannot prosper if it is on a hand-to-mouth basis so far as finance and personnel are concerned. The quality of the staff the Council recruits, especially in respect of graduates in basic sciences who are in demand from other industries, will depend very much on the kind of research that is being undertaken in the departments that train these recruits. This problem is likely to be aggravated as the 'bulge' descends on the universities, to reduce even further the opportunities university teachers have for personal research.

The reports from the individual institutes are brief and give little information beyond the range of the work that is being undertaken. One cannot, therefore, judge the emphasis that is being placed on the various lines, or estimate the progress that is being made. By way of compensation there are some excellent reviews on several aspects of research in Great Britain along the lines followed in the previous year's report. Because these reviews have a perspective, they are really more valuable than the strictly factual routine report. An outstanding review is that covering foot-and-mouth disease. One sees that the scope of the work being undertaken at the Pirbright Institute has very much more than local implications, and illustrates very effectively the importance of the Council's work to the world at large.

Following the same line of thought, it is heartening to see a reference to the secondment of research workers to countries which have recently achieved self-government, in order to fill the scientific gap created by the retirement of expatriate staff. Countries like Ghana and the Sudan urgently need help, and they are unlikely to obtain it by offering short-term contracts, for there is no certainty that the appointee will get suitable employment when the contract terminates. If, however, he knows that his post is open for him on his return, and that a colleague will replace him abroad to maintain the continuity of his work, then a very different atmosphere is created.

Unfortunately, if we in Britain do not provide this help it will be obtained from other countries, to the detriment of our relations with the emergent countries. This is well evidenced by what is happening in the Sudan. The need for this help exists not only in research but also in teaching, especially at the university level, and also in the provision of technical assistance. It is to be hoped that these initial steps are the fore-runner to a more comprehensive scheme of assistance to countries that need our help.

M. McG. COOPER

* Report of the Agricultural Research Council, 1958–59. Pp. 213. (Cmnd. 1069.) (London: H.M. Stationery Office, 1960.) 9s. net.

THE BACTERIAL GENERA *PSEUDOMONAS* AND *ACHROMOBACTER*

THE summer conference of the Society for Applied Bacteriology was held at the University College of North Wales, Bangor, during July 5–7. A paper-reading session occupied the first day, the last two days being devoted to a symposium on "*Pseudomonas/Achromobacter*".

The contributions to this session covered a wide field of both fundamental and applied problems concerning these two groups of bacteria, but the themes which recurred and which promoted most discussion were differentiation and classification. As interests varied widely from the bacterial flora of meat, eggs, fish, water and soil to human and plant diseases, there were wide contrasts of approach and this led to useful exchanges of ideas.

In an introduction to the symposium, Dr. M. Ingram (Low Temperature Research Station, Cambridge) traced the history of the two genera through

the various editions of Bergey's "Manual of Determinative Bacteriology". He showed how over the years there has been a change of emphasis with regard to the importance of flagellation and pigmentation in the definitions of *Pseudomonas* and *Achromobacter*. Some species previously included in the latter genus have now been transferred to the former because of their polar flagellation; previously they had been excluded from the genus *Pseudomonas* because they showed no evidence of pigmentation. Even now that these two genera have been more clearly defined, reconsideration of the placing of some species seems called for. Dr. Ingram made it clear that he in no way wished to decry the value of the "Manual", and this point was later taken up in discussion when the meeting was reminded that the value of the contents of Bergey's "Manual" depends on the standard of work of the bacteriologists whose published descriptions of bacteria are included in it.

Dr. J. M. Shewan (Torry Research Station, Aberdeen) followed with an account of the methods used in his laboratory for the differentiation and classification of the Gram-negative rods associated with fish and for the broad grouping of *Pseudomonas* isolates. For initial separation, these methods depend on the following tests: colony form, pigment production, Gram's stain, motility and morphology (using phase-contrast microscopy), mode of insertion of flagella, antibiotic sensitivity, the oxidase test (Kovacs' method) and metabolism of glucose (Hugh and Leifson's test). *Pseudomonas* isolates are thus divided into three groups. Group I produce a soluble green pigment, oxidize glucose with the production of 2-keto acid and are generally resistant to terramycin. Group II are non-pigmented, oxidize glucose but are usually sensitive to terramycin. Group III are also non-pigmented but fail to oxidize glucose, giving a negative or alkaline reaction in Hugh and Leifson's test. Gram-negative coccoid rods which are non-motile and non-pigmented are classified as *Achromobacter* or *Alcaligenes* according to whether or not they oxidize glucose, while peritrichous rods are classed as Enterobacteriaceae. Other Gram-negative rods recognized are: *Vibrio*, *Aeromonas*, *Flavobacterium* and *Cytophaga*.

Basically the same procedure is being followed at the Low Temperature Research Station, Cambridge, for the examination of isolates from chilled poultry; in addition, they have found the arginine test useful for distinguishing *Pseudomonas* species from *Achromobacter*.

Prof. J. C. Ayres (Food Technology, Iowa State University) has employed further tests for the differentiation of *Pseudomonas* species isolated from poultry, meat and eggs, namely: growth temperature, gelatin liquefaction, fat hydrolysis, nitrate reduction and citrate and carbohydrate utilization. He groups *Pseudomonas* isolates according to whether they resemble *Ps. fluorescens*, *Ps. geniculata*, or *Ps. fragi*.

For isolates from soil, Dr. A. J. Holding (Edinburgh School of Agriculture) has used a similar range of tests; but he has found that litmus milk reactions and nitrogen utilization tests give useful additional information. Unlike workers in the fish and poultry fields, he classes as *Achromobacter* organisms which are motile and predominantly rod-shaped.

A note of caution was sounded by Dr. K. Klinge (Hygienischbakteriologisches Institut, University of Erlangen) in connexion with undue reliance being placed on individual biochemical tests. He instanced the oxidase test where, using Graby and Hadley's method, he found that the number of strains of *Ps. aeruginosa* giving a positive reaction depend on the medium in which they are grown. A yeast extract medium has proved the most favourable.

Dr. A. M. Paton (Department of Bacteriology, Aberdeen) described media that can be used in the isolation and identification of plant pathogenic bacteria. He has found that a gluconate basal broth is semi-selective and is a useful enrichment medium prior to plating on nutrient agar and 5 per cent sucrose agar. With regard to the latter medium, it is important to realize that production of lævan from sucrose is not restricted to certain plant pathogens but is characteristic also of some saprophytic pseudomonads associated with plants. Other tests for identification of plant pathogens suggested by workers in this field were, phage sensitivity and the ability to produce poly-β-hydroxy-butyric acid, a sudanophilic substance, which is characteristic of certain of the non-fermentative Gram-negative rods.

It was evident both from the main papers and from subsequent discussions that the approach of each worker to questions of differentiation and classification depended on the particular problems encountered in his own field. Some, notably those concerned with fish and flesh, wanted at an early stage to be able to separate the non-pigmented *Pseudomonas* from *Achromobacter*. Dr. Holding indicated a further difficulty with soil isolates; saprophytic *Xanthomonas* strains which have lost their ability to form pigment appear to be indistinguishable from the non-pigmented *Pseudomonas*. In contrast to the workers in the above fields, the medical bacteriologists required tests for the rapid detection of *Ps. aeruginosa* and of relatively few other non-fermentative Gram-negative rods. Dr. Klinge described tests he had used to distinguish *Ps. putida* and *Ps. fluorescens* from *Ps. aeruginosa* and also mentioned *Bacterium antitratum*, which he and some other workers have suggested should be included in the genus *Achromobacter* (this view has been questioned by others). For Dr. K. B. Rogers (Children's Hospital, Birmingham), speed of diagnosis is an urgent necessity, and his aim is to find a means of recognizing *Ps. aeruginosa* within 12 hr. of culturing. Plant bacteriologists also were seeking means of distinguishing the pathogenic from the saprophytic *Pseudomonas* within a reasonable period.

Although differentiation on the basis of a few tests was the primary task of most, many were deeply concerned with the classification of their isolates. Several speakers made a plea that the two should not be confused, though it was recognized that what proved to be a useful scheme for differentiation might also be a logical basis for classification. None appeared entirely satisfied with the present position regarding the two genera, *Pseudomonas* and *Achromobacter*, but there was no move to make drastic changes at this stage. The main need seemed to be for all named species to be very fully described and for them to be available in the culture collections. Prof. Ayres stressed the need for rigid standardization of the constituents of media and other factors such as temperature, age and size of inoculum and growth-medium when characterizing bacteria. He also pointed out that the present system of classification is based to a great extent on unstable characters. A number of workers, in the fields of fish, food and water bacteriology, have been using an electronic

computer to analyse their collected results, applying the theory that, in classification, every feature of an organism should be given equal weight. For this procedure, a minimum of 80 different features was quoted as necessary.

Apart from problems of differentiation and classification, considerable attention was paid to the ecology and development of *Pseudomonas* and *Achromobacter*. Workers at the Torry Research Station have found that, while on fresh fish *Achromobacter* species are present in rather larger numbers than *Pseudomonas* species, after about 15 days on ice the latter become dominant. Many of them are dependent on sea-water and can multiply at 0° C. Similarly, it was found at the Low Temperature Research Station that non-pigmented *Pseudomonas* species become dominant on stored chilled poultry. They are associated with 'putrid' off-flavours compared with 'fruity' ones produced by *Achromobacter*. Prof. Ayres has also found that on raw flesh the dominant organisms are coccoid, motile, aerobic and non-pigmented. On eggs, he has encountered various *Alcaligenes* and *Pseudomonas* species, but only a small proportion can penetrate the inner membrane and cause spoliation. Dr. J. Brooks gave an account of factors which limit bacterial multiplication in egg-white; they included lysozyme, *p*H and the inavailability of protein and of iron, biotin and probably other trace elements. He has found that, so far as penetration of the egg membrane is concerned, age is an important factor, and by the twelfth day entry by infecting organisms is much more rapid.

A description of the distribution of Gram-negative organisms, including *Pseudomonas* species, in fresh-water, by Miss Vera G. Collins (Freshwater Biological Association, Windermere) threw light on the importance of layering effects on the distribution of bacteria in lakes, while the final paper of the symposium, by Dr. Rogers, showed how a single species, *Ps. aeruginosa*, could persist in and heavily infect surgical apparatus which could not be sterilized by heat. This organism proved highly resistant to the non-corrosive chemical disinfectants and the use of infected apparatus could lead to severe and even fatal infections in children. From the discussion which followed, it appeared that dairy cows have become more liable to infection by this organism in recent years.

Two remaining papers dealt with fundamental approaches to two distinct problems. The first was by Prof. J. de Ley (Microbiology Laboratory, State University, Ghent), who gave a clear and convincing account of the carbohydrate metabolism and localization of enzymes in micro-organisms related to *Pseudomonas*. During the discussion which followed, there was a plea that bacteriologists and the biochemists should work more closely together in the future. It was the feeling of several workers that knowledge of metabolic pathways is of fundamental importance in the classification of bacteria. In the second paper, Dr. A. M. Paton (Department of Bacteriology, Aberdeen), discussed the role of *Pseudomonas* in plant disease. He welcomed the recent increase in knowledge of the metabolism of members of this genus, though as yet the results referred to relatively few species and their general validity is still unknown. After referring to various fundamental problems concerning plant/*Pseudomonas* relationships, he went on to describe the use of plant tissues embedded in nutrient agar for the investigation of pathogenicity mechanisms. He thought that, until more is known of such mechanisms, progress in plant disease control will be limited.

The papers read at the symposium and also contributions to the discussion on "Methods of Isolation and Differential Techniques" will be published in full in the *Journal of Applied Bacteriology*.

EVE BILLING

PHYSIOLOGY OF THE BANANA PLANT

COMPREHENSIVE investigations of the physiology of the banana plant are now being undertaken by Prof. F. C. Steward and colleagues in Cornell University. Of the three parts which have now appeared (*Ann. Bot.*, N.S., 24, 83, 117, 147; 1960) Part 1 deals with the detection and estimation of biochemical substances in the banana plant, in particular, the nitrogenous constituents of alcohol-soluble extracts, and keto-acids and non-volatile organic acids. The classes of nitrogen compounds to which attention is given are the amino-acids and their amides, certain volatile amines, ureido and guanido compounds, and certain indole compounds. In view of the large amount present in fruit of the Gros Michel variety, free histidine was isolated and critically identified. The use of various reagents and tests for these various classes of substances on paper chromatograms are described.

The range of substances which have been detected by these means in the banana leaf, leaf-sheath, fruit (pulp and peel) and stem exudate is shown by their location on paper chromatograms. Evidence is presented which indicates qualitatively the degree of prominence of the different substances in the tissues or extracts which have been examined.

Part 2 relates to factors which affect the nitrogen compounds of the fruit of several varieties subsequent to harvesting. In Gros Michel from Honduras, the amides (asparagine and glutamine) and histidine are of special importance in the soluble nitrogen fraction of the fruit. Prominent changes occur in the nitrogen compounds as the fruit ripens, and these are shown to be markedly influenced by the conditions that obtain during the development of the fruit. The nitrogenous composition of the fruit (Gros Michel) is markedly affected by the season of the year at which it forms; this affects the balance between the amides (asparagine and glutamine) and histidine, and also influences the post-harvest metabolic behaviour in ways which are described. While the total protein of the fruit is relatively stable in its amino-acid composition, certain differences were noted which seem to characterize the Gros Michel as it grows in Central America, and some shifts in the amino-acid balance in the protein seem to occur with ripening. It was also ascertained that the very young inflorescence is at first relatively rich in soluble nitrogen compounds.

After the early phase of growth, involving cell division, has elapsed, the fruit utilizes its soluble

nitrogen in synthesis faster than it is supplied to the fruit, so the soluble nitrogen complement falls to a low level; thereafter it increases again to a new higher level at harvest. The composition of the soluble nitrogen fraction as stored at harvest is quite different from that which obtains in the inflorescence in which the fruit is being initiated. The latter emphasizes the amides (asparagine and glutamine) and histidine; the former emphasizes alanine and glutamine as the only prominent amide.

In Part 3, nitrogen compounds of the leaves are considered. The materials analysed were obtained from plants grown in sand cultures either supplied with full nutrient solution or with solutions deficient in each of the several major nutrient elements. The growth was continued long enough to establish the conditions characteristic of these nutrient treatments. Extracts of leaves, sampled according to their position on the axis, have been made from plants grown in full nutrient solution; these extracts have been examined by chromatographic methods to detect and determine the various nitrogen compounds they contain.

The relative proportions of the soluble nitrogen compounds of the banana leaf are quite different from those of the fruit and, in response to the deficiency of specified mineral nutrients, both the total amount and the relative composition of the soluble nitrogen fraction are greatly affected. The results are interpreted in terms of the more active accumulation of soluble compounds in young leaves and the maintenance of a low amide (glutamine)-level in leaves engaged in protein synthesis. The accumulation of soluble nitrogen compounds when growth and synthesis are arrested, and the relative accumulation of a specified number of nitrogenous substances, due to the lack of a nutrient element, indicate that metabolic blocks in reaction pathways occur.

THE NUCLEUS OF THE ANDROMEDA NEBULA

IN 1959 the electronic camera developed by Lallemand and Duchesne in Paris was taken to the Lick Observatory on Mount Hamilton, California, and installed at the focus of the coudé spectrograph of the 120-in. reflector. Among the objects chosen for observation was the nucleus of the Great Nebula in Andromeda, *M* 31. The nucleus appeared on the slit as almost stellar, the inner parts of the nebula which are normally so conspicuous on photographs being invisible.

The results of the observations have been reported by A. Lallemand, M. Duchesne and M. F. Walker (*Pub. Astron. Soc. Pacific*, 72, 76; 1960). The first spectrogram of the nucleus was made in very good seeing when a stellar image was about half a second of arc in diameter, and the image of the nucleus was of diameter 4·4″. It showed at once that the *H* and *K* lines of Ca II, which were the only ones clearly visible, were markedly inclined through the nucleus. Subsequent observations confirmed this. The observations have been interpreted on the assumption that the inclination of the lines is produced by the rotation of the nucleus, and, when converted to the equivalent velocities in circular orbits, the measures yield a maximum circular velocity of 87 km./sec. at a distance of 2·2″ from the centre of the nucleus. Beyond this distance the velocity appears to decrease, a velocity of 42 km./sec. being measured at 4·2″ from the centre

Previous observations of the rotation of *M* 31 refer to points farther from the centre, the innermost point being at 25″ from the centre. The velocity apparently has a minimum somewhere in the region of 10″ from the centre, a maximum at 3′, another minimum at 9′, and an increasing velocity for greater distances. If one assumes that the nucleus is spherical, of radius 2·2′, and that it rotates as a solid body with a maximum circular velocity of 87 km./sec., its properties may be calculated. Its radius is 7·4 parsecs, its mass $1 \cdot 3 \times 10^7$ solar masses, its average density $1 \cdot 5 \times 10^3$ solar masses per cubic parsec and its rotation period $5 \cdot 2 \times 10^5$ years. Its mass-to-luminosity ratio is about 3·6 in solar units. The nucleus is therefore similar in size to a giant globular cluster, but one hundred times more massive and twenty times as dense and as luminous. It rotates one to two orders of magnitude faster than the rest of *M* 31. The results indicate that the nucleus is a separate dynamical entity, although spectroscopic evidence suggests that its stellar composition is like that of the surrounding central regions.

RESULTS OF THE OCCULTATION OF REGULUS BY VENUS, JULY 7, 1959

By DR. G. de VAUCOULEURS and DR. D. H. MENZEL
Harvard College Observatory, Cambridge, Mass.

1. Ingress and Egress Observations

TABLE 1 gives the times T_1, T_2 of the half-intensity phase, $\Delta m = 0 \cdot 75$ mag., at ingress and egress derived from visual, photographic and photoelectric observations secured by members of the Harvard College Observatory (stations 1*a*, 2, 3, 4, 5, 7) and Smithsonian Astrophysical Observatory (stations 1*b*, 6) expeditions. Rain and clouds prevented observations at two other stations (Castel Gandolfo, Asiago). Additional observations (stations (8–24) were received by letter or taken from published sources. Station co-ordinates, observers and sources are listed in Table 2. Published observations

Table 1. Observed Times of Ingress and Egress at Half-intensity*

No.	Station	T_1	T_2	T_2-T_1	T_m	$(O-C)_1$	$(O-C)_2$	Sec β	Obs.†
1	Madrid	19m. 34 2s.	30m. 41·8s.	667 6s.	25m. 08 0s.	+ 0 87s	+ 0·11s.	1 274	2V
2	Le Houga	20 10 2	30 28·5	618 3	25 19·5	+ 0·38	+ 2 91	1·382	V + Pe
3	Merate	21 30 5	30 26 5	536 0	25 58 5	+ 1·03	− 1 89	1 578	Pg
4	Catania	21 49 0	32 05 0	616·:	26 57·:	− 0·81	(+ 6 21)	1 400	V
5	Beirut	24 41·2	33 03·8	502·6	28 52 5	− 0 09	− 1 59	1·687	V + Pg
6	Shiraz	27 10 5	—	—	—	− 2·20	—	2·150	2V
7	Bloemfontein	24 52 2	38 49 7	837 5	31 51 0	+ 0·47	− 0 46	1·018	V + Pe
8	Pretoria	24 51·8	38 57·2	845·4	31 54·5	+ 0·33	− 0·35	1 008	V
9	Hartebespoort	24 47·8	38 55 2	847·4	31 51·5	− 1 83	− 0·25	1·009	2V
10	Utrecht	21 23·5	29 21·5	478 0	25 22 5	− 5 53	+ 2·93	1·806	2V
11	Copenhagen	22 47·5	28 31 5	344·1	25 39 5	− 3·15	− 4·28	2·453	V
12	Uppsala	24 27 5	27 12 5	165·:	25 50·.	− 0 50	+ 1 86	5·179	V
13	Johanneshov	24 26 5	27 20·5	174·:	25 53 5	+ 2 09	− 0 32	4 793	V
14	Munich	21 56·5	—	—	—	− 0 94	—	1·739	V
15	Mulhouse	21 20·5	30 02 0	521 5	25 41 2	− 1·41	− 2 90	1 624	V
16	Armagh	20 22·7	—	—	—	+ 0·08	—	1 696	V
17	Dunsink	20 19 0	28 52 3	513 3	24 35·7	+ 1 03	+ 1 13	1·651	V
18	Ascot	20 44·0	—	—	—	+ 0 75	—	1·648	V
19	Uccle	21 17 5	29 29 0	491·5	25 23 2	+ 4·45	− 3 82	1·714	V
20	Leyden	21 18·7	—	—	—	− 5·49	—	1 795	V
21	Zurich	21 28·8	30 08 4	519·6	25 48 6	− 0 96	− 2 00	1·632	V
22	Innsbruck	21 39·5	30 16 0	516·5	25 57 7	(−12 09)	+ 1 06	1 688	V
23	Bucharest	23 47·0	30 56 7	429·7	27 21·8	+ 0·50	+ 2 04	1·984	V
24	(South Africa)	24 50 8	38 57 0	846 2	31 53·9	− 0 70	− 0 60	1·008	2V

* Interpolated and corrected for personal equation where required. All times are U.T. 14 hr. +.
† *V*, visual; *Pg*, cinematographic; *Pe*, photoelectric (ingress only).

Table 2. Stations Co-ordinates, Instruments, Observers and Sources

No.	Station	Longitude	Latitude	Altitude (m.)	Instrument cm.	×	Observers	Sources
1*a*	Madrid	+ 03° 41′ 15″	+ 40° 24′ 30″	650	15*r*	250	H. O. Ingrao	H.C.O.
1*b*	Madrid				12*r*	—	J. A. Hynek	S.A.O.
2*a*	Le Houga	+ 00° 11′ 15″	+ 43° 46′ 40″	140	20*r*	*Pe*	G. de Vaucouleurs	H.C.O.
2*b*	Le Houga				20*r*	300	A. de Vaucouleurs	H.C.O.
3	Merate	− 09° 25′ 42″	+ 45° 41′ 54″	334	49*r*	*Pg*	R. O. Doyle H. W. Ocker	H.C.O. Boeing Co.
4	Catania	− 15° 05′ 11″	+ 37° 30′ 13″	049	15*r* 30*r*	— —	D. H. Menzel M. G. Fracastoro	H.C.O.
5	Beirut	− 35° 28′ 11″	+ 33° 54′ 22″	038	30*r* 12*r*	*Pg* —	O. Gingerich M. Lesley	H.C.O.
6*a*	Shiraz	− 52° 31′ 34″	+ 29° 38′ 40″	1,596	18*R*	110	C. F. Capen	S.A.O.
6*b*	Shiraz				15*R*	80	V. W. Capen	
7*a*	Bloemfontein	− 26° 24′ 21″	− 29° 02′ 18″	1,387	33*r*	*Pe*	J. Anderson H. Haffner	Boyden (H.C.O.)
7*b*	Bloemfontein				30*R*	—	C. Hoffmeister	I.A.U. circ. 1684 MNASSA, 18, 97
8	Pretoria	− 28° 13′ 44″	− 25° 47′ 18″	1,542	188*R*	720	A. D. Thackeray	MNASSA, 18, 63
9*a*	Hartebespoort	− 27° 52′ 38″	− 25° 46′ 22″	1,220	15*r*	—	H. C. Lagerweij J. A. Bruwer	MNASSA, 18, 52
9*b*	Hartebespoort				20*r*	—	Th. Walraven J. W. Muller	Union Obs. Annex Comm. by W. Finsen
10*a*	Utrecht	− 05° 07′ 48″	+ 52° 05′ 10″	012	25*r*	—	(Staff)	Sterrewacht Sonneborgh
10*b*	Utrecht				40*R*	—	(Staff)	Comm. by M. Minnaert
11	Copenhagen	− 12° 27′ 11″	+ 55° 42′ 13″	014	11*r*	180	J. Trier P. Darnell	I.A.U. Circ. 1683
12	Uppsala	− 17° 37′ 30″	+ 59° 51′ 29″	021	36*r*	200	A. Walenquist L. Peterson	Comm. by G. Larsson-Leander
13	Johanneshov	− 18° 06′ :	+ 59° 18′ .	—	15*R*	290	L. Dahlmark	Comm. by G. Larsson-Leander
14	Munich	− 11° 36′ 30″	+ 48° 08′ 45″	529	28*r*	250	W. D. Heintz	Mitt. St. München, I, Nr. 9
15	Mulhouse	− 07° 18′ 11″	+ 47° 44′ 39″	—	20*R*	210	H. Kern	L'Astron., 73, 383
16	Armagh	+ 06° 38′ 51″	+ 54° 21′ 13″	062	25*r*	100	Papworth	Irish A.J., 5, 212
17	Dunsink	+ 06° 20′ 16″	+ 53° 23′ 13″	086	30*r*	—	M. A. Ellison	Irish A.J., 5, 212
18	Ascot	+ 00° 38′ 20″	+ 51° 24′ 38″	—	15*r*	—	R. L. Waterfield	I.A.U. Circ. 1684
19	Uccle	− 04° 21′ 30″	+ 50° 47′ 55″	105	13*r*	100	A. Velghe	I.A.U. Circ. 1684
20	Leyden	− 04° 29′ 02″	+ 52° 09′ 20″	006	?	—	A. G. Jansen	I.A.U. Circ. 1685
21	Zurich	− 08° 32′ 50″	+ 47° 22′ 02″	469	30*r*	85	R. A. Naef	I.A.U. Circ. 1684; Orion, No. 66
22	Innsbruck	− 11° 22′ 51″	+ 47° 16′ 08″	605	18*r*	—	O. Schneider J. Fuchs	I.A.U. Circ. 1688
23	Bucharest	− 26° 05′ 48″	+ 44° 24′ 50″	083	?	—	C. Christescu	I.A.U. Circ. 1683
24	(South Africa)	− 28° 14′ 39″	− 25° 46′ 46″	1,440	30*R* 15*R*	305 77	N. M. Hoogenhout P. G. van der Byl	MNASSA, 18, 52, 62 MNASSA, 18, 52, 62

r, refractor; *R*, reflector; ×, magnification (visual observation); *Pg*, photographic; *Pe*, photoelectric.

at more than twenty other stations were found too discordant or incomplete for inclusion in the final solution. The 'observed' times in Table 1, when derived from visual observations, are interpolated to $\Delta m = 0{\cdot}75$ mag. with the help of the theoretical light curve derived from the photoelectric observations of ingress at stations 2 and 7 and are corrected where required for a personal equation of 0·2–0·3 sec. on the average.

2. Geometric Results

The observed mid-eclipse times $T_m = \frac{1}{2}(T_1 + T_2)$ and durations $D = T_2 - T_1$ were compared with the values computed from the apparent co-ordinates of Venus and of α Leonis (α = 10h. 06m. 12·193s., $\delta = +12°\ 09'\ 56{\cdot}424''$) derived from the American ephemeris data. The ephemeris radius and parallax of Venus were $R_V = 14\ 25''$, $R_E = 14{\cdot}91''$ for a dis-

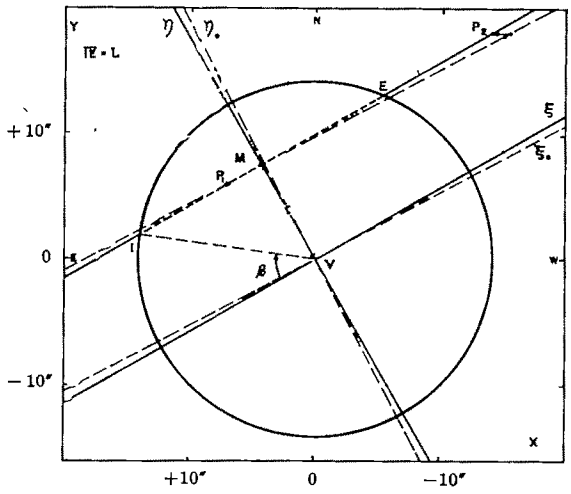

Fig. 1. Projection on plane tangent to celestial sphere of apparent motion of Regulus with respect to Venus. P_1, P_2, apparent positions at 14h. 24m. and 14h. 36m. U.T. I, ingress; E, egress; M, mid-occultation point ($MV = r$). Dashed lines, geocentric paths

tance $\Delta = 0{\cdot}59005$ A.U. ($\sigma_1 = 8{\cdot}41''$, $\pi_\odot = 8{\cdot}80''$). The speed of the apparent motion of Venus was approximately $\dot{s} = 0{\cdot}0339''$ per sec. of time in position angle $\theta = 118° 37'$, the exact values varying slightly from station to station.

The mean O–C for the mid-eclipse time from nineteen stations, $\Delta t = T_m$ (observed U.T.) $- T_m$ (computed E.T.) $= -28{\cdot}1$s. $\pm 0{\cdot}2$s.*, can be interpreted as a determination of Ephemeris Time from the motion of Venus in longitude. A provisional value for 1959·5 derived at the U.S. Naval Observatory from observations of the Moon is $\Delta t_{☾} = -32{\cdot}4$s. (Markowitz, W., personal communication). The 4·3 sec. difference between the two values is well within the possible errors in the star position and in the Venus ephemeris (several tenths of a second of arc).

If ΔR, Δr are the corrections to the ephemeris values of the radius of Venus R_e and of the minimum distance r_e between the star and the centre of the disk (Fig. 1), the difference O–C between the observed and computed durations $D = T_2 - T_1$ is to the first order:

$$\dot{s}\,(D_o - D_c)\cos\beta_e = \Delta R - \Delta r \sin\beta_e \qquad (1)$$

with $\sin\beta_e = r_e/R_e$. Starting from first-approximation values of ΔR, Δr determined graphically, a least-squares solution for sixteen stations leads to:

$$\Delta R = +0{\cdot}150'' \pm 0{\cdot}005'',\ \Delta r = +0{\cdot}315'' \pm 0{\cdot}010''$$

The corrections Δt and Δr when applied to the ephemeris data give the following values for the observed differential geocentric co-ordinates (α Leo – Venus) on July 7, 1959, at 14h. 24m. 00s. Universal Time:

$$\Delta\alpha\cos\delta = +9{\cdot}110'' \pm 0{\cdot}010''$$
$$\Delta\delta = -0{\cdot}334'' \pm 0{\cdot}010''$$

The final O–C of the ingress and egress times computed with these corrected co-ordinates and the observed planetary radius $R_0 = R_e + \Delta R = 14{\cdot}400''$ are listed in Table 1 and plotted in Fig. 2 as a function of $\sin\beta = r/R$. All residuals are less than $\pm$ 6s., except at ingress in station 22 (rejected), and at egress in station 4, where observation was interfered with by a thick haze; the average deviation for the other stations is $\pm$ 1·6s. at ingress ($n = 23$), $\pm$ 1·7s. at egress ($n = 18$). The mean O–C is $-0{\cdot}51$s. $\pm$ 0·22s. ($n = 23$) at ingress and $-0{\cdot}36$s. $\pm$ 0·27s. ($n = 18$) at egress. However, the photoelectric light curves of ingress at Le Houga and Bloemfontein (section 3) give $(O-C)_1 = +0{\cdot}4$s. $\pm$ 0·3s. and $+0{\cdot}3$s. $\pm$ 0·4s., respectively, and the excellent visual observations at Pretoria $(\overline{O-C})_{1,2} = 0{\cdot}0$s. $\pm$ 0·3s. No residual correction is indicated.

The observed radius $R_0 = 14\,400''$ does not refer to the cloud-level, but to a much higher level in the upper atmosphere where the differential refraction effect amounts to 0·75 mag. This radius must be further corrected for the total refraction $\omega_0 = 0{\cdot}016''$ at this level (section 3), since the observed durations are shortened by refraction (Fig. 3). The corresponding radius at unit distance then is:

$$\sigma_1(z_0) = (R_0 + \omega_0) \times \Delta = 8{\cdot}506'' \pm 0{\cdot}003''$$

This value demonstrates that the numerous filar micrometer determinations of the semi-diameter of Venus in excess of 8·5″ are in error; the best measurements with double-image micrometers during transits or with the filar micrometer on the narrow crescent phases give $\sigma_1 = 8{\cdot}41'' \pm 0{\cdot}01''$ in agreement with the ephemeris value. The altitude of the occulting shell (at half intensity) then is:

$$\sigma_1(z_0) - \sigma_1(z_c) = 0{\cdot}096'' \pm 0{\cdot}011''$$

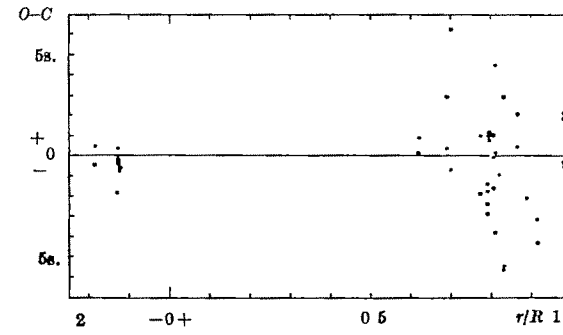

Fig. 2. Residuals O–C of ingress (●) and egress (○) times at half-intensity for corrected elements versus $\sin\beta = r/R$

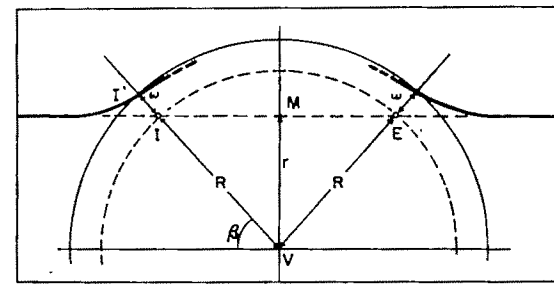

Fig. 3. Effect of atmospheric refraction on duration of occultation. At the times of apparent ingress in I, and egress in E, the geometric positions of the star are in I and E; the apparent radius $R = VI = VE$ corresponding to the observed duration $D = T_2 - T_1$ of the occultation is less than the true radius $R' = VI' = VE'$ of the occulting shell; the difference $\omega = II' = EE'$ is the total deviation by refraction

* All errors quoted are p.e.

or :

$$z_0 - z_c = 70 \pm 8 \text{ km.}$$

above the cloud-level.

3. Photometric Results

The fading phase of ingress at the dark limb was successfully observed photoelectrically at the Péridier Observatory, Le Houga, France (station 2), and at the Boyden Observatory, Bloemfontein, South Africa (station 7). The unsmoothed readings at 0·24-sec. intervals are compared in Figs. 4 and 5 with theoretical light curves computed from the classical theory of extinction by differential refraction in a homogeneous atmosphere[1,2]. It was not found possible to fit the observations with a constant scale height $H = RT/mg$, that is, a homogeneous isothermal atmosphere; both curves indicate a small, but definite, increase of H with altitude. In the observable range $|z - z_0| < 20$ km., the scale height may be written :

$$H(z) = H(z_0)\left[1 + \frac{1}{H}\frac{\partial H}{\partial z}(z - z_0)\right]$$

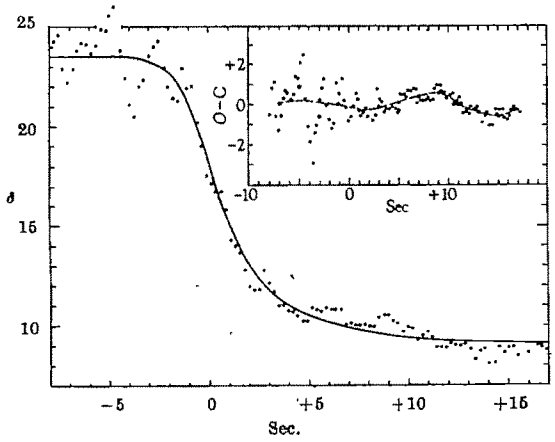

Fig. 4. Photoelectric observations of ingress at the Péridier Observatory, Le Houga, France, compared with theoretical curve for adopted scale height. Inset: residuals, note damping of scintillation during fading phase

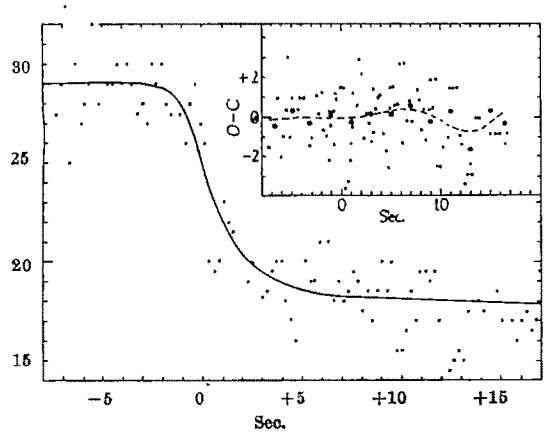

Fig. 5. Photoelectric observations of ingress at Boyden Observatory, Bloemfontein, South Africa, compared with theoretical light curve for adopted scale-height. Inset, residuals

with :

$$H(z_0) = 6{\cdot}8 \pm 0{\cdot}2 \text{ km.}$$

(corresponding to a total refraction angle $\omega_0 = H/\Delta = 0{\cdot}0160''$)[2] and :

$$\frac{1}{H}\frac{\partial H}{\partial z} = +\,0{\cdot}010 \pm 0{\cdot}002 \text{ km.}^{-1}$$

The residuals are shown in the insets; the variation of H with height, although small, seems real, since it was not possible to secure a satisfactory fit with a constant value. Note that because of the different geometry of the occultation in France (sec $\beta = 1{\cdot}38$) and in South Africa (sec $\beta = 1{\cdot}02$), the actual time-scales for fading are notably different in the two stations; the satisfactory fit of both curves by a single set of parameters is therefore a significant check.

With the acceleration of gravity $g(z_0) = 860$ cm. sec.$^{-2}$, we have :

$$\frac{T}{m} = 1{\cdot}03\,H$$

or, for $H = H(z_0)$:

$$T(z_0) = 7{\cdot}0\,\overline{m}$$

For the plausible value $m = 42{\cdot}5$, corresponding to the assumed volume composition carbon dioxide = 0·90, nitrogen = 0·09, argon + others = 0·01 :

$$T(z_0) = 297 \pm 10^\circ \text{ K.}$$

(280° K. for nitrogen/carbon dioxide = 1, $m = 36$; 308° K. for nitrogen/carbon dioxide = 0, $\overline{m} = 44$).

Further, if we assume that $\partial\overline{m}/\partial z = 0$ (that is, no photodissociation of carbon dioxide or nitrogen in the range $z_0 \pm 20$ km.), the value of $\partial H/\partial z$ implies :

$$\frac{\partial T}{\partial z} \simeq +\,3^\circ \text{ km.}^{-1}$$

or a range of variation from 240° K. near $z - z_0 = 50$ km. to 360° K. near $z - z_0 = 90$ km.

The total pressure at altitude z_0 is :

$$p(z_0) = 2{\cdot}6 \pm 0{\cdot}13 \text{ dynes cm.}^{-2};$$

it is practically independent of the adopted mixing ratio nitrogen/carbon dioxide. The corresponding mass and reduced thickness above z_0 are :

$$m(z_0) = 3{\cdot}0 \times 10^{-3} \text{ gm.}$$
$$h(z_0) = 1{\cdot}7 \text{ cm. N.T.P.}$$

The reduced thickness of the atmosphere *along* the light path for the grazing ray at z_0 is :

$$X(z_0) = 1{\cdot}3 \text{ m.}$$

Absorption effects by known or suspected atmospheric gases must therefore be entirely negligible and the observed light curve can be safely interpreted in terms of pure differential refraction effects.

Given the photometric curve for a central occultation (Fig. 6) and the corrected elements of section 2, it is easy to compute the magnitude loss $\Delta m = -\,2{\cdot}5 \log I/I_0$ at the observed instants of disappearance T_D

Table 3. MAGNITUDE DIFFERENCES AT DISAPPEARANCE AND REAPPEARANCE

No.	Station	T_D	$\frac{O-C}{\sec\beta}$	Δm_D	T_R	$\frac{O-C}{\sec\beta}$	Δm_R	$D-R$ mag.	Tel. cm.	Tel. ×	Remarks
1*a*	Madrid	19m. 37 1s.	+ 2 98s.	2 15	30m. 42 3s.	+ 0·47s.	0 50	+ 1 65	15*r*	250	
1*b*	Madrid	36 9	+ 2·83	2·08	41 3	− 0 31	0 94	+ 1·14	12*r*	—	
2*b*	Le Houga	20 13 1	+ 2·31	1 90	30 25·7 ?	+ 0 07	0 72	+ 1·18	20*r*	300	*
3	Merate	21 31 0	+ 0 95	1 30	30 27·5	− 0·57	1·10	+ 0·20	49*v*	*Pg*	*
4	Catania	21 49·7	− 0·07	0 70	32 09 7 :	+ 7 79	rej.	+ 0·70	15*r*, 30*r*	—	*
5	Beirut	24 43 5	+ 1 31	1 47	33 05·5 .	+ 0 06	0 72	+ 0 75	12*r*	—	
6*a*	Shiraz	27 14·7	+ 0·93	1 29	—	—	—	+ 1 29	18*R*	105	*
6*b*	Shiraz	14 6	+ 0·88	1 25	—	—	—	+ 1 25	15*R*	80	
7*b*	Bloemfontein	24 59·8 :	+ 7·96	3 17	38 49·3	− 0·88	1·25	+ 1·92	30*R*	—	
8	Pretoria	24 58 3	+ 6·75	3 00	38 54·8	− 2 78	2 03	+ 0·97	188*R*	720	
9*a*	Hartebeespoort	24 49 2	− 0·40	0 54	38 55 7	+ 0·20	0·65	− 0·11	15*r*	—	
9*b*	Hartebespoort	49 3	− 0·30	0·59	55·8	+ 0 30	0·59	0 00	20*r*	—	
10*a*	Utrecht	21 31 1	+ 1 16	1 39	29 25·0	+ 3 54	0 00	+ 1 39	25*r*	—	
10*b*	Utrecht	30·9	+ 1·05	1 35	22 2 :	+ 1·99	0 05	+ 1 30	40*R*	—	
11	Copenhagen	22 50·8	+ 0·04	0 79	28 32·6	− 1·30	1·46	− 0 67	11*r*	180	
12	Uppsala	24 29·5 :	+ 0·29	0 94	27 14 5 :	+ 0·75	0·35	+ 0 59	36*v*	200	*
13	Johanneshov	24 33·5 :	+ 1·90	1 64	27 32 5 :	+ 2 44	0·03	+ 1·61	15*R*	290	*
14	Munich	21 58 8	+ 0·81	1 22	—	—	—	—	28*v*	250	
15	Mulhouse	21 22 7	+ 0 49	1 05	30 02 7	− 1 35	1·49	− 0 44	20*R*	210	
16	Armagh	20 25·0	+ 1 42	1·53	—	—	—	—	25*r*	100	
17	Dunsink	20 24·8	+ 4·12	2·46	28 50·8 ?	− 0 24	0 90	+ 1 56	30*r*	—	*
18	Ascot	20 46 3	+ 1·82	1·70	—	—	—	—	15*r* ?	—	
19	Uccle	21 19 8	+ 3 91	2 40	29 29 8	− 1 75	1 67	+ 0·73	13*r*	109	
20	Leyden	21 23 4	− 0·45	0·52	—	—	—	—	?	—	
21	Zurich	21 29·6	− 0·12	0 68	30 09 2	− 0 73	1 16	− 0 48	30*r*	85	*
22	Innsbruck	21 41·8	− 5·81	rej.	30 16 8	+ 1·13	0·20	− 0·20	18*r*	—	
23	Bucharest	23 52 2	+ 2 87	2·10	30 57·6	+ 1·46	0·12	+ 1 98	?	—	
24*a*	(South Africa)	24 53 2	+ 1.69	1·65	38 57 5	− 0·10	0 92	+ 0 73	30*R*	305	

T_D (or T_R), time when last seen at ingress (or first seen at egress), corrected for personal equation; $O-C$, observed T_D (or T_R) minus computed ingress (egress) times at half-intensity T_I (or T_E), Δm, magnitude difference read on standard light curve at time $t = T_I$ (or T_E) + $(O-C)/\sec\beta$; $D-R$, $\Delta m_D - \Delta m_R$.

Station 2*b*: T_R, doubtful at 25 7s., definite at 28·8s. Station 3: T_R, doubtful at 25·5s., definite at 27 5s. Station 17: T_R, doubtful at 50·8s., definite at 53 8s. Station 12: T_D, ± 10s. (clouds). Stations 3, 4, 6*a*, 12 (T_R), 13 (T_D), 16, 21: hazy sky.

and reappearance T_R (Table 3). At both ingress and egress the gain in Δm for large telescopes was only slight; on the average $\Delta m_D = -0{\cdot}5 + 1{\cdot}5 \log A$ at ingress, and $\Delta m_R = -1{\cdot}4 + 1{\cdot}5 \log A$ at egress, if A is the telescope aperture in cm. On the average, $\Delta m(D) - \Delta m(R) = +0{\cdot}9$ mag., that is, the star was not detected at the bright limb until it was more than twice as bright as when last seen at the dark limb. For instruments in the range $A =$ 10–40 cm., $\overline{\Delta m_D} \simeq 1{\cdot}5$ mag., $\overline{\Delta m_R} \simeq 0{\cdot}6$ mag. with a dispersion $\sigma \approx \pm 0{\cdot}3$ mag.; in stations with a bright, hazy sky $\Delta m_D \approx 0{\cdot}5$ to $1{\cdot}0$ mag. and $\Delta m_R \approx 0{\cdot}0$ (with T_R occasionally late by 5–10 sec. or more); in stations with good seeing and dark blue sky $\Delta m_D \approx 2{\cdot}0$ to $2{\cdot}5$ mag.

4. Atmospheric Model

A tentative atmospheric model incorporating the occultation results is shown in Fig. 6. The schematic temperature curve is based on the following data:

(1) Surface temperature: $T(0) = 580°$ K. (from micro-wave observations).

(2) Lower stratospheric temperature: $T(z^*) = 285°$ K. (from spectroscopic observations) at an estimated altitude $z^* \approx (580 - 285)/10 = 29{\cdot}5$ km. for an assumed mean adiabatic gradient $\Gamma = -10 \pm 1°$ K. per km.; according to Kuiper, the top of the cloud layer is about 0 46 H lower, hence $z_c \approx 27 \pm 5$ km.

(3) Upper stratospheric temperature: $T(z_r) = 235°$ K. (from the radiometric observations) at an estimated altitude $z_r - z_c \approx 40$–50 km. or $z_r \approx 65$–75 km.

(4) Occultation-level temperature: $T(z_0) = 297°$ K. at $z_0 - z_c \approx 70$ km. or $z_0 \approx 95$–100 km.

With this temperature curve the mean temperature between z_0 and z_c is $\bar{T} = 260 \pm 10°$ K. and the mean scale height $\bar{H} = 6{\cdot}0 \pm 0{\cdot}2$ km., so that:

$$\log p(z_c) - \log p(z_0) = (z_0 - z_c)/2{\cdot}30\,\bar{H} = (z_0 - z_c)/13{\cdot}7$$

If we assume for the pressure at the top of the cloud layer the commonly accepted value $p(z_c) = (1{\cdot}6 \pm 0{\cdot}2) \times 10^5$ dyne cm.$^{-2}$, the observed pressure at the occultation-level $p(z_0) = (2\ 6 \pm 0{\cdot}13)$ dyne cm.$^{-2}$ implies an altitude difference:

$$z_0 - z_c = (5{\cdot}20 - 0{\cdot}41) \times 13{\cdot}7 = 65{\cdot}5 \pm 2{\cdot}5 \text{ km.}$$

in good agreement with the observed value 70 ± 8 km. The pressure distribution $p(z)$ corresponding to the temperature curve and the adopted value of $p(z_c)$ is shown in Fig. 7. The surface pressure of the

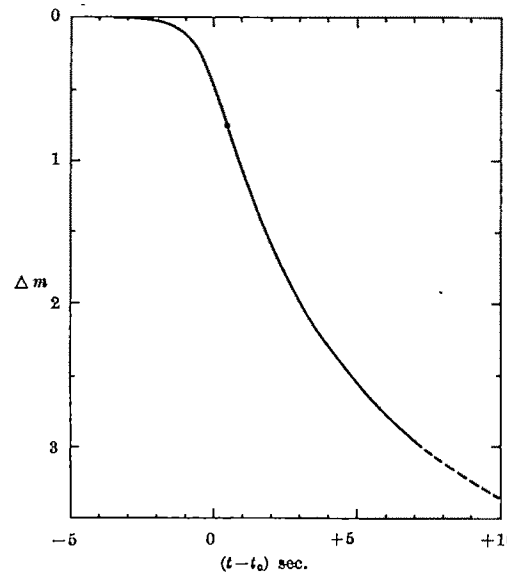

Fig. 6. Standard light curve for central occultation ($\beta = 0$) on July 7, 1959, with $H(z_0) = 6{\cdot}8$ km., $\partial H/\partial z = +0{\cdot}01\,H$

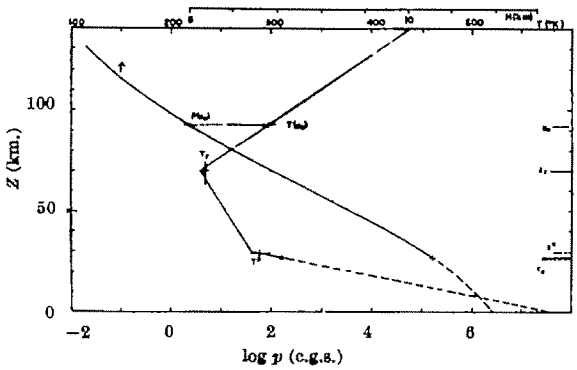

Fig. 7. Atmospheric model incorporating micro-wave, radiometric, spectroscopic and occultation data. Schematic temperature distribution (scale at top) and derived pressure curve for $p(z_c)$ = 160 millibars at top of cloud layer ($z_c \approx$ 27 km.). The occultation pressure $p(z_0)$ = 2·6 dyne cm.$^{-2}$ obtains at $z_0 - z_c$ = 65 5 km, where $T(z_c)$ = 297° K.

model, $p_0 \approx 2{\cdot}5$ atm., uncertain by a factor 2–3, is not directly relevant to the interpretation of the optical data.

If $\sigma_1(z_0) = 8{\cdot}506'' \pm 0{\cdot}003'' = 6{,}165 \pm 2$ km., $z_0 - z_c = 65 \pm 2{\cdot}5$ km. and $z_c = 27 \pm 5$ km., the optical semi-diameter of Venus then is $\sigma_1(z_c) = 8{\cdot}506'' - 0{\cdot}090'' = 8{\cdot}416'' \pm 0{\cdot}005'' = 6{,}100 \pm 4$ km. and the radius of the solid globe $\sigma_1(0) = 8{\cdot}506'' - 0{\cdot}127'' = 8{\cdot}379'' \pm 0{\cdot}008'' = 6{,}089 \pm 6$ km. = $0{\cdot}955_5 \pm 0{\cdot}001$ ($\delta = 1$).

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VARIATION WITH TEMPERATURE OF YOUNG'S MODULUS OF POLYCRYSTALLINE GRAPHITE

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It is well known that at 1,000° C. the elastic moduli of artificial graphites rise with temperature[1,2]. It is also often assumed that this positive variation with temperature exists down to room temperature, although there appear to be no actual measurements to confirm this. Some fairly precise measurements of Young's modulus from 20° to 1,000° C. which we have made indicate that the variation with temperature is not always positive; there is, in fact, a well-defined minimum in the region of 200° C. This is a result of considerable importance in connexion with work on the structure of polycrystalline graphite artefacts, and is also of fundamental interest in indicating that the basic graphite crystallite probably exhibits a negative temperature coefficient of one or other of its elastic moduli, in conformity with most crystalline materials.

The only other evidence of a negative temperature coefficient for a carbon in this temperature-range appears to be that given by Davidson *et al.*[2] for an artefact heat-treated to 1,400° C. They found a net negative variation of rigidity modulus between 0° and 1,000° C. and continuing up to 1,400° C., but with no indication of this variation becoming positive.

Representative results obtained in the present investigation are shown in Fig. 1. These relate to a nuclear reactor grade carbon stock, heat-treated to final temperatures of 1,200°, 2,100° and 2,600° C. respectively. The modulus was measured in all cases in a direction parallel to the extrusion axis. The measurements were made by an adaptation of the flexural vibration method first described by Forster[3]. The specimens, 4 in. long and ⅛ in. diameter, were suspended horizontally in a platinum-wound mullite furnace tube by two graphitized cellulose threads connected respectively to the vibrator and the pick-up units. The vibrator was driven from a Muirhead decade oscillator and the resonance condition determined with a cathode-ray oscilloscope. The pick-up units were mounted on water-cooled supports and shielded from the furnace winding so as to keep their temperature below 50° C. The whole assembly was operated in a vacuum chamber at a pressure of 10^{-4} mm. mercury. The fundamental frequency ranged from about 800 to 2,000 c./s. for all the materials considered. The variation with temperature is relatively small, and at 1,000° C. the frequency can be as little as 50 cycles above the value at room temperature. In all cases specimens were given a preliminary degassing run to 1,000° C., under vacuum, before making measurements.

In addition to the pronounced minima, a noteworthy feature of these results is the hysteresis between heating and cooling (the direction of change of temperature is indicated in Fig. 1 by the arrows); this is, in general, more pronounced for the higher treatment temperatures. On re-cycling four or five times, the degree of hysteresis showed a tendency to diminish very slightly. Heating and cooling were

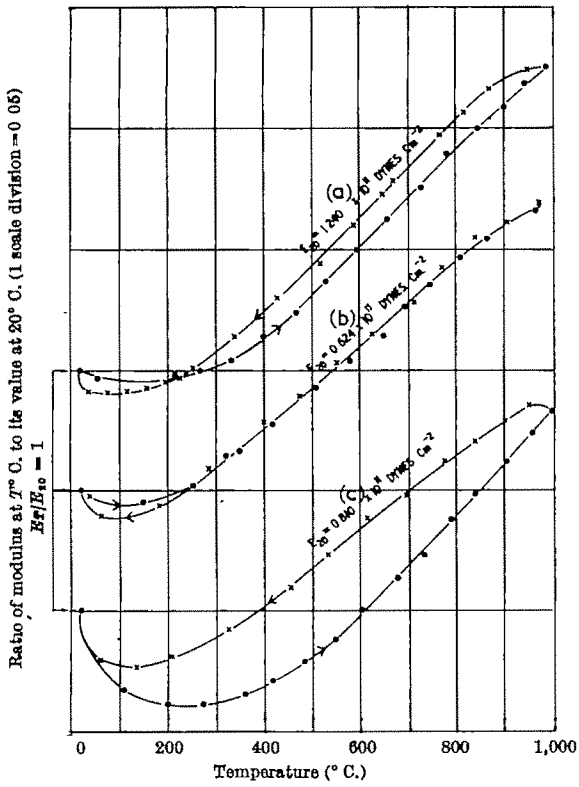

Fig. 1. Relative variation of Young's modulus as a function of temperature for Acheson reactor grade carbon (*a*) heat-treated to 1,200° C.; (*b*) heat-treated to 2,100° C.; (*c*) heat-treated to 2,600° C.

each normally carried out over a period of about 3 hr. It was observed that, if the temperature was held at some intermediate value during heating, the modulus would tend to rise toward the cooling curve. But the holding time has not yet been extended long enough (more than 19 hr.) actually to reach the 'cooling' condition. No such effect was observed on holding during cooling.

The temperature at which the minima occur is not constant but appears to lie between 100° and 300° C., depending on the nature of the material. As indicated above, the region of negative variation with temperature is of great interest, and experiments now in progress indicate that this extends down to a temperature of − 196° C. It is considered that this behaviour reflects either the behaviour of the crystal shear modulus (C_{44}) or a dilatational modulus (C_{11} or C_{33}), all of which are expected to fall with rising temperature in accordance with general theory. The occurrence of a minimum and a subsequent rise of modulus may then be attributed to some structural change which becomes important at about 200° C.

There are two possible explanations of the positive variation with temperature, and both depend on the anisotropic nature of the graphite single crystal. The first, proposed by Mrozowski[4], is that, on heating, internal cooling stresses introduced during manufacture (that is, on cooling from the final heat-treatment temperature) become relieved, with consequent increase in strength and modulus. The other, described by Hove[5], is that, on heating, the large *c*-axis expansion of the crystallites, hitherto accommodated in the voids between the crystals, enables a filling-in of these voids to take place, thus tightening up the structure; this, incidentally, allows the *c*-axis component to play an increasingly larger part in the artefact expansion as the temperature rises. At this stage it is possible to raise three objections to the first, or 'strain', hypothesis: (i) Present results indicate that any built-in strains would cease to be effective below 200° C. There is no obvious reason why this should be so. (ii) The time-dependent nature of the heating curve and the relative stability of the cooling curve suggest that annealing does go on at these temperatures, and hence that there would be little tendency for strains to build up during the much slower cooling conditions of manufacture. (iii) Greater strains (at room temperature) should be induced by the higher heat-treatment temperatures, thus resulting in steeper modulus variations. This is not in agreement with the experimental results.

Davidson and Losty[6] have objected to the second, or 'void', hypothesis. They suggest that Wigner growth of the crystal resulting from neutron irradiation ought to be related to the consequent increase of modulus of the artefact in a manner parallel to the thermal case, whereas in fact it is found that under irradiation the modulus of the artefact increases far more rapidly than in the thermal case.

However, the present facts seem to favour the void hypothesis. On elementary grounds one would expect, on the basis of either hypothesis, accompanying changes in expansion coefficient. As already pointed out, the void hypothesis requires both the modulus and the expansion coefficient to change in the same sense. On the other hand, the strain hypothesis implies that modulus and expansion should change in opposite senses. For, in this case,

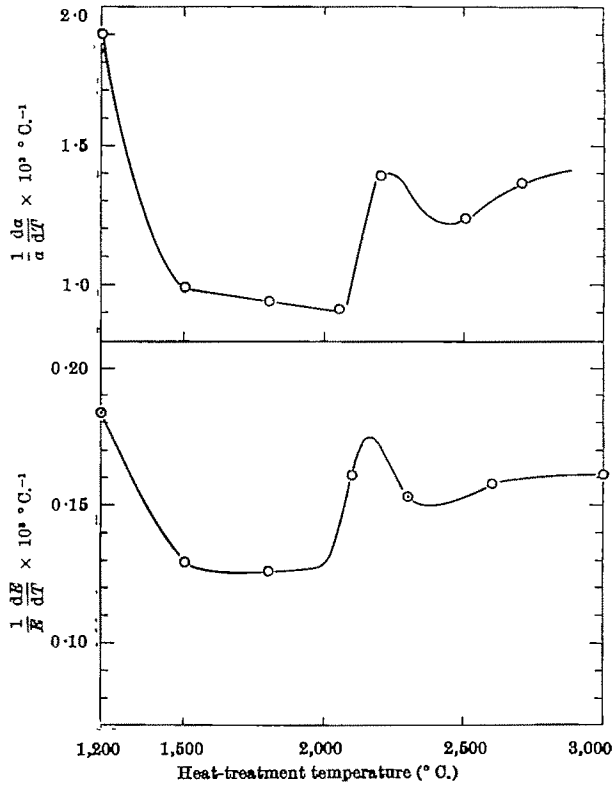

Fig. 2. Temperature variations of thermal expansion coefficient (*a*) and Young's modulus (*E*) as functions of heat-treatment temperature at ambient temperature of 600° C.

any increase in modulus must presumably arise from a net effective reduction in molecular spacing, and this would result in a fall in expansion coefficient. In Fig. 2 are shown, plotted together, the variations with temperature of modulus and expansion coefficient as functions of heat-treatment temperature. The modulus variations have been determined from the cooling curve and correspond to an ambient temperature of around 600° C. The expansion data were obtained by Mr. T. Beirne, using the push-rod-and-tube technique on ½-in. diameter specimens in a nitrogen atmosphere. The variations have again been calculated for 600° C. ambient temperature.

There is a striking similarity in the shapes of the two curves, showing that elastic modulus and expansion coefficient follow one another very closely. It should be noted that although both modulus and expansion measurements were obtained from respective single specimens for each treatment-temperature, the two sets of specimens were cut from two distinct 8 in. × 8 in. × 32 in. blocks of carbon. The general variation with heat-treatment temperature is thus quite genuine and cannot be attributed to in-block variations in structure (although no doubt there are minor variations between specimens which would preclude a perfect agreement). This result thus gives support to the void hypothesis.

The changes in expansion are roughly ten times the changes in modulus. This is reasonable if it is assumed that the effect depends mainly on the micropores. The filling-in of these would not affect the mechanical structure very much, but it could lead to large changes in the contribution to the artefact expansion made by the *c*-axis component of individual crystallites.

Assuming then that void filling is the dominant mechanism, the hysteresis could arise from the inability of crystallites to expand cleanly without overcrowding their neighbours. Some general plastic yielding would then take place before the crystallites reached their full extent, and before the expansion coefficient reached the maximum for the particular temperature in question. On cooling down, the crystallites would shrink back, and this would be a relatively clean process involving rather less plastic yielding. As noted above, dependence of the cooling curve on time has not been detected.

Since the position of the minimum is always close to 200° for materials the pore structure of which is quite different, it is pertinent to ask whether this point does not represent a specific plastic yield temperature rather than some function of the pore structure. The existence of such a yield temperature would be of great interest in interpreting other properties of graphite.

Further investigations are being directed to varying the source material and to exploring thoroughly the low-temperature region.

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INFLUENCE OF PTERIDINES ON THE PRODUCTION OF VITAMIN B_{12} BY TRYPANOSOMID FLAGELLATES*

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IT was noted several years ago that a protozoan parasite of mosquitoes, *Crithidia fasciculata*, required for growth inordinately high levels of a conjugated pteridine; folic acid or still higher levels of folinic acid fulfilled the requirement[1]. The lower efficiency of folinic acid emphasized that the role of conjugated pteridines in this organism differs from the microbial pattern in which folic acid functions only in one-carbon metabolism.

The puzzle of this strange pteridine requirement was solved when it was shown[2] that conjugated pteridines serve two functions in the metabolism of this hæmoflagellate: (1) The usual role in one-carbon metabolism; (2) As a precursor of a new class of growth factors, the unconjugated pteridines, previously called the '*Crithidia* factor' by Nathan and Cowperthwaite[3]. We now know that the 2-amino, 4-hydroxy pteridines, which have good *Crithidia* factor activity, are those which are substituted in the 6-position with either—CH_2OH or a longer aliphatic chain with two vicinyl hydroxy groups.

So far a direct approach to the elucidation of the role of the *Crithidia* factor has been unsuccessful; we have been unable to bypass the growth requirement for the *Crithidia* factor. However, we have recently shown that 2,4,5-triamino-6-hydroxy pyrimidine plus some sugar, such as glucose, can replace *Crithidia* factor[4]. Apparently the protozoan can use the pyrimidine as a pteridine-precursor by converting it to an activated form and closing the incomplete pyrazine ring with glucose.

Now that there are several ways available for satisfying the pteridine requirement of *C. fasciculata* (Table 1, column 1), one way to study the function of the *Crithidia* factor is to measure the variation in key products formed as a function of the compounds used to satisfy the multiple pteridine requirement. Vitamin B_{12} seemed a key product to measure because it is known that, in certain diseases involving vitamin B_{12}, folic acid sometimes relieves symptoms, whereas in other B_{12}-linked diseases, such as pernicious anæmia, folic acid potentiates neurological involvement. To check the validity of measuring the vitamin B_{12} formed by *C. fasciculata*, the B_{12}-products formed by

* Substance of a report presented at the third International Symposium on the B-Vitamins at Poznan, Poland, during September 1959.

Table 1. EFFECT OF VARIATIONS IN PTERIDINES SUPPLIED EXOGENOUSLY ON VITAMIN B_{12}-ACTIVITY PRODUCTION BY *Crithidia fasciculata*

Compound supplied/ml.		mgm. dry cells per litre	μgm. B_{12}/gm. dry cells *Euglena* assay	μgm. B_{12}/gm. dry cells *Ochromonas* assay	μμgm. B_{12}/l. supernate *Euglena* assay	μμgm. B_{12}/l. supernate *Ochromonas* assay	μμgm. B_{12}/l. (cells + supernate) *Euglena* assay	μμgm. B_{12}/l. (cells + supernate) *Ochromonas* assay
Folic acid	1 0 μgm.	220	15,000	680	700	4,500	4,000	4,654
Folic acid + 2-NH_2, 4-OH, 6-trihydroxy-propyl pteridine	1 0 mμgm. 1 0 mμgm.	222	18,900	5,500	2,150	4,000	6,368	5,221
Thymidine + 2-NH_2, 4-OH, 6-trihydroxy-propyl pteridine	20 0 μgm. 1 0 mμgm.	180	28,900	4,000	2,000	3,000	7,200	3,720
Folic acid + 2,4,5-triamino, 6-OH pyrimidine (and glucose from the basal medium)	1 0 mμgm. 5 0 μgm.	200	0	0	0	0	0	0

Strigomonas oncopelti, a related protozoan which requires *p*-aminobenzoic acid but no pteridine, were also assayed.

Two-litre batches of *Crithidia fasciculata* (*Anopheles* strain, *ATCC* 11745) were grown in a defined medium[5] modified by increased levels of several of the mineral components (a reflexion of the decrease in amounts of contaminating inorganic ions in the organic components of the medium and in the distilled water which is now prepared in a glass still). The organisms were allowed to incubate at about 28° C. until there were about 200 mgm. of cells (dry weight) per litre of culture. The cells were then collected by centrifugation and preserved in a lyophilized state until they were prepared for assay. The culture supernatants were twenty times concentrated and stored at 6° C. until they were prepared for assay.

Strigomonas oncopelti (*ATCC* 12982) was grown in the medium given in Table 2. Because this trypanosomid does not require hæmin as a growth factor, the *p*H-range for growth may be extended below *p*H 7·6, where hæmin would ordinarily be precipitated from the medium. For these experiments *S. oncopelti* was grown at *p*H 7·9–8·1, as was *C. fasciculata*, to eliminate the possibility of differences of product due to difference of *p*H. The same methods were used for incubation, harvesting and storage of both organisms.

250 mgm. of lyophilized cells were homogenized in 25 ml. of *p*H 4·5 aconitic acid buffer which contained 0·5 per cent metabisulphite[6]. This homogenate was autoclaved at 121° C. for 30 min., diluted to 1·0 mgm. cells/ml. with distilled water, and assayed. Culture supernatants were diluted 1 : 3 (v/v) with buffer, autoclaved, filtered through paper and assayed.

Table 2. DEFINED MEDIUM FOR *Strigomonas oncopelti*

Potassium phosphate	0 02 per cent
Crystalline magnesium sulphate	0 08 per cent
Calcium (as chloride)	0 3 mgm. per cent
Copper (as sulphate)	0 04 mgm. per cent
Metals mix*	2 0 mgm. per cent
Sodium chloride	0 05 per cent
Triethanolamine	0 5 per cent
L-Arginine	0·03 per cent
L-Glutamic acid	0·1 per cent
L-Histidine	0 02 per cent
DL-Methionine	0·02 per cent
Vitamin mix†	1 0 ml./100
p-Aminobenzoic acid	1 0 μgm per cent

* Metals mix: 2 0 mgm. = iron, 0·2 mgm. per cent as $Fe(NH_4)_2(SO_4)_2.6H_2O$; zinc, 0·1 mgm. per cent as $ZnSO_4.7H_2O$; manganese, 0 1 mgm. per cent as $MnSO_4.H_2O$; copper, 0·008 mgm. per cent as $CuSO_4.5H_2O$; cobalt, 0 01 mgm. per cent as $CoSO_4.7H_2O$; boron, 0·01 mgm. per cent as H_3BO_3; molybdenum, 0 005 mgm. per cent as $(NH_4)_6Mo_7O_{24}.4H_2O$; vanadium, 0 001 mgm. per cent as $Na_3VO_4.16H_2O$.

† Vitamins mix: 1·0 ml. = thiamine hydrochloride 0·1 mgm., nicotinic acid 0·1 mgm., calcium pantothenate 0 1 mgm., pyridoxamine dihydrochloride 0 1 mgm. per cent; biotin 1·0 μgm.

Vitamin B_{12} was measured with *Ochromonas malhamensis* and *Euglena gracilis*. We have been accustomed to assume that *O. malhamensis* measures only 'true B_{12}', that is, those forms of vitamin B_{12} utilizable by humans, and that *E. gracilis* measures 'total B_{12}', that is, those forms to which *O. malhamensis* responds plus other forms (pseudos) which are inactive for humans. Neither of these organisms responds to factor B or nucleotides in place of vitamin B_{12}. These assays could detect 1·0 μμgm./ml. of B_{12} activity.

As the materials used to satisfy the pteridine requirements of *C. fasciculata* were varied, the amount and kind of B_{12}-activity produced also varied (Table 1). When B_{12} was detectable there was, in the cells, more total than true B_{12}. On the other hand, for culture supernatants, the results of the assays seemed theoretically impossible: there was more *Ochromonas*-active than *Euglena*-active material (Table 1). Such a disturbing result has been noted before with human sera[7] and in our unpublished results with sera from patients with liver diseases. There may be a differing ability of the 'true', *Ochromonas*-active and 'pseudo', *Euglena*-active B_{12} to leak out of the cells, and if so, one might expect varying results for the culture supernatants freed of cells. However, one would not expect the amount of B_{12} as assayed by *Ochromonas* to exceed that given by *Euglena*. The factor responsible for greater production of *Ochromonas*-active material may either be a special form of vitamin which is only active for *Ochromonas* (and by implication for humans); or it may be some material which releases inhibition of the synthesis of B_{12} from smaller parts already present; or it may be the long-sought B_{12}-bypass factor.

The role of pteridines in the production of B_{12}-like materials is clearer. For *C. fasciculata*, when there was only enough folic acid present to satisfy the one-carbon function and all the unconjugated pteridines had to be synthesized, presumably from the 2,4,5-triamino, 6-hydroxy pyrimidine also supplied, there was no B_{12}-activity produced (Table 1). For this organism at least, (*a*) the supply of unconjugated pteridines determines whether B_{12} will be synthesized and (*b*) the amount of available conjugated pteridines, or their one-carbon metabolism products (for example, thymidine), influence the kind of B_{12} produced.

The role of pteridines in B_{12} synthesis is more strikingly demonstrated in *S. oncopelti* (Table 3). A series was arranged in which *p*-aminobenzoic acid, folic acid, or *p*-aminobenzoic acid plus various pteridines was used to satisfy the *p*-aminobenzoic

Table 3. EFFECT OF ADDITIONS OF PTERIDINES TO THE GROWTH MEDIUM ON THE PRODUCTION OF VITAMIN B_{12} BY *Strigomonas oncopelti*

Source of *p*-aminobenzoic acid and of pteridines	(μgm./ml)	B_{12} (μμgm.) per 225* mgm. dry cells	
		Euglena assay	*Ochromonas* assay
p-aminobenzoic acid	0·1	0	0
Folic acid	0·50	67,500	45,000
p-aminobenzoic acid +	0·1		
2-NH_2, 4-OH, 6-trihydroxy propyl-pteridine	0·005	67,500	45,000
p-aminobenzoic acid +	0·1		
Folic acid +	0·005		
2-NH_2, 4-OH, 6-trihydroxy propyl-pteridine	0·005	67,500	45,000

* ± 10 mgm. This is the cell crop per litre of medium. The supernatant fluids contained no B_{12}.

acid requirement and to supply possible stimulators for B_{12} synthesis. Production of B_{12}-activity in *S. oncopelti* cells was unusually high: 300 μμgm. *Euglena*-active material/mgm. cells as compared with 28 μμgm./mgm. cells for the best *C. fasciculata* yield and 200 μμgm. *Ochromonas*-active material/mgm. cells as compared with 5 μμgm./mgm. cells for the best *C. fasciculata* yield. Moreover, there was no effect on the balance between *Ochromonas*-active and *Euglena*-active material when the pteridines given to *S. oncopelti* were varied; it was uniformly high. In parallel with the results obtained with *C. fasciculata* (Table 1), there was no assayable B_{12} produced when no exogenous pteridine supply was introduced.

The relatively large quantities of B_{12} compounds produced by *S. oncopelti* (Table 3) suggest the use of this organism for the concentration and identification of the various forms of the vitamin produced and for the later identification of *C. fasciculata* products. The high yields and the absence of the need for exogenous hæm also point to the use of *S. oncopelti* for enzymatic studies of B_{12} synthesis.

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TURNOVERS OF ERYTHROCYTES AND PLASMA PROTEINS IN MAMMALS

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MUCH work has been carried out on the survival of erythrocytes and plasma proteins in different animals. In general, a clear pattern has emerged. Plasma proteins disappear from the circulation exponentially, as illustrated by curve *A* in Fig. 1 (refs. 1, 2). Under favourable conditions of iodination, the rates of disappearance of iodinated proteins or passively transferred antibody globulins (including protein molecules of all ages) are the same as those obtained with proteins after ^{14}C-amino-acid labelling (in which most labelled molecules are of a similar age)[1,2]. It follows that removal of plasma proteins from the circulation is a random process which is largely independent of the age of the protein molecules.

This process stands in sharp contrast to the removal of erythrocytes from the circulation. There is substantial evidence that the normal disappearance of erythrocytes from the circulation is linear rather than exponential[3] (Fig. 1*B*). Cells labelled by incorporation of isotopic glycine into hæm show survival curves of the type illustrated in Fig. 1*C*. Apart from an initial rapid breakdown, they remain at approximately constant level for a certain period, about 100 days in man, after which they rapidly disappear from the circulation[3,4]. This suggests that the factor determining their breakdown in or removal from the circulation depends primarily on some property of the aged cell, while external factors are of secondary importance. The life-span of erythrocytes seems to be controlled by an internal process.

In this article an attempt will be made to show that the turnovers of erythrocytes and plasma proteins, which at first sight seem so dissimilar, may in fact depend on comparable mechanisms. Although reticulocytes contain demonstrable ribonucleic acid[5], it is generally agreed that mature erythrocytes have no nucleoprotein[6]. Since there is substantial evidence that nucleic acid is involved in protein synthesis, it is scarcely surprising that mature erythrocytes cannot

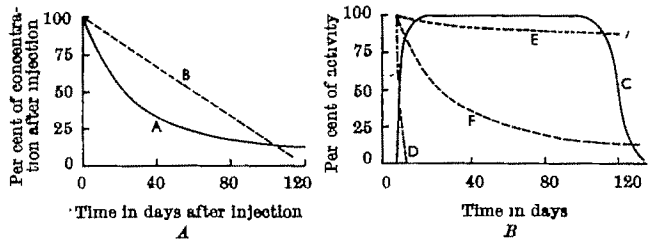

Fig. 1. *A*, concentration of labelled plasma albumin in circulation at various times after injection into human subjects; *B*, concentration of donor erythrocytes at various times after transfusion into normal human recipients; *C*, concentration of isotopically labelled hæm in circulation after a single injection of labelled glycine in human subjects; *D*, concentration of tricarboxylic acid cycle and hæm-synthesizing enzymes in human erythrocytes as a function of their age; *E*, concentrations of enzymes showing slow decrement rates (for example, lactic dehydrogenase) in human erythrocytes as a function of age; *F*, concentration of enzymes showing intermediate decrement rates and of adenosine triphosphate in human erythrocytes as a function of age

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synthesize hæmoglobin or stromal protein[7]. It is a reasonable deduction that the metabolism of the non-nucleated erythrocyte, upon which the maintenance of a functional cell-membrane and hæmoglobin are known to depend, must be carried out by enzymes inherited from the immature, nucleated precursor. The suggestion has therefore been made, and supported by experimental evidence, that there is no synthesis of enzymes in mature erythrocytes and an exponential decay of enzyme activities at different rates during their life-spans[8].

In human erythrocytes, activities of hæm-synthesizing and tricarboxylic acid cycle enzymes decline very rapidly, so that there is no measurable activity in mature cells[9] (Fig. 1*D*); this decline parallels the disappearance of mitochondria from maturing cells. Certain other enzymes, for example, lactic dehydrogenase[10] and purine nucleoside phosphorylase[11], show only slight decrements in activity in old erythrocytes (Fig. 1*E*). However, several enzymes show exponential falls in activities in ageing human erythrocytes at rates intermediate between these two extremes (Fig. 1*F*); such behaviour is shown by glucose-6-phosphate dehydrogenase, phosphoglyceraldehyde dehydrogenase, DPNH·H^+ methæmoglobin reductase, catalase and cholinesterase[9,10,11]. It is noteworthy that the concentration of adenosine triphosphate follows a similar curve in ageing human[10] and rabbit[12] erythrocytes, suggesting that its generation is limited by decline in activity of one or more enzymes at this rate. Since adenosine triphosphate is the immediate source of energy for many important reactions in the erythrocyte, including active uptake of glucose and phosphate and active transport of ions across the cell-membrane[9], it would not be surprising if fall in concentration of adenosine triphosphate to a critical level results in the disordered metabolism and demise of the cell. It is unlikely that the hexose monophosphate shunt pathway is critical in maintaining the metabolic viability of erythrocytes under normal conditions, since subjects with considerably reduced erythrocyte glucose-6-phosphate dehydrogenase activities show normal life-spans unless exposed to primaquine or other hæmolytic agents[13].

It is of interest that curves 1*A* and 1*F* (Fig. 1) are almost superimposable, which suggests that enzymes in erythrocytes decrease in activity at rates comparable with the rates of disappearance of plasma proteins from the circulation. The decrement in enzyme activity in ageing erythrocytes is not due to diffusion out of the cells, since no activity of most of these enzymes is demonstrable in the plasma. It must be due to inactivation within the erythrocyte. Observations on erythrocyte life-spans in different species suggest that the rates of enzyme inactivation in erythrocytes, as well as rates of turnover of plasma proteins, are related to overall metabolism. It has been established and adequately documented[14–16] that small animals have higher specific metabolic rates than large animals under comparable conditions. The metabolic rates of terrestrial mammals can be expressed by the equation $O_2 = 0{\cdot}0633\ B.W.^{-0{\cdot}27}$, where O_2 is the oxygen consumption in ml. per gm. tissue per min. and *B.W.* is the body-weight in gm. (equation 1). Several fairly satisfactory methods for determining life-spans of erythrocytes have now been applied to a number of mammalian species. These methods include differential agglutination and hæmolysis after injection of cells differing in blood-group specificity from those of recipients, labelling hæmoglobin with radioactive iron and isotopic glycine, and labelling of cells with radioactive di*iso*propylfluorophosphonate. The use of radioactive chromate gives comparable results within species, but not between species, owing to differences in rates of elution from erythrocytes. Nucleated avian erythrocytes can also be labelled with phosphorus-32 in deoxyribonucleic acid. A review of these methods and their limitations has recently been published by Berlin *et al.*[3].

Representative results for different species are summarized in Table 1 (refs. 17–27). In general, there is a reasonable measure of agreement among the results for a single species, although some rather large discrepancies remain to be resolved by further work. From the data in Table 1 it is clear that the erythrocytes of small mammals have shorter life-spans than those of large mammals. When the results are presented graphically (Fig. 2), it appears that there is a straight-line relationship between erythrocyte life-span and the logarithm of body-weight. The regression of life-span (Y) in logarithm of body-weight (X) can be calculated by the least squares method and described by the equation $Y = 23{\cdot}95X - 1{\cdot}89$ (equation 2). The sheep erythrocyte has a somewhat longer life-span than expected from this relationship. However, in some experiments with sheep considerable random destruction is evident[28], so that the average erythrocyte life-span is probably less than 120 days.

From Fig. 2 and equation (1) it can be concluded that erythrocyte life-span is inversely proportional to the logarithm of metabolic rate. In keeping with such a concept is the report that in human patients with hyperthyroidism erythrocyte life-span is significantly diminished[29]; the same appears to be true from the data presented for rats made hyperthyroid[30]. Conversely, in marmots kept in the cold, erythrocyte life-spans are prolonged, the effect being very striking in hibernating animals[31]; similar observations have been made with hamsters[32]. If there are comparable activities of critical enzymes at the beginning and end of the lives of erythrocytes of different species, it can also be concluded from data summarized in Figs. 1 and 2 that the logarithmic rates of enzyme decrement are proportional to logarithms of metabolic rates.

Birds have high body temperatures and metabolic rates, and it is noteworthy that the life-spans of their nucleated erythrocytes are relatively short[23–25] despite some capacity for continued protein synthesis in the circulation. However, the life-span of nucleated erythrocytes of the cold-blooded turtle is reported to

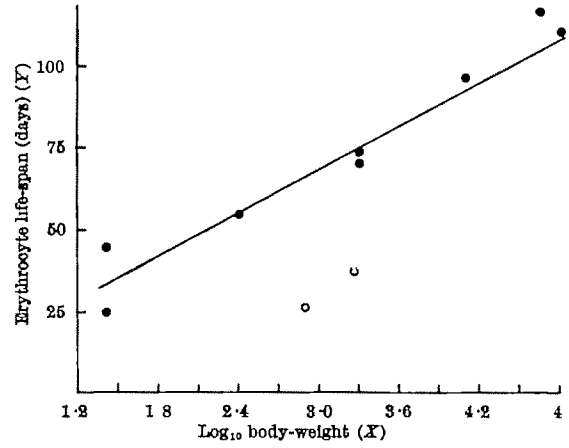

Fig. 2. Regression of erythrocyte life-span against logarithm of body-weight in various mammals (●) and two birds (○)

Table 1. LIFE-SPANS OF ERYTHROCYTES OF VARIOUS SPECIES DETERMINED BY DIFFERENT METHODS

Species	Body-wt. (gm.)	Potential life-span (days)	Method	Ref.
Mouse	23	20–30	Fe-59	17
Mouse	23	41–45	DFP-32	18
Rat	250	50–60	Fe-59	19
Rat	250	(55)	DFP-32	18
Rabbit	2,000	50–75 (70)	N-15 glycine; Fe-59	3
Cat	2,000	68–77 (73)	N-15, Fe-59	20, 21
Dog	13,000	90–135 (95)	N-15, Fe-59	3
Sheep	70,000	120	Fe-59	22
Man	65,000	100–135 (118)	N-15; diff. agglutination	3
			DFP-32	
Fowl	700	28–35 (31)	N-15 glycine;	23
			P-32	24
Duck	1,300	39	^{14}C-glycine	25
Turtle	120	> 11 months	^{14}C-glycine	26

Values in brackets are most probable mean life-spans from available data. Body-weights, unless given, are taken from ref. 27.
DFP, radioactive diisopropylfluorophosphonate.

Table 2. NUMBER OF TIMES ERYTHROCYTES OF VARIOUS MAMMALS ARE DEOXYGENATED (REFS. IN BRACKETS)

Species	Blood vol. (ml.)	Cardiac output (ml./min.)	Life-span (days)	No. of times deoxygenated
Rat	20 ((33)	47 (27)	55	186, 120
Dog	1,000 (34)	1,300 (27)	95	177, 840
Man	5,500 (27)	5,100 (27)	120	160, 344

Table 3. HALF-LIVES OF PLASMA ALBUMIN IN DIFFERENT ANIMALS

Group	Species	Body-wt. (gm.)	α-life (days)	Ref.
	Cow	185,000	20 7	36
A	Man	65,000	15·0	36
	Dog	13,000	8 0	36
	Rabbit	2,000	5·7	36
	Guinea pig	730	2·8	37
B	Rat	250	2 5	36
	Mouse	25	1 9	37
	Man	65,000	23	1
C	Baboon	20,000	16	38
	Rabbit	3,000	8·8	2
	Rat	250	2·6	39

be greater than 11 months[26]. The rates of incorporation of labelled glycine into circulating turtle erythrocytes were low, suggesting a low rate of replacement of cells and protein. Presumably turtle erythrocytes use up their enzymes so slowly that synthesis in the circulation can nearly maintain the *status quo*.

The relationship between decline in enzyme activity of erythrocytes and metabolic rate may be due to direct effects upon the metabolism of erythrocytes: it is reported, for example, that triiodothyronine increases phosphate turnover by erythrocytes *in vitro*[35]. But it might also be due in part to variations in cardiac output, which would affect the rates of oxygenation and deoxygenation of erythrocytes. This process, accompanied as it is by ionic fluxes across the cell membrane, is an important metabolic event for the erythrocyte. Assuming random circulation through various organs, the number of times an erythrocyte is oxygenated and deoxygenated is $C.O. \times L.S./B.V.$, where $B.V.$ is the blood volume, $C.O.$ is the cardiac output in the same units of volume per unit time, and $L.S.$ is the average life-span of the cell in the same units of time. This calculation can only be made approximately because of the difficulty of obtaining reliable and representative figures for cardiac outputs. Nevertheless it is of interest that, as shown in Table 2, the number of times an erythrocyte is oxygenated and deoxygenated appears to be of the same order in man, the dog and the rat, species differing considerably in body-weight. In view of the arguments presented here, it is of interest that the rates of turnover of plasma proteins show a similar dependence on body-weights and hence on metabolic rates of mammals. The results vary somewhat, depending on the technique of labelling, and it has been considered advisable to make independent comparisons of results obtained in two different laboratories where most of the investigations have been undertaken, the Department of Pathology, University of Pittsburgh, and this Institute (groups *A*, *B* and *D*, and *C* and *E*, respectively, in Tables 3 and 4). When the logarithms of the half-lives of plasma proteins (Y) are plotted against logarithms of body-weights (X), straight lines are observed (Figs. 3 and 4). Certain considerations deserve special note, however. In the first place, the points for turnover of serum albumin in rodents evidently fall on a different regression line from those of other mammals, suggesting that the metabolism of albumin is different in rodents. This may perhaps be related to the renal glomerular filtration, re-absorption and catabolism of albumin which have been reported in rodents[41]. Secondly, it has recently been found that in albuminæmic human subjects the half-life of albumin is greatly prolonged[42], which suggests that the normal mechanism for removal of albumin is poorly developed. Further evidence that plasma protein turnovers are related to metabolism is provided by observations that half-lives of albumin

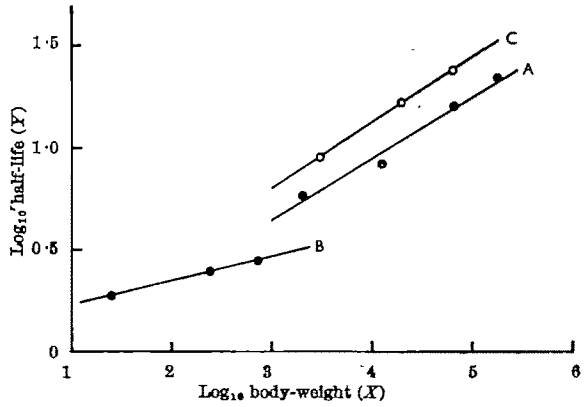

Fig. 3. Regressions of logarithms of half-lives of plasma albumin in different mammals, as shown in Table 3, against logarithms of body-weights. The values for rodents (curve *B*) fall on a different regression line from those in other mammals (curves *A* and *C*). The equations defining these regressions are: (*A*) $Y = 0{\cdot}29X - 0{\cdot}24$; (*B*) $Y = 0{\cdot}12X + 0{\cdot}12$; (*C*) $Y = 0{\cdot}31X - 0{\cdot}14$

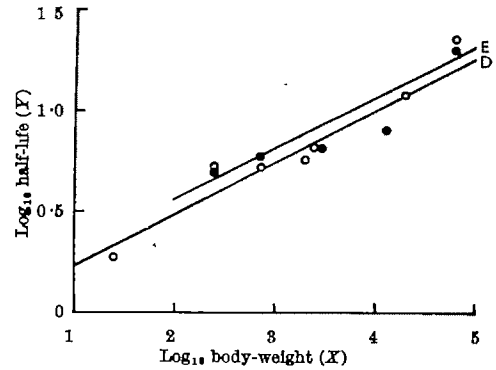

Fig. 4. Regressions of logarithms of half-lives of γ-globulins, as shown in Table 4, against logarithms of body-weights. The equations defining these regressions are: (*D*) $Y = 0{\cdot}26X - 0{\cdot}03$, (*E*) $0{\cdot}25X + 0{\cdot}06$

Table 4. Half-lives of γ-Globulin in Various Mammals

Group	Species	Body-wt. (gm.)	Half-life (days)	Ref.
D	Man	65,000	20·3	40
	Dog	13,000	8·0	40
	Monkey	2,500	6·6	40
	Rabbit	2,000	5·7	40
	Guinea pig	730	5·4	40
	Rat	250	5·5	40
	Mouse	25	1·9	37
E	Man	65,000	23	1
	Baboon	20,000	12	38
	Rabbit	3,000	6 6	2
	Guinea pig	730	6 0	1
	Rat	250	5·4	39

and γ-globulin are both shortened by administration of thyroid hormones to experimental animals[34,40].

I am indebted to Drs. J. H. Humphrey and J. L. Fahey and Miss M. V. Mussett for advice and to Dr. A. S. McFarlane for permission to quote unpublished findings.

Note added in proof. Since this article was submitted for publication, Drs. Humphrey and Fahey have obtained evidence that the half-life of normal mouse γ-globulin is 4·6 days. Hence the regression proposed in Fig. 4 is probably not valid. The relationship of albumin half-life to body-weight shown in Fig. 3 still stands, which suggests that—as might be expected—the mechanisms of albumin and γ-globulin turnover are different.

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TRITANOPIA AND TWO-COLOUR IMAGE SYNTHESIS

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FURTHER investigations have shown the conclusions of an earlier article[1] to be essentially correct and in harmony with the interpretations of Judd[2], Walls[3,4] and Wilson and Brocklebank[3,4], but in need of clarification and the replacement of generalities with precise information. The topic originates in the fact that, under certain conditions, the image of a scene synthesized with two primary colours that approximate red and blue-green may be as acceptable to an observer anticipating a full gamut of colours as is the image conventionally rendered with three primaries[6]. Furthermore, provided additional conditions are fulfilled, the initial pair of synthesizing primaries may be chosen somewhat arbitrarily, for example, red and white (both incandescent and arc-light) or yellow and green—instead of being limited to red and blue-green[5-7].

What is distinctive in such bichromatic systems is not the red and green photographic separations used as a starting point—for these analysing primaries are common to conventional trichromatic systems as well—but the unused blue-violet separation. Thus, as with any visual system which ignores blue-violet light ($\lambda < 490$ mμ approx.), the adjective 'tritanopic'[9,16,17] applies.

There are three principal constituent phenomena at work, to each of which observers are not all equally sensitive. The first, referred to earlier[1] as "revision of the original primaries", and which will also be called the zero-order hue-change effect, is identified with 'discounting the illuminant' in the 'surface mode of perception', as proposed by Helmholtz and developed by Helson and Judd[8,9,18]. That is, on being presented with an unorthodox image, the observer's involuntary cortical processes must, in converting stimulus into perception, make a psychological choice among three possibilities: (1) a two-dimensional pattern of mere coloured patches; (2) the representation of a scene under white illumination with objects of colours the raw stimuli would evoke in isolation; or (3) the representation of a scene under tinted illumination with objects of the colours left after discounting the apparent illuminant. For example, with red and white synthesizing primaries, the choice—if not the trivial case (1)—is between (2) a white-lit scene with red, pink and grey objects, and (3) a scene with red,

white, and blue-green objects under a discounted pink illuminant.

It is convenient to employ, by way of abbreviation, the established terms[8,9,18] 'aperture' and 'surface' (or object) 'mode of perception' to indicate the choices (2) and (3), respectively. The favouring of the latter choice depends on factors of psychological significance, which may include the depiction of reality, including surface textures, or the presence of some feature seeming to be a diffuse or specular reflector of the apparent illuminant. Analogy may be drawn with another psychological problem, Necker's cube[10], where the choice is between (1) a two-dimensional pattern of twelve line segments, and (2, 3) the representation of a cube in one of two orientations with one of two corners nearest the observer. In the absence of any clues favouring one over the other, the observer's choice, in this particular case, involuntarily oscillates between (2) and (3). It is not surprising that in all such cases of cortical adaptation to a bias a choice may be made without perceptible delay; in tasks such as reading, a printed word or phrase may be recognized in an interval so short it is difficult to appreciate that a dozen or more decisions or bits of information must have been processed in that interval without conscious effort. Due to the difference and distance between stimulus and perception, a mechanical limiting of the stimulus-receiving interval, as with a 1/250-sec. shutter[12], does not necessarily prevent the processing of the stimuli during a subsequent and relatively longer blank interval, following which the perception is delivered full-grown. It is also known that no matter how short the duration of an optical stimulus, the resulting neural activity carries on for at least 1/20 sec.

In synthesized images, the chromaticity of the tinted, or biased, apparent illuminant is represented by the mixture of the synthesizing primaries, whatever their number. If the resultant is to be easily discounted to reveal a wide range of apparent underlying surface colours, it should in general be highly desaturated like the naturally occurring tinted illuminants which do not conceal too much evidence of how the underlying surface colours might appear in daylight. A light pink, for example, is especially satisfactory. Among the saturated apparent illuminants that can be simulated, only yellow (interpretable as white minus blue) is satisfactory, as it resembles the desaturated illuminants in its high intrinsic luminosity and ability to be reflected to some extent by objects of nearly all colours. In order to be discounted, a scene's apparent illuminant may be deduced from highlights or any other features which might be expected to reflect it diffusely or specularly[1], but in the absence of such clues, an average of the luminance and chromaticity integrated within the frame of the image[8,9] (in effect, a 'virtual neutral-cue') can be readily substituted[2]. Images which lack specular highlights, but are nevertheless surface-mode inducing, result when suitably crossed polarizing filters are located between photoflood lamps and camera[12], or, more simply, when the subject has a mat but textured surface, as does a woollen tapestry or carpet. Appraisal of the quality of images having nothing whatever to serve as a balance-indicating grey scale cannot, however, be intelligently undertaken, lest the seeming richness of some colours be a matter of unbalance in projector intensity rather than a genuinely enhanced effect.

Qualitatively, discounting the deduced apparent illuminant involves its subtraction—or, addition of its complementary—over the image area. To be more precise, the Judd formulæ[8] should be used. The construction of Fig. 2. of ref. 1 rapidly gives a qualitatively similar, though less precise, result. In this construction it may perhaps be logical to modify each of the original synthesizing primaries by addition of the complementary of their mixture (W) rather than the complementaries of each other. Thus S′ and L′ could lie on SW* and LW*, respectively, where W* is located between S* and L*. There is little difference in the final result beyond a foreshortening of S′L′. Another logical correction would be to replace the symbol S with the letter M throughout[2], because it is the responses of the original scene to the *l*ong and *m*iddle wave-lengths of visible light that have been recorded, while the short-wave-length response has been ignored.

In its simplest form, the zero-order hue-change effect may be demonstrated with the coloured-shadow display described by Goethe[13]. By combining on a neutral screen the light from two coloured sources, arranged so that an opaque obstacle casts two shadows, the colour of each shadow is seen to be that of one of the light sources combined with the after-image or contrast complementary of the mixture. Thus, for example, orange and yellow-green lights combine to give a very pale yellow field against which desaturated red (orange minus yellow) and desaturated bluish green (yellow-green minus yellow) shadows appear without perceptible delay. The shadow hues (the revised primaries) are a complementary pair; if the original primaries are capable of producing a white field by being nearly complementary and in balance at the outset, no revision takes place. That is, the question of a zero-order hue change does not arise in a two-colour image unless the synthesizing primaries are non-complementary or unbalanced at the outset. Furthermore, it will be seen later that if the synthesizing primaries (whether original or after revision) do not approximate red and blue-green, there will be little or no hue change beyond this point.

In exchanging two new for two old primaries, the zero-order effect has not in general converted a one-degree-of-freedom line of chromaticities into a two-degrees-of-freedom plane of chromaticities; the image is still bichromatic. However, certain hues, like red and blue-green, do change slightly when undergoing desaturation or when varying in luminance relative to a fixed grey scale[9,11]. For example, increased desaturation yields slight red → orange and blue-green → green shifts at increased luminance as well as slight red → purple and blue-green → blue shifts at decreased luminance. These first-order hue changes, which constitute the second constituent phenomenon and are included in the Judd-Helson formulation[8,9], can be observed in the demonstration of Fig. 1(*c*) of ref. 1. Thus, if $M'L'$ (formerly $S'L'$) roughly parallels the x axis (ref. 1, Fig. 2) the chromaticities perceived may now be chosen from a narrow ellipse of which $M'L'$ is the major axis. Other primary or revised-primary hues, such as yellow-green and violet, however, exhibit little or no such effect[11].

The zero- and first-order hue-conversion effects are essentially universal, for they occur with virtually all observers and under a variety of non-critical conditions. Much less universal is a third constituent phenomenon, to be called 'second-order hue shift,' which has been identified as an interchange between colours of equal lightness along a tritanopic confusion locus. (The effect was referred to less precisely in ref. 1 as "overlapping in the subjective distinctions between

colours of equal lightness and adjacent hue.") These particular hue shifts, which alone depart appreciably from a red : blue-green axis, require very critical photographic procedures[12], and are in general very prone to differences among individuals and dependent on subtense and context[3,4,14]. For example, in a large audience one typically finds a few young women who perceive no important hue shifts away from a red : blue-green axis, although they perceive all the lower-order hue changes readily, and are surrounded by a large body of neighbours who all see a very full gamut of hues without the slightest difficulty. For these reasons, and others given above, it is most convenient to treat the second-order effects separately, and not consider them to be lumped with the grosser lower-order effects, as Judd does[2].

In colour space, the tritanopic confusion loci are lines of constant lightness (Munsell 'value') and constant 'warmth' or 'coolness'. Typical confusion loci are those joining pale pink with warm yellow, and dark reddish brown with deep purple. The second-order shifts along these loci usually occur in the sense opposite to that of tritanopic reduction[15–17], so the term 'anti-tritanopia' may be adopted. In anti-tritanopia, a slightly greenish yellow hue component can be inserted if luminosity is high but less than that of white, while a blue-violet component can be inserted if luminosity is low but greater than that of black. Such a result might also have been predicted by the Helson effect[18] by noting that the discounted illuminant in any short-wave-deficient arrangement would be expected to be yellowish (although, in the case of red and carbon-arc-white synthesizing primaries (ref. 6, for example) the mixture is not physically yellowish at all), and that Helson specifies that a result of brightness adaptation to such an illuminant is to have relatively light patches take on the (yellowish) hue of the supposed illuminant while relatively dark patches take on the (blue-violet) hue of its complementary. However, it is difficult to identify positively anti-tritanopic shifts with the Helson effect, because the former may be so dependent on the observer, the context, or the subtense. In addition, Helson effect would not allow for the neutral sensations which are retained at all brightness levels.

The blue-violet content of natural and artificial illuminants is extremely variable and is often negligible in the latter. In addition, a part of the foveal region of the retina possesses some short-wave-absorbing pigmentation (the basic purpose of which may perhaps be to reduce chromatic aberration in a high-resolution region). Thus, the perception centres of a normal trichromat would be accustomed to the hue changes, along tritanopic confusion loci, that occur when an image moves on to the affected area of the retina, or when the illuminant varies in short-wave content, and psychological choices would frequently arise. For example, a pale pink patch could be either (1) a pink patch viewed with trichromatic organs in wide-band light or (2) a warm yellow patch viewed with short-wave-deficient organs (if of small subtense) and/or under a short-wave-deficient illuminant (if of arbitrary subtense). The involuntary favouring of choice (2) with little or no perceptible delay could be aided by factors of psychological significance, such as familiarity with the object portrayed or the fact that, in a scene, choice (1) would have led to a less complete[13] or less æsthetic picture, embodying two instead of three degrees of freedom.

Anti-tritanopia is readily demonstrated in its own right with a bichromatic set of six Munsell chips in red and blue-green hues only. The 1/2-in. mat chips 7·5 *R* 5/12 (red), 7·5 *R* 7/8 (pink), 7·5 *R* 8/4 (pale pink), 7·5 *BG* 6/6 (blue-green), 7·5 *BG* 4/5 (dark blue-green), and 7·5 *R* 3/5 (dark brown), mounted well apart and in order on a very light grey (*N* 8/0) background, are recommended. Suitable viewing conditions may be established either at arbitrary subtense with any illuminant lacking wave-lengths shorter than about 490 mμ but otherwise unselective, or at moderately reduced subtense (10′–1°, depending on the individual and the illumination-level) under white light. In either case, the sensations reported are not red, pink, pink, etc., but red, orange, yellow, green, blue and purple, respectively[3,4].

In conclusion, the perception of a multiplicity of hues in a well-executed two-colour synthesis of the image of a scene appears to be due to rapid cortical adaptation or orientation to an apparent illuminant seeming to fall on the objects in the scene. Two qualities of the apparent illuminant may be deduced : the quality of being biased away from neutrality, and the quality of being tritanopic, or of rendering only two degrees of freedom. In assessing the second quality, whether or not the first is present, what matters is not the deficiencies in the synthesizing primaries, but the supposed deficiencies in the apparent illuminant simulated by their mixture. The perceived colours are therefore formed from the original stimuli first by discounting the chromatic bias, if any, of the apparent illuminant, and then by discounting the tritanopic reduction due to its apparent omission of short-wave response and the third degree of freedom. Syntheses, the stimuli of which are not converted as described, and are therefore of great significance to some[2,7], would be merely patterns which in some way fail to be consistent with, or invite involuntary cortical interpretation as, a representation of surfaces upon which the discountable illuminants fall.

I am indebted, for exchanges of information, to Messrs. Wilson and Brocklebank (who also helped perfect the 'Tritanope's Palette'), W. B. Wintringham (who suggested that tritanopic confusion be considered), D. B. Judd, F. Pollak, and J. M. Adams. The continued interest and encouragement of R. L. Gregory and Prof. W. R. Hawthorne are gratefully acknowledged.

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LETTERS TO THE EDITORS

PHYSICS

Effect of Hydrogen-Ion Bombardment on the Oxides of Aluminium and Magnesium

COMMERCIAL high-purity, polycrystalline samples of aluminium oxide and magnesium oxide have been subjected to bombardment by a 300-μamp. beam of hydrogen ions having an energy distribution with a maximum at 500 eV. At this energy, the maximum penetration into the substances would be of the order of 100 Å., and therefore any changes of property observed would, in the main, be confined to these regions. Changes in electrical resistance have been recorded as a convenient means of following the effect of the bombardment.

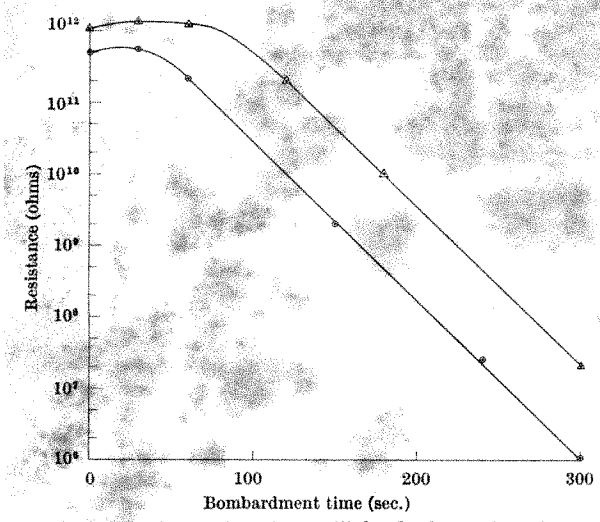

Fig. 1. Variation of resistance with bombardment time of: ⊙, magnesia; △, alumina

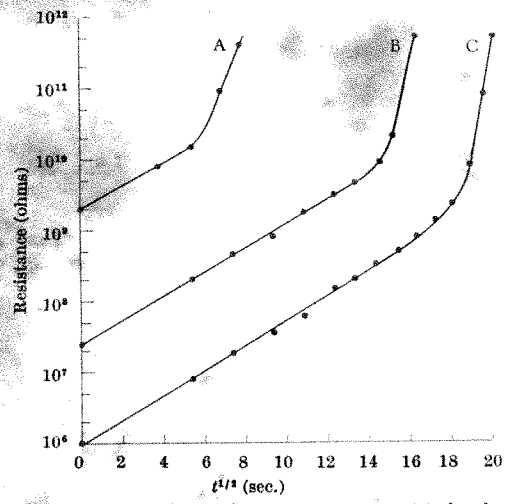

Fig. 2. Recovery of electrical resistance subsequent to bombardment, as a function of $t^{1/2}$ (sec.) for MgO. *A*, Bombarded for 150 sec.; *B*, bombarded for 240 sec.; *C*, bombarded for 300 sec.

Fig. 1 illustrates the variation of resistance with time of bombardment, and, as can be seen, there is no sign of the observed effect becoming saturated within the time-scale used. Subsequent to bombardment, it was found that the electrical resistance recovered to its original value; this is shown in Fig. 2 for the case of magnesium oxide. Aluminium oxide exhibited a similar behaviour. The full recovery process took place at room temperature, suggesting an activation energy of about 0·1 eV. In addition, the strong dependence of the recovery process on $\sqrt{t}$ (where t is time) is suggestive of a diffusion mechanism. However, further work is required before a full understanding of this effect, which may conceivably have important practical implications, is obtained.

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Submillimetre Waves by Harmonic Generation from Cold Cathode Arcs

THE use of the mercury pool arc for microwave harmonic generation has already been described[1,2]. The purpose of this communication is to report some preliminary results obtained with solid cathodes.

As before, the driving power used was a few watts obtained from a continuous-wave Q-band klystron operating at 35 Gc./s. The arc was mounted in a Q-band wave-guide and was so oriented that the $\frac{1}{2}$-mm. diameter tungsten-wire anode was parallel to the microwave electric vector. The cathode material in the form of a thin slab was mounted adjustably through the H-plane wall of the wave-guide beneath the wire anode. The arc was struck by applying d.c. to the anode (via a variable resistance) and then moving the cathode until contact was made between it and the pointed end of the anode. The cathode was then withdrawn so that an arc less than 0·1 mm. in length was formed. Harmonic output was collected by means of a smaller wave-guide protruding through an E-plane wall of the Q-band wave-guide close to the arc. No effort was made to match the arc to the output wave-guide.

At high gas pressures (for example, 20 atmospheres argon) disintegration of the cathode material under the action of the cathode spot is much reduced; the cathode spot is clearly emitting at a very high current density, yet the cathode remains 'cold'. It seems that, in principle, any conductor may be used for harmonic generation, but for most materials the cathode spot wanders from beneath the anode wire, thus lengthening the arc and producing a startling drop in harmonic output. Calcium is the most successful cathode tried to date, but even with this material a small movement of the spot can be seen

and this produces a fluctuation in the harmonic power generated. For calcium the d.c. potential across the arc drops from about 15 volts to between 0 and 8 volts when the Q-band drive is switched on. The d.c. current (usually about 0·25 amp.) is adjusted by means of the variable resistance to give maximum harmonic output. This adjustment is very critical.

With a calcium cathode, the ninth harmonic at 315 Gc./s. ($\lambda = 0{\cdot}95$ mm.) was found, using a Golay infra-red detector for receiver. The highest output so far obtained at this frequency is about 10^{-8} watt, but if the output system can be matched to the arc, the power should approach 1 microwatt. The variation of output power with increasing harmonic number suggests that the ninth harmonic is probably not the highest present, and it is hoped to use a second arc as frequency charger for superheterodyne detection of these higher harmonics.

This communication describes work forming part of the research programme of the National Physical Laboratory, and is published by permission of the Director of the Laboratory.

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Dislocations in Non-metallic Layer Structures

A POINT not mentioned by Amelinckx and Delavignette in their communication[1] concerning dislocations revealed in thin flakes of non-metallic layer structures by transmission electron microscopy is the ready observation of grids of crossing dislocations, as distinct from hexagonal net-works, in talc and mica (Fig. 1, cf. Fig. 1 of Amelinckx and Delavignette's communication and Fig. 2).

These grids are generally remarkably stable and may be moved slightly to and fro by varying the intensity of the electron beam, although if the flake is overheated the dislocations vanish suddenly.

Fig. 1. Grid of crossing dislocations in talc (a hexagonal network is just resolvable in the bottom left-hand corner)

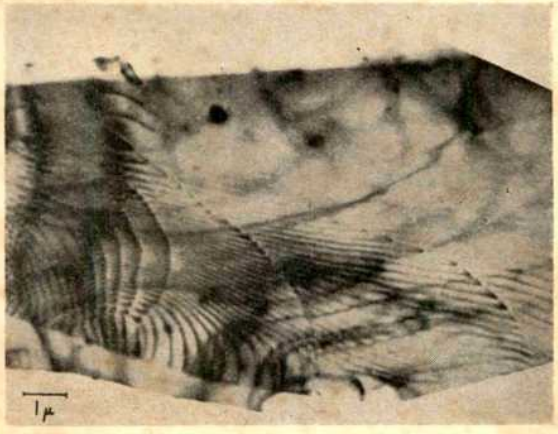

Fig. 2. Crossing of two systems of dislocations in mica

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An Electron Microscope Study of Graphite Oxidation

LATTICE or surface imperfections may play an important part as active sites in the oxidation of graphite, and an attempt at observing these and how they behave on oxidation has been made by electron microscopy.

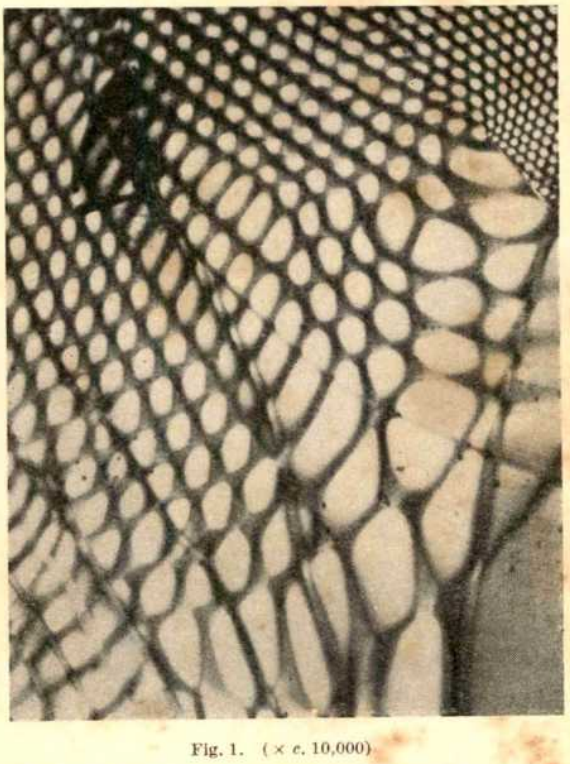

Fig. 1. (× *c.* 10,000)

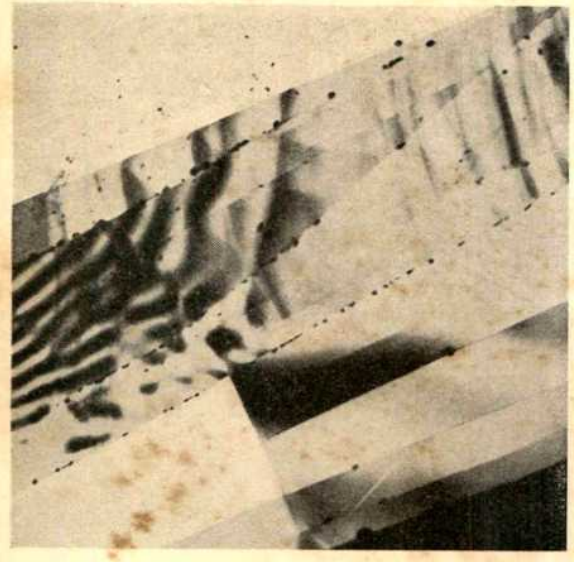

Fig. 2. (× c. 16,000)

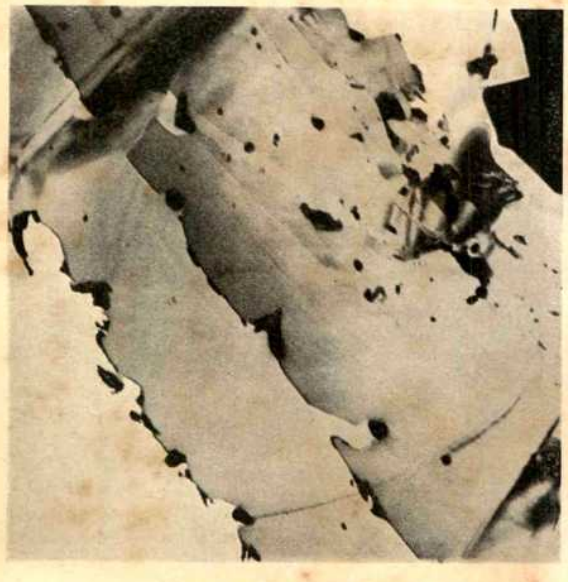

Fig. 3. (× c. 16,000)

Thin films of graphite were prepared by smearing microscope grids over the surface of natural Madagascar flake for examination in an *E.M.*6 Metropolitan Vickers electron microscope. These appeared as large areas of flat graphite sheets the basal planes of which were predominantly normal to the electron beam. Dislocations in the basal planes were frequently observed, the estimated density being 10^9/cm.^{2}.

Graphite is also particularly prone to the incidence of stacking faults. The basal plane dislocation splits into partials forming a ribbon of stacking fault 700–1000 Å. wide according to the equation :

$$a[10\bar{1}0] \rightarrow a/3[11\bar{2}0] + a/3[2\bar{1}\bar{1}0]$$

From measurements of the radius of curvature of dislocation nodes the stacking fault energy of graphite was estimated at approximately 0·25 erg/cm.^{2}. Interaction of partials to form networks is shown in Fig. 1.

Due to the fortuitous relative rotation of graphite sheets, moiré fringes are often observed, with dislocations imaged as extra planes. These extra lines are associated with dislocations lying in the basal planes and as these do not pass through the film the analysis of Pashley and Bassett[1] cannot be applied.

Thin films heated in air at 600° C. and examined in the microscope show that attack occurs preferentially at crystal edges and cleavage steps (Fig. 2). Further attack occurs inwards from the initial points (Fig. 3). It would be expected that greater reactivity would occur where dislocations end at crystal edges. Due to the high mobility of these dislocations, considerable movement occurs during heating and cooling and no definite conclusions can be drawn from thin films which have been oxidized outside the microscope. To overcome this, a heating stage has been designed and made for the *E.M.*6 microscope and work is now proceeding to oxidize specimens during examination.

I wish to thank the Directors of C. A. Parsons for permission to publish this communication and D. R. Ashworth for supervising the initial work.

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Ultra-violet Absorption Spectra of the Molecules H_2O, HDO and D_2O

WE are in complete agreement with Barrett and Mansell[1] concerning the absorption spectrum of water down to 185 mμ, and also in their implied criticism of the work of Golding[2]. Independently of Barrett and Mansell, we had failed to observe with a Unicam *SP*.500, flushed with nitrogen, the fine-structure described by Golding, and the results were therefore checked on a vacuum grating spectrophotometer[3] and extended down to 180 mμ using silica cells of 1 cm. and 1 mm. path-length. Plotted as log *A* against wave-length, the absorbance of water rises nearly linearly down to at least 180 mμ, with no trace of fine-structure. At about 20° C. the absorbance values for 1 cm. path-length were found to be 0·1 at 192 mμ, 1·0 at 186 mμ and 10 at 181 mμ very nearly. More complete and precise results will be published elsewhere.

In the course of private correspondence by one of us with Mr. Golding, a letter from him almost identical with that which follows Barrett and Mansell's communication was received and a full reply was sent. Normal spectrophotometric precautions for work in this region were not observed if the monochromator was not flushed with nitrogen ; even in a Beckman *DK*2 spectrophotometer, the greater part of the light-path lies within the monochromator. Stray light cannot be estimated by using a shutter in the way described ; even if it could, it is of interest to compare the percentages of stray light (calculated from the figures given for maximum optical densities with less than 1 per cent error) with corresponding values determined in a more orthodox manner by Stich, Rotzler and Reichstein[4] for a specially selected *DK*2 spectrophotometer with complete nitrogen flushing (Table 1).

Table 1

	Wave-length	186 mμ	188 mμ	190 mμ	195 mμ
Percentage stray light	Golding	0·53	0·47	0·18	0·05
	Stich *et al.*	4·0	1·3	0·4	0·02

The true stray light will also not in general be appreciably dependent on width of slit; however, if any air remains in the light-path, an effect in the opposite sense to that described by Golding may be observed at the maxima of the Schumann–Runge oxygen absorption bands. Here, as the slits are made narrower, the stray light increases significantly, as might be anticipated; the sharp minima in Golding's spectra occur at the wave-lengths of these oxygen maxima, and together with the abrupt fall at still shorter wave-lengths present an excellent example of the misleading effects of stray light. The statement that Lambert's (rather than Beer's) law is obeyed must be taken with some reserve; it quite certainly would not be obeyed at the wave-lengths of the Schumann–Runge peaks. Sulphuric acid has a remarkably low absorbance down to 185 mμ, so the effect of adding water is not surprising, and of course the same is true for the effect of a solute added to one of a pair of cells containing water—in each case the increase in absorbance results in the appearance of the stray light effects.

Dr. Wilbur C. Kaye of Beckman Instruments, Inc., has informed us that with a properly flushed *DK*2 spectrophotometer the spectrum of liquid water is in agreement with the results of Barrett and Mansell, and does not show the maximum or fine structure described by Golding.

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CRYSTALLOGRAPHY

Crystal Structure of 1-3-7-9 Tetramethyluric Acid and the Molecular Packing in Hydroxymethyl Purine Crystals

THE ability of 1-3-7-9 tetramethyluric acid to solubilize polycyclic aromatic hydrocarbons in water and to form 1 : 1 and 1 : 2 crystalline complexes from organic solvents, first pointed out by Weil-Malherbe[1], has recently attracted considerable interest[2,3].

Since solubilization and complex formation are closely related, we have investigated the crystal structure of some 1-3-7-9 tetramethyluric acid hydrocarbon complexes by X-ray diffraction hoping to obtain information on the interaction between the purinic and the hydrocarbon molecules. The present investigation of the crystal structure of 1-3-7-9 tetramethyluric acid was undertaken as a first step.

X-ray diffraction photographs were recorded from single crystals of 1-3-7-9 tetramethyluric acid using a Weissenberg camera and copper $K\alpha$ radiation. The unit cell dimensions are: $a = 15{\cdot}59$ Å., $b = 8{\cdot}87$ Å., $c = 8{\cdot}46$ Å., $\beta = 118°$, $V = 1033$ Å.^{3}, $Z = 4$, $d_{\text{theor.}} = 1{\cdot}430$, $d_{\text{exp.}} = 1{\cdot}422$.

The space group is $P2_1/a$ if a few extremely weak reflexions are ignored.

Both optical[4] and calculated Fourier transforms[5,6], as well as Patterson projections on 010 and 100 were used in the first stage of the structure determination. When a sufficiently large fraction of the observed amplitudes could be assigned correct signs, Fourier projections on 010 and 100 were computed (Figs. 1 and 2).

Atomic co-ordinates were refined through reiterate cycles of structure factor calculations carried out on a 650 *IBM* electronic computer[7]. The molecules

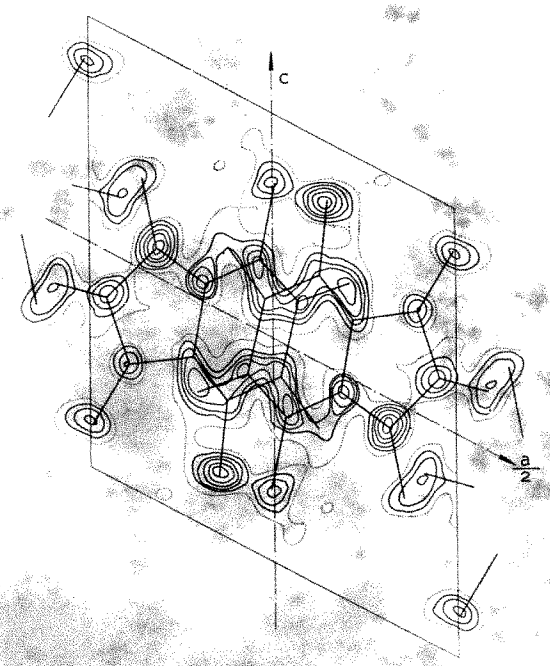


Fig. 1

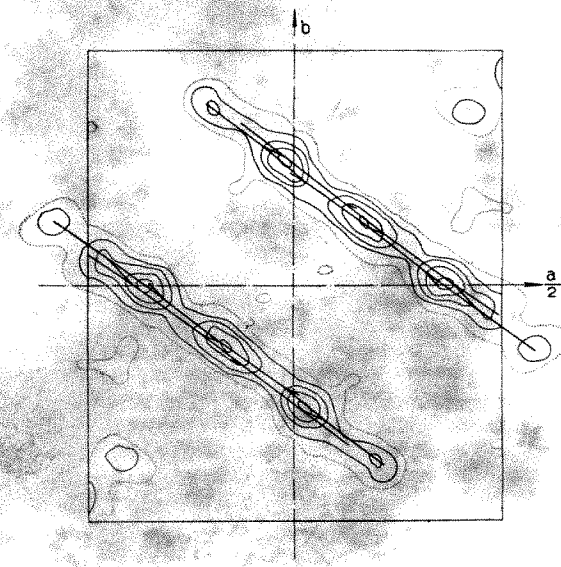


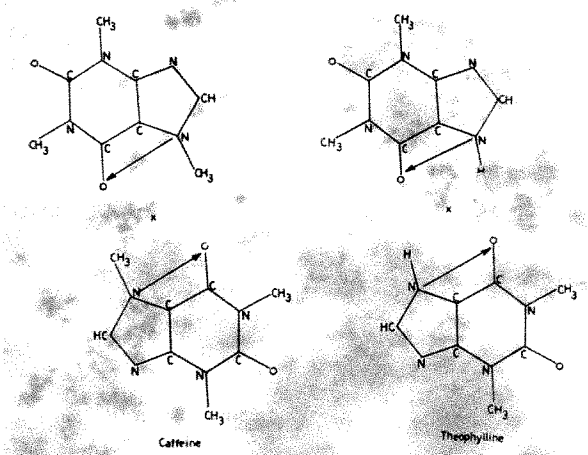
Fig. 2

appear to be planar with an average distance of the atoms from the molecular plane:

$$0{\cdot}0187\,x + 0{\cdot}4416\,y - 0{\cdot}3655\,z = 1$$

of $\pm\,0{\cdot}02$ Å.

It is interesting to compare the arrangement of the molecules in the crystal with that of the two parent methylhydroxypurines, theophylline and caffeine[8]. All these structures are monoclinic, with the space-group $P2_1/a$ (ignoring weak forbidden reflexions). However, whereas the crystal structures of theophylline and caffeine are closely related, that of 1-3-7-9 tetramethyluric acid is based on a different type of packing. In caffeine and theophylline, the pairing takes place in the same plane (or almost in the same plane), according to the following scheme:



In the case of 1-3-7-9 tetramethyluric acid the two paired molecules lie in parallel planes 3·5 Å. apart, as shown in Fig. 3.

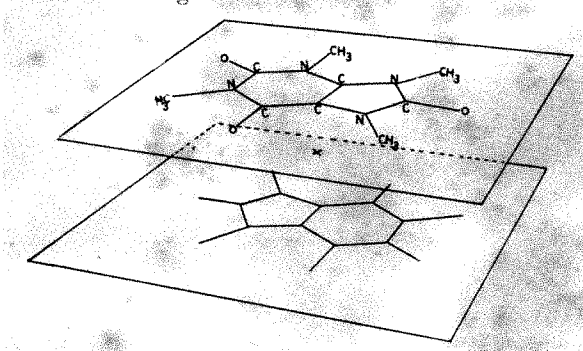


Fig. 3

From the structure of theophylline alone it might be inferred that hydrogen bonding between $>$C=O and $>$N—H groups is responsible for the pairing. However, the occurrence of a similar pairing between caffeine molecules, where hydrogen bonding is ruled out by the methylation of the nitrogen, indicates that dipole–dipole interaction may be dominant in both cases. The ring nitrogen atoms forming three σ bonds probably contribute their lone pair electrons (p_z^2) to the π molecular orbitals. A large fraction of these electron pairs should be localized around the more electronegative oxygen atoms of the $>$C=O groups. The mode of pairing of theophylline and caffeine could be to the strongest $\overset{+}{N}$—$\overset{-}{O}$ dipole, which arises from the charge-distribution in one molecule being antiparallel to the corresponding dipole in the opposite molecule, as indicated above.

In the case of theophylline, a certain degree of hydrogen bonding might be present in addition to the dipole–dipole interaction, but it would be weakened by misalignment of the oxygen lone pair orbital moments and the N—H bond moments to which hydrogen bonding is sensitive[9]. The radical change in the mode of pairing observed in going from caffeine to the 1-3-7-9 tetramethyluric acid structure can thus be explained by the weakening of the $\overset{+}{N}-\overset{-}{O}$ dipoles resulting from the introduction of one more $>$N—CH_3 and $>$C=O group. It would appear that the strongest $\overset{+}{N}$—$\overset{-}{O}$ dipoles are now roughly perpendicular to the long axis of the molecules, and that interaction between these dipoles is the main factor responsible for the pairing of the 1-3-7-9 tetramethyluric acid molecules in parallel planes (see Fig. 3). The role of dipole–quadrupole, quadrupole–quadrupole and higher multipole terms is difficult to estimate without calculating the π charge-distribution in the molecule.

Our results show that hydrogen bonding is not necessarily the only specific interaction responsible for the pairing of hydroxymethyl purine molecules, since dipole–dipole interaction may predominate in favourable cases.

A similar suggestion has been recently made by Cannon[10] concerning the interaction between $>$N—H and $>$C=O groups of amide bonds.

We wish to thank Dr. F. Ascoli for a gift of 1-3-7-9 tetramethyluric acid crystals. We are indebted to Prof. M. F. Perutz for valuable criticism and for reading the manuscript of this communication. This work was supported by the Consiglio Nazionale delle Ricerche and by a grant from the Rockefeller Foundation.

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As part of a programme of work on the investigation of the bond lengths and bond angles in purines[1], the crystal structure of 1,3,7,9-tetramethyluric acid has been determined. In the preceding communication, de Santis, Giglio and Liquori have reported the crystal structure of this substance, but describe a different polymorphic form from the one given here.

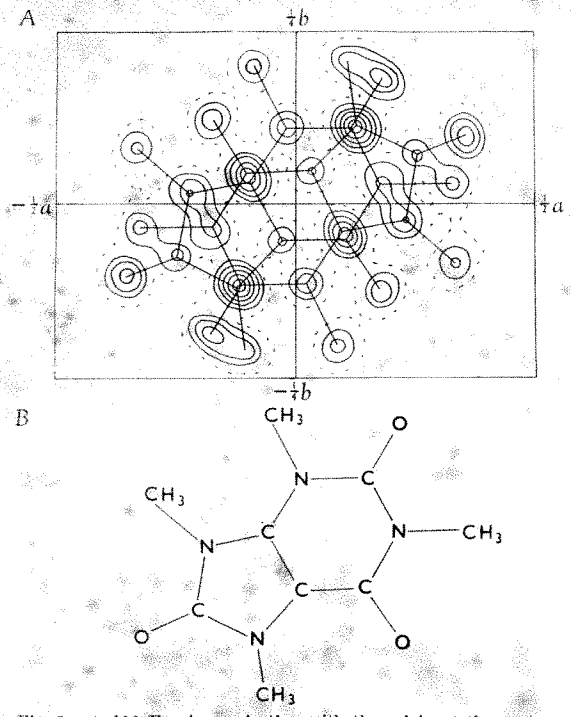

Fig. 1. *A*, *hk*0 Fourier projection with the origin at the centre. Contours are at arbitrary but equal intervals with the zero contour broken. *B*, 1,3,7,9-tetramethyluric acid showing the positions of the carbon, nitrogen and oxygen atoms in the above projection

I have found that 1,3,7,9-tetramethyluric acid crystallizes from water in two polymorphic forms. Crystals of one form are those described by de Santis *et al.*, and also by Groth when his *c* axis is halved. The dimensions of the unit cell given by de Santis *et al.* are :

$$a = 15{\cdot}59\ \text{Å.},\ b = 8{\cdot}87\ \text{Å.},\ c = 8{\cdot}46\ \text{Å.},\ \beta = 118°,\ V = 1033\ \text{Å.}^3$$

The space group is $P2_1/a$ if some fairly weak reflexions of the type *h*0*l* with *h* odd are ignored, but these constitute about 17 per cent of the total number of 'forbidden' reflexions. Crystals of the other form are needles elongated along the *c* axis, and the unit cell dimensions obtained from rotation and Weissenberg photographs are :

$$a = 10{\cdot}11\ \text{Å.},\ b = 14{\cdot}89\ \text{Å.},\ c = 6{\cdot}75\ \text{Å.},\ \beta = 100{\cdot}4°,\ V = 999\ \text{Å.}^3$$

The space group is $P2_1/a$, there being no 'forbidden' reflexions as in the first form, and the unit cell contains four molecules. The smaller volume of this cell indicates that the packing of the molecules is more economical. These crystals appear more suitable for a full structure determination, and hence they were chosen for the present investigation.

The orientation of the molecules and their positions within the unit cell have been determined from the *hk*0 and 0*kl* sharpened Patterson functions in conjunction with structure factor graphs. The co-ordinates so obtained have been refined by successive Fourier syntheses, and by the method of least squares, the computations being carried out on *Mercury* in the University of London. At the present stage of refinement, the *R*-factor for the *hk*0 projection is 17 per cent and an *hk*0 Fourier projection is shown in Fig. 1.

Molecules related by a centre of symmetry lie in parallel planes approximately 3·3 Å. apart, and pairs of molecules are related by screw axes. A similar arrangement exists in the other form, the distance between parallel planes being 3·5 Å. A comparison of the two completed structures should prove interesting and should show whether there are any significant differences in the molecular dimensions brought about by the transition from one polymorphic form to the other. The occurrence of weak 'forbidden' reflexions in the other structure suggests that the polymorphic change in 1,3,7,9-tetramethyluric acid represents the rearrangement of an ordered lattice in the structure described here into a disordered one.

Full details of this structure determination and the final results will be published elsewhere.

I should like to thank Prof. E. Boyland of the Chester Beatty Research Institute for the gift of 1,3,7,9-tetramethyluric acid, and the University of London for the award of an I.C.I. Fellowship.

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METALLURGY

A Determination of the Melting Point of Element 43 (Technetium)

A SMALL quantity (0·11 gm.) of technetium-99 metal has recently been loaned to us by Oak Ridge Laboratories (U.S. Atomic Energy Commission) and we have taken the opportunity to measure the melting point, as there does not appear to be a value reported in the literature.

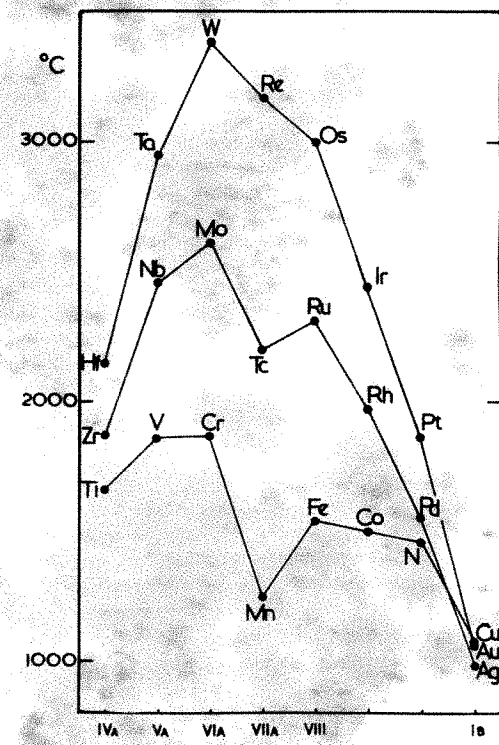

Fig. 1. Melting points of metals of the transition series plotted in order of ascending atomic number

The metal, in the form of coarse powder, was contained in a small thoria crucible, and was melted under argon in a tungsten tube resistor furnace of the type described by Haworth and Hume-Rothery[1]. The temperature was measured with a Tinsley double-scale disappearing-filament optical pyrometer, by observation through a small hole in the crucible lid. The quantity of metal was not sufficient for the direct observation of melting, but after heating to 2,150° C. the metal had not melted, while after heating to 2,250° C. the powder had melted into a small shiny bead. The melting point may therefore be taken as 2,200 ± 50° C. The molten metal did not attack the thoria, nor does it appear to be volatile at the melting point, only traces of radioactivity being detected on the radiation screens above the crucible of melt.

The melting points of metals of the three main transition series are plotted in Fig. 1 for metals of the Groups IV*A* to I*B* of the Periodic Table. It may be seen that technetium resembles manganese inasmuch as its melting point is lower than that of either of the adjacent metals in the series, the melting points of molybdenum and ruthenium, determined in the same apparatus, being 2,610 ± 20° C. and 2,310 ± 20° C. respectively.

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Crystallization of Amorphous Niobium Oxide during Anodic Oxidation

Studies of the anodic oxidation of metals such as tantalum, niobium, zirconium and titanium have been confined, in general, to temperatures of 25° C. where the thin films formed can be regarded as homogeneous dielectrics and the relationship between $V - t$, $1/C - V$ and $1/C - t$ is rectilinear.

During a study of the anodic oxidation of niobium in a variety of electrolytes (acetic, formic, phosphoric, oxalic, chloracetic, boric acids, etc., sodium chloride, strong acids and bases) it has been observed that temperature and current density have a marked influence on the anodizing characteristics. The results are illustrated in Figs. 1, 2 and 3, which show the voltage-time, weight gain-time and voltage–reciprocal capacity relationships respectively for niobium anodized in 1 *M* acetic acid at a constant current density of 1 m.amp./cm.² at various temperatures.

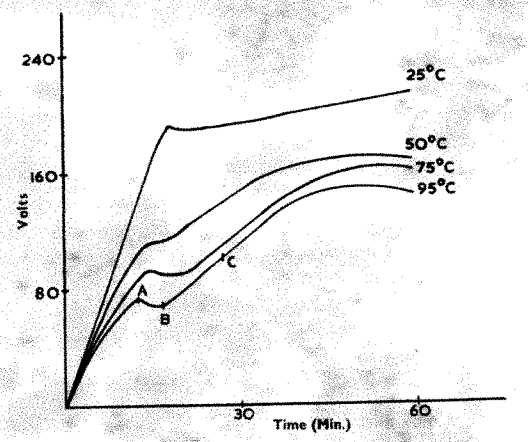


Fig. 1. Anodic oxidation of niobium in 1 *M* acetic acid at a constant current density of 1 m.amp./cm.². Voltage-time relationship at various temperatures showing plateau formation at temperatures greater than 50° C.

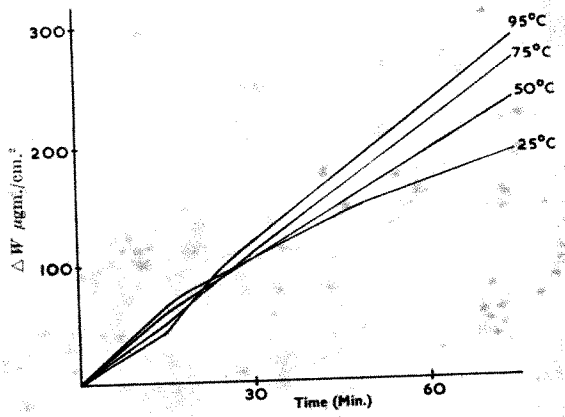


Fig. 2. Anodic oxidation of niobium in 1 *M* acetic acid at a constant current density of 1 m.amp./cm.². Weight gain (ΔW)–time relationship at various temperatures

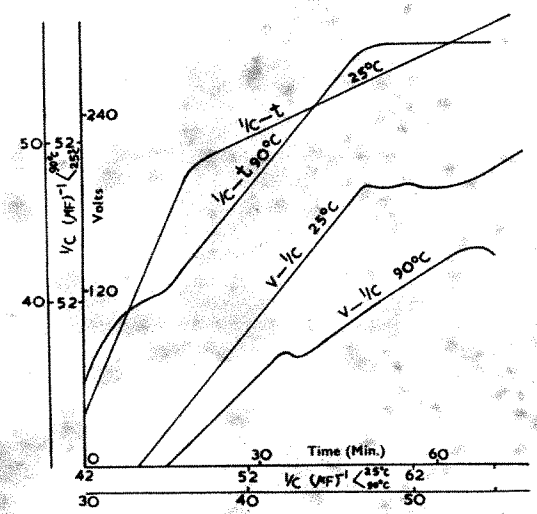
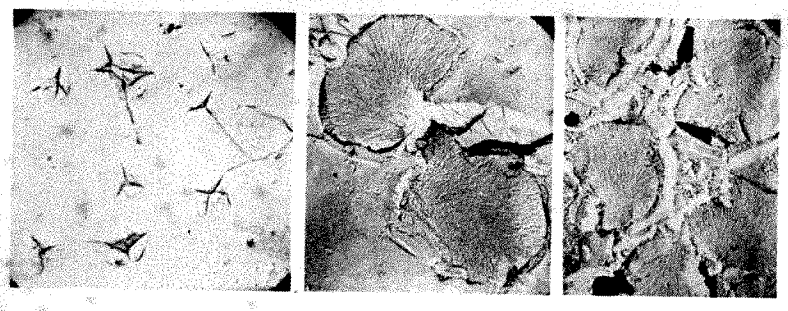


Fig. 3. Anodic oxidation of niobium in 1 *M* acetic acid at a constant current density of 1 m.amp./cm.². Reciprocal capacity–time and voltage–reciprocal capacity relationship at 25° C. and 90° C. showing corresponding changes in the slope to those in Fig. 1

At 25° C. the $V - t$ curve is rectilinear up to ~190 V. and oxidation proceeds with the formation of interference films, but at higher temperatures the $V - t$ curve is characterized by a plateau, and it is evident that the higher the temperature the lower the voltage at which the plateau occurs. Fig. 2 shows that at 90° C. there is a sudden increase in the $\Delta W - t$ curve which corresponds with the charge required for plateau formation. Similar discontinuities are evident in the $V - 1/C$ and $1/C - t$ curves (Fig. 3).

A similar plateau has been observed with the other electrolytes studied, under appropriate conditions of concentration, temperature and current density.



(a) (b) (c)

Fig. 4. Electron micrographs *a*, *b* and *c* correspond to points *A*, *B* and *C* (Fig. 1) and show the initial cracking of the film and subsequent appearance at the surface of the crystalline oxide. Magnification, *a* and *c* × 4,250, *b* × 6,500

Electron diffraction studies of films formed at various voltages at 25° C. and 90° C. have shown that at the lower temperature the oxide surface remains amorphous, but at 90° C., although the oxide gives diffuse haloes of Nb_2O_5 below the plateau, at and above the plateau the structure corresponds to crystalline Nb_2O_5.

Figs. 4*a*, *b* and *c* show electron micrographs obtained at points *A*, *B* and *C* (Fig. 1) and reveal the initiation of cracks in the surface at the plateau and the subsequent projection of crystals of Nb_2O_5 through the overlying amorphous surface layer. At 25° C., although similar cracks (similar to Fig. 4*a*) appeared at the surface at ~190 V., there was no visible evidence of crystallization even after prolonged passage of charge.

From the present work it is evident that initially the oxide surface is continuous and amorphous and that the arrest in the rise in voltage, that is, the plateau, is associated with the formation of discontinuities in the oxide which are caused by crystallization of the amorphous oxide.

Cathcart *et al.*[1] have found that during the high-temperature oxidation of niobium at 350–500° C. the growth law is initially parabolic, but, at a critical thickness which depends on temperature and time, becomes linear owing to cracking of the oxide. From marker experiments they conclude that film growth is due to anion migration through the oxide and that cracking results from the stresses which arise from the formation of the oxide at the metal/metal oxide interface.

Vermilyea[2] has described the phenomenon of field crystallization where anodically formed amorphous Ta_2O_5 has been shown to crystallize in the presence of a strong electric field and considers that rupture of the amorphous oxide is due to this crystallization which occurs within the amorphous oxide. The similarity of the photomicrographs (Fig. 4) to those obtained by Vermilyea for tantalum indicates that the phenomenon observed in the present work is due to field crystallization and that a similar mechanism is applicable.

Recent electron diffraction studies of thermal oxide films on niobium[3] have shown that the oxide is amorphous when protective but is crystalline when non-protective, indicating that film rupture is due to crystallization.

It is apparent from the present work that there are many similarities in the behaviour of niobium during anodic and thermal oxidation, as in both cases film thickening results in discontinuities in the oxide so that oxidation continues linearly. It should be observed that a protective oxide from the point of view of anodic oxidation is one where film growth proceeds to only a limiting thickness and then practically ceases owing to an alternative electrode process, that is, gas evolution. Fig. 2 shows that film growth of the anodic oxide continues owing to crystallization and consequent film rupture so that the oxide cannot be regarded as truly protective.

It is possible, therefore, that a similar mechanism occurs during the thermal oxidation of niobium and that crystallization of the amorphous oxide, rather than oxide formation at the metal/metal oxide interface as postulated by Cathcart *et al.*, is the main cause of the stresses which result in discontinuities in the oxide and a linear growth law.

Acknowledgments are made to the U.K. Atomic Energy Authority (Development and Engineering Group, Springfield) for sponsoring this research.

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RADIATION CHEMISTRY

Role of Ferrous Hydride in the Oxidation of Ferrous Ion by Hydrogen Atoms

THE oxidation of ferrous ion by atomic hydrogen was recently postulated to proceed by hydride ion formation[1]:

$$Fe^{2+} + H \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} FeH^{2+} \qquad (1)$$

$$FeH^{2+} + H^+ \xrightarrow{k_2} Fe^{3+} + H_2 \qquad (2)$$

Recently the work of Dainton and Peterson[2] demonstrated the use of nitrous oxide for discrimination between various forms of hydrogen atoms (or their analogues) in γ-irradiated aqueous solutions. This technique may be applied in the establishment of the oxidation mechanism of ferrous ion by hydrogen atoms.

In the *p*H region up to 2 the radiation-chemical oxidation of ferrous ion solutions containing nitrous oxide by H atoms will proceed by (1) and (2) or alternatively by:

$$H + N_2O \xrightarrow{k_3} N_2 + OH \text{ (or } N_2OH) \qquad (3)$$

$$OH + Fe^{2+} \rightarrow Fe^{3+} + OH^- \qquad (4)$$

This scheme leads to the following results:

$$\text{(I)} \qquad G(N_2) = \frac{G_H}{1 + \dfrac{k_1\beta[Fe^{2+}]}{k_3[N_2O]}}$$

$$\text{(II)} \quad G(H_2) = G_{H_2} + \frac{G_H}{1 + \dfrac{k_3[N_2O]}{k_1\beta[Fe^{2+}]}}$$

where :

$$\beta = \frac{[H^+]}{(k_{-1}/k_2) + [H^+]}$$

and hence :

$$\text{(III)} \quad \frac{G(N_2)}{G(H_2) - G_{H_2}} = \frac{k_3[N_2O]}{k_1[Fe^{2+}]}\left(\frac{k_{-1}}{k_2}\right)\frac{1}{[H^+]} + \frac{k_3[N_2O]}{k_1[Fe^{2+}]}$$

The linear plot (Fig. 1) is obtained in good agreement with equation III. From the ratio of the slope to intercept we obtain $(k_{-1}/k_2) = 0{\cdot}05$ mole litre^{-1}. These results cannot be readily reconciled with any alternative mechanism previously proposed for this reaction :

$$(1{\cdot}1) \quad Fe^{2+}H_2O + H \rightarrow Fe^{3+}OH^- + H_2$$
$$(1{\cdot}2) \quad Fe^{2+} + H + H^+ \rightarrow Fe^{3+} + H_2$$
$$(1{\cdot}3) \quad H + H^+ \rightleftarrows H_2^+$$
$$(2{\cdot}3) \quad Fe^{2+} + H_2^+ \rightarrow Fe^{3+} + H_2$$

Mechanism (1·1) is not consistent with the dependence on pH of the Gs ratio, while according to the triple collision or the oxidation mechanism involving H_2^+ the intercept in Fig. 1 should be zero.

The oxidation of the ferrous ion by hydrogen atoms externally generated in an electrode-less discharge was recently re-investigated in our laboratory[3] over a wide region of H^+ and Fe^{2+} ions concentration. These results yield the value of k_{-1}/k_2 in the region of 0·05–0·02 mole litre^{-1}, in good agreement with the radiation-chemical results.

This ratio of rate constants is consistent with the pH independence of the relative rates of competing reactions of Fe^{2+} and methanol for hydrogen atoms[4]. However, the investigation of the competition between Fe^{2+} and oxygen[5] requires that k_{-1}/k_2 should be of the order of 0·01.

These results indicate the identity of hydrogen atoms produced by ionizing radiation at low pH and atomic hydrogen externally generated. From Fig. 1 we obtain $k_1/k_3 = 60$ and the application of the value of k_1 independently obtained[1,3] leads to $k_3 \sim 10^3 - 10^4$ litre mole^{-1} sec.$^{-1}$. Thus the interaction of hydrogen atoms as such with nitrous oxide is a relatively slow process, while at pH above 3, efficient decomposition occurs[2]. This behaviour is analogous to that of hydrogen peroxide in neutral[6] and acid[7] solutions. It appears that the hydrogen atom precursor in neutral solutions is the solvated electron, while the 'acid form' is the genuine hydrogen atom. The assumption that the acid form of atomic hydrogen involves only H_2^+ is in disagreement with the slowness of its formation[8]. This species is of importance only in acid solutions where no alternative efficient scavenging of hydrogen atoms occurs, as in the oxidation of I^- by hydrogen atoms[1,8].

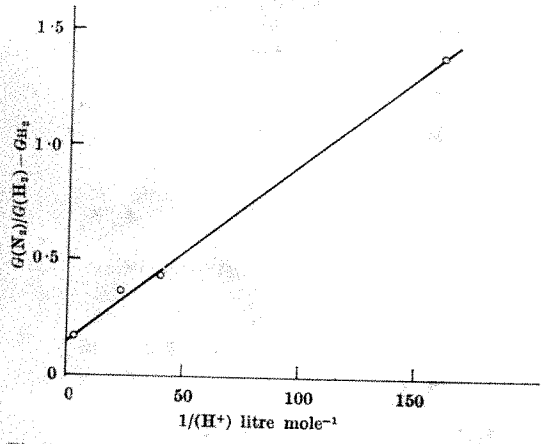

Fig. 1. Plot of the experimental results (ref. 2) for the radiation-chemical oxidation of 10^{-3} M ferrous sulphate solutions containing 0·01 M nitrous oxide

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Detection of Photochemical Oxidation of Sulphur Dioxide by Condensation Nuclei Techniques

THE purpose of the tests reported in this communication was to prove that condensation nuclei techniques could be used in a qualitative way in the determination of the predominating reaction. Since quantitative performance depends on controlling several variables, proof that qualitative determinations were possible was needed to justify further work. Since sulphuric acid particles have been found to act readily as condensation nuclei, the manner of their formation from sulphur dioxide in the atmosphere was chosen as the subject of the investigation.

Several investigations have been made of the conversion of sulphur dioxide in the air to form sulphuric acid ; for example, those of Blacet[1] and of Gerhard and Johnstone[2]. They indicate that oxidation of the sulphur dioxide by ozone is insignificant compared to the action initiated by the absorption of the radiation by the sulphur dioxide molecule. The molecule then becomes activated. The series consists of the following reactions :

$$SO_2 \rightarrow SO^*_2 \quad (1)$$
$$SO^*_2 + O_2 \rightarrow SO_4 \quad (2)$$
$$SO_4 + O_2 \rightarrow SO_3 + O_3 \quad (3)$$
$$SO_3 + H_2O \rightarrow H_2SO_4 \quad (4)$$

They showed that reaction (5) is of minor importance.

$$SO_2 + O_3 \rightarrow SO_3 + O_2 \quad (5)$$

As an example they pointed out that the addition of nitrogen dioxide, which produces ozone catalytically, did not measurably change the rate of production of sulphuric acid, whereas the rate at which sulphuric acid was produced was directly proportional to the amount of sulphur dioxide present.

The tests made here confirm their results. The production of sulphuric acid was detected by a condensation nucleus detector[3]. It has been found that the condensation nucleus detector is highly sensitive to the presence of sulphuric acid particles in

the air, a sensitivity in some cases better than one part in 10^{12}. However, because several variables affect performance, it was only possible to establish a threshold sensitivity. Some of these variables are the length of time the gas is irradiated by the light, the amount of time that the nucleogenic molecules have to coagulate, and the presence of water vapour to aid in the coagulation process.

Two different arrangements of the apparatus were made to determine what process might predominate. They were designed so that if ozone were the predominant factor in the conversion, the first arrangement would be the more sensitive, whereas if sulphur dioxide irradiation was the predominant factor, the second arrangement would be the more sensitive. In the first arrangement the air was irradiated by the ultra-violet while the sulphur dioxide that was mixed with it was not irradiated. When this procedure was followed no condensation nuclei were produced for several minutes. Those occurring at this time are believed to be due to backward diffusion from the reactor volume of sulphur dioxide into the irradiator, due in part to the pulsating flow of the condensation nuclei detector.

In the second arrangement, the irradiation tube was thoroughly purged with sulphur dioxide so that no air would be irradiated. With the light off, the mixture of sulphur dioxide and air did not produce condensation nuclei. When the irradiator was turned on, the condensation nuclei meter became saturated as soon as the irradiated sulphur dioxide had a chance to pass through the reactor volume to the detector. Due to the extreme sensitivity, it was impossible to introduce such a small amount of irradiated gas that the detector did not become saturated.

Indications are that the life-time of the irradiated sulphur dioxide is quite long. Saturated response was still obtained 30 hr. after irradiation. Evidence that the irradiated sulphur dioxide gas might have been adsorbed by the glass tubing was obtained. It was necessary to purge the tubing for several hours before there was no indication of release of irradiated gas into the condensation nuclei detector. Back diffusion of the irradiated gas into the lecture bottle used as a source of gas necessitated a change to a fresh bottle after a few experiments had been performed.

The irradiator consisted of a special mercury vapour lamp in a quartz tube parallel to another quartz tube through which the air or gas sample could pass. This allows the ozone-producing 1849 Å. radiation to reach the air in the sample tube, as well as passing those lines responsible for absorption in sulphur dioxide.

This experiment shows that it is possible to use the condensation nucleus technique in making analytical studies of reactions in the atmosphere. It has corroborated results made by more elaborate analysis.

I am grateful to Mrs. J. H. Winn for technical assistance.

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Rapid Analysis of Erbium by Neutron Activation followed by γ-Ray Spectrometry

IT is known that when natural erbium is irradiated with neutrons, erbium-167*m* (2·5 sec.) is formed[1].

In the present work, a sample (10^{-3} gm.–1 gm., sealed in a polyethylene capsule) is placed in the nuclear reactor *JRR*–1 for 3 sec. to be irradiated with neutrons at a flux of 4×10^{10} neutrons per cm.^{2}/sec. (when operated at 5-kW. level), cooled for 5 sec., counted for 3 sec., again cooled for 2 sec. and counted for 3 sec. This is done by manual operation. The counting apparatus used is a 256-channel pulse height analyser attached to a 2-in. thick sodium iodide crystal.

In the resultant gamma spectrum the height of photopeak due to 0·208-MeV. gamma-ray of erbium-167*m* is measured.

The relation between photopeak height and the amount of erbium has been obtained by use of standards which involve erbium in various amounts ranging from 0·01 to 1 mgm.

The coefficient of variation of single analyses has been obtained by use of seven standard samples, each of which includes 156 μgm. of erbium. The coefficient estimated from seven values is 9·9 per cent, when the average photopeak height is 116 counts per channel and the average area of the peak is $1 \cdot 9 \times 10^3$ counts. Most of the variation seems to originate from error in time measurement, especially for the beginning of irradiation.

Results of analyses are shown in Tables 1 and 2.

Table 1. RESULTS OF ANALYSES FOR SYNTHETIC SAMPLES* MADE OF RARE EARTHS

Sample	Amount of rare earths except erbium (mgm.)	Erbium added (μgm.)	Erbium found (μgm.)	Recovery (per cent)
A	0·39	94	94	101
B	1·95	156	164	105
			124	80
C†	1·95	44	28	64
D	1·95	18·7	19·5	104
E	1·95	8·7	9·0	103

* Rare earth elements, except erbium, were mixed in the ratio of natural mixtures (ref. 1).
† The ratio of erbium to other rare earths is equal to that in the natural mixtures.

Table 2. RESULTS OF ANALYSES FOR SAMPLES TO WHICH NO ERBIUM WAS ADDED

Sample	Amount of sample (mgm.)	Erbium found (p.p.m.)
A (Monazite, Malay)	4·57	$3 \cdot 5 \times 10^3$
B (Orthite, Korea)	42·4	$< 9 \times 10^1$
C (Soil, dried)	290	$< 3 \cdot 8 \times 10^1$
D (Vegetable, dried)	1,291	$< 4 \cdot 0 \times 10^0$
E (Holmium oxide)	14·2	$< 3 \cdot 0 \times 10^2$

It is hoped to publish a full account of this work in the *Nippon Kagaku Zasshi*.

I am indebted to Prof. Shoji Makishima for helpful suggestion, to Dr. Toshio Nakai for use of laboratory facilities, and to Mr. Muneo Handa for helpful assistance.

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CHEMISTRY

Formation of Vibrationally Excited Carbon Monosulphide and Sulphur by the Flash Photolysis of Carbon Disulphide

It has recently been shown[1] that a measurable over-population of the excited vibrational levels of a diatomic molecule can be achieved by subjecting it to a high-intensity flash of ultra-violet light in the presence of a high pressure of inert gas, which maintains isothermal conditions. With nitric oxide, electronic excitation :

$$NO.X^2\Pi + h\nu \rightarrow NO.A^2\Sigma^+$$

was followed either by fluorescence or quenching, and by both mechanisms, molecules were produced in the ground electronic states with vibrational energy in excess of the zero point in high quantum yield. The excitation was made to occur without chemical reaction. These phenomena will be of considerable value in the study of energy transfer.

We describe here an extension of the same principle and method to the vibrational excitation of a transient species, produced by photochemical dissociation of a stable molecule. Electronic excitation of the transient by secondary absorption of light ultimately results in the formation of vibrationally excited ground electronic state molecules.

We have found that the carbon monosulphide molecule, produced by flash photolysis of carbon disulphide, is a suitable molecule for a preliminary search for this effect, since it is long lived and has a high absorption coefficient. The main system of carbon monosulphide ($A^1\Pi - X^1\Sigma^+$) (refs. 2, 3, 4) was first observed in absorption by Kondratiev[5] and later by Porter[6], who showed that the $C^1\Sigma - B^1\Sigma$ system also occurs in absorption and thereby identified the $B^1\Sigma$ state with the $X^1\Sigma^+$ ground-state. Our re-investigation of the flash photolysis of carbon disulphide, using a medium quartz spectrograph (Hilger *E* 498), has revealed four important new features.

(1) The carbon monosulphide molecules can be observed in the ground-state with up to at least four vibrational quanta, and the simultaneous cascading of these vibrationally excited molecules down to the level $v'' = 0$ can be followed by kinetic spectroscopy. An example of this is illustrated by Fig. 1, where the charge composition was 0·5 mm. carbon disulphide with 750 mm. of argon, 2,000 joules energy ; bands of carbon monosulphide with v'' up to 3 are marked below the diagram. Similar results were obtained using nitrogen as inert gas. The larger the value of v'', the faster is the rate of decay. It was demonstrated that the vibrational energy was out of thermal equilibrium, by carrying out similar experiments using various pressures of carbon dioxide as inert gas, in which case the absorption spectra of carbon monosulphide molecules with $v'' > 0$ were not observed. If the production of vibrationally excited molecules had been due to an increase of temperature, the effect would have been similar to any inert gas, provided the heat capacity of the system was kept constant. The vibrational energy is probably transferred rapidly to carbon dioxide if it is used as inert gas. Similar proof that the vibration energy is out of equilibrium was obtained by including butene-1 in the carbon disulphide/argon mixtures, which at quite low partial pressures (1 mm.) reduced markedly the concentration of $CS.X^1\Sigma^+(v > 0)$, and greatly increased their rate of decay. The *Q* heads of the main system of carbon monosulphide are suitable for quantitative measurement by plate photometry, and the change with time of the vibrational distribution is being investigated. Preliminary measurements show that the rate of production of $CS.X^1\Sigma^+(v > 0)$ depends roughly on the square of the flash energy, and it may be concluded that the mechanism of vibrational excitation is similar to that referred to above for nitric oxide. The concentration of carbon monosulphide is proportional to the flash energy and the rate of vibrational excitation by secondary absorption of light is proportional to the flash energy, to give an overall square dependence.

Also shown in Fig. 1 are the formation and decay of part of the $v'' = 0$ progression of sulphur. In experiments where even the smallest trace of oxygen was present, the spectrum assigned by Jones[7] to sulphur monoxide (S_2O_2) in the wave-length region 2700 Å.–3300 Å. was observed very strongly in absorption.

(2) The sulphur vapour spectrum ($B^3\Sigma_u^- \leftarrow X^3\Sigma_g^-$) in the region 2900 Å.–3700 Å., arising from reactions of sulphur atoms produced in the primary step, showed that a fraction of these molecules are also produced with excess vibrational energy ; transitions were observed corresponding to v'' up to at least 7. Polymerization of the sulphur occurred rapidly, causing a fast decay of molecules with all v'' values. The fast decay of sulphur relative to carbon monosulphide was reported by Porter[6].

(3) In addition to the two known systems of carbon monosulphide, some new bands, probably of carbon monosulphide, were observed in absorption, an apparently single-headed band being particularly strong at 2589·04 Å. (air), shaded to the red, which may occur from a transition from the zeroth vibra-

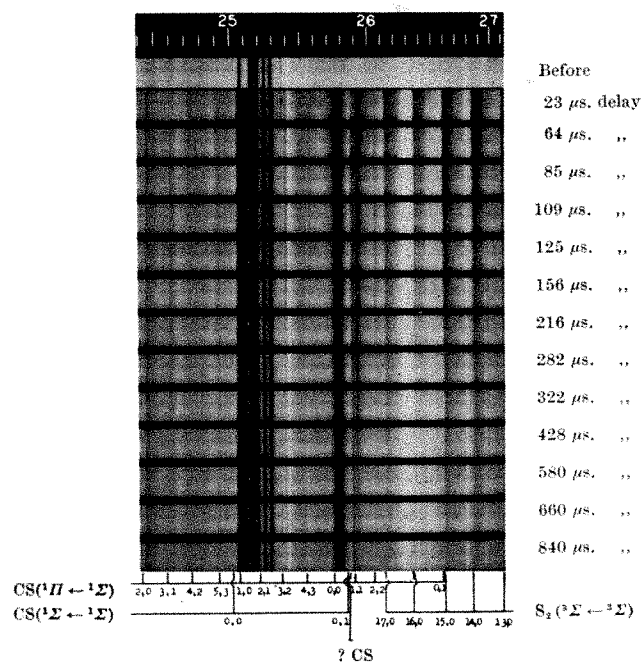

Fig. 1. Formation and decay of vibrationally excited carbon monosulphide by the flash photolysis of carbon disulphide. 0·5 mm. carbon disulphide with 750 mm. argon. 2,000 joules

tional level of the $X^1\Sigma^+$ state. (An alternative explanation is that the new bands are due to an impurity which is formed with, and decays with, carbon monosulphide. However, we were unable to relate them to known spectra which might arise from contamination of carbon disulphide.)

(4) With low pressures of carbon disulphide, $< 0 \cdot 05$ mm., the fluorescent spectrum of carbon monosulphide was excited with such intensity by the photolytic flash that the $v' = 0$, 1 and 2 progressions could be recorded on Ilford *HP*3 plate from one exposure with a slit width of 0·01 mm. The band at 2589·04 Å. referred to under (3) occurred only very weakly in emission. At the higher pressures of carbon disulphide that were required to produce a measurable over-population of the vibrational levels of carbon monosulphide, the fluorescence was completely quenched.

Thus we summarize the mechanism of vibrational excitation of carbon monosulphide as follows:

$$CS_2 + h\nu \rightarrow CS(?) + S(?)$$
$$CS(?) \rightarrow CS.X^1\Sigma^+(v = 0)$$
$$CS.X^1\Sigma^+(v = 0) + h\nu \rightarrow CS.A^1\Pi\,(v = 0 \text{ and } 1)$$
$$CS.A^1\Pi\,(v=0 \text{ and } 1) + M \rightarrow \rightarrow CS.X^1\Sigma^+(v = n) + M$$

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Influence of Moisture on the Spontaneous Heating of Coal

RESEARCH into the spontaneous heating of coal has been concerned in the past with three well-defined problems. These are measurements of rates of oxidation of coal, measurements of heat produced by oxidation and thirdly the establishment and solution of differential equations describing rises in temperature in oxidizing coal. Recently, measurements of the heat of oxidation of coal in air of controlled humidity have been reported and also heats of desorption and adsorption of water vapour[1,2].

In these experiments, sub-bituminous coals (Table 1) always showed a greater rate of loss of heat by evaporation of moisture in a dry air stream than their rate of heat generation by oxidation. This effect is illustrated in Fig. 1, which compares heat produced by oxidation of 4 gm. of coal with loss of heat by drying the same coal in a stream of dry nitrogen of 10 ml./min.

As a result of these experiments it has recently been pointed out that transfer of heat by evaporation of moisture can be of over-riding importance in spontaneous heatings although this factor has previously been neglected[3]. For example, the linear transfer of

Table 1. TYPICAL ANALYSIS OF SUB-BITUMINOUS COAL, OHAI, SOUTHLAND

As received basis (per cent)		By ash-free and sulphur-free basis (per cent)	
Moisture	17	Carbon	75·0
Ash	5	Hydrogen	5·4
Volatile matter	37	Nitrogen	1·1
Fixed carbon	41	Oxygen	18·5

Gross calorific value, 10,000 B.T.U.
Sulphur 0·5 per cent

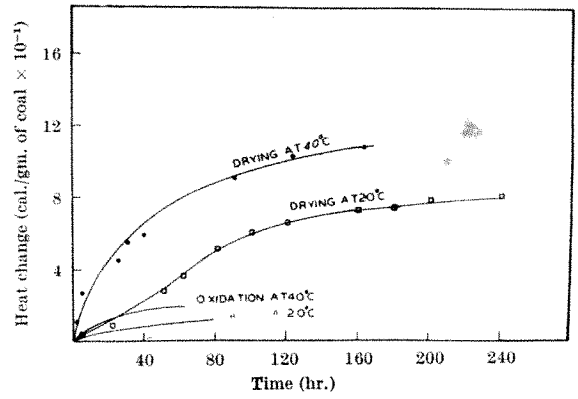

Fig. 1

heat by conduction across a temperature gradient in crushed coal is about 3×10^{-4} cal./sec./cm.^{2}. If saturated air travels across this gradient and remains saturated but rises in temperature by 1 deg. C., then the increase in heat content of the air is 1×10^{-2} cal./ml. of air and a flow as low as 0·03 ml./sec. across 1 sq. cm. can be responsible for transfer of heat equal to that caused by conduction. Observations of spontaneous heating of coal heaps in New Zealand mines confirm that air travelling through the heaps does remain saturated, though as yet rates of air flow have not been measured.

These results have led to an investigation of the behaviour of sub-bituminous coal the moisture of which has been removed in a vacuum of 0·05 mm. mercury, at 105° C. The coal was crushed to the sizes shown in Table 2 and evacuated in less than 5 min. to minimize oxidation.

Table 2. SIZE ANALYSIS OF COAL USED IN SPONTANEOUS HEATING LABORATORY EXPERIMENTS

+ 1/10 in.	B.S.S.	19 per cent
− 1/10 in. + 60 mesh	B.S.S.	68 per cent
− 60 mesh	B.S.S.	13 per cent
		100 per cent

It has been found that 3 kgm. of coal treated in this way will fire spontaneously in 30 min. from a temperature of 22° C. when oxygen saturated with moisture at this temperature is passed through it at 1 litre/min. The coal is contained in a light aluminium foil cylinder, 12 cm. in diameter and 24 cm. high, with an open top. Air or oxygen enters the coal at a central point 2 cm. from the bottom of the cylinder through a 3-mm. diameter glass tube pushed through the coal from its top surface. Saturated air at 1 litre/min. caused ignition in 12 hr. while dry oxygen ignited the coal in 12 hr. from a temperature of 18° C.

Besides providing a striking demonstration of the importance of humidity in spontaneous heating, this experimental technique allows the spontaneous heating of coals to be studied in the laboratory under conditions of heat transfer resembling those found in practice.

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Fractionation of Polystyrene by Gel Filtration

In a recent paper[1], Porath and Flodin have described a simple and rapid method for the fractionation of water-soluble substances. In this method, which they call gel filtration, aqueous solutions of the substances are applied to the top of a column containing swollen insoluble grains of cross-linked dextrans and are eluted with water; fractions are collected from the bottom of the column in order of decreasing molecular weight. Porath and Flodin ascribe this phenomenon to a form of molecular sieving, the efficiency of which depends on the mesh size of the swollen cross-linked beads. For example, small molecules which penetrate the gel particles will be retarded, while large molecules, which are completely excluded from the gel phase, will migrate without retention in the interstitial fluid.

This communication reports some preliminary experiments in which this technique has been applied to a non-aqueous system, the fractionation of a sample of polystyrene in benzene solution.

Since polystyrene is soluble in non-aqueous solvents such as benzene it is necessary to use substances which swell in these solvents for packing the column. Insoluble cross-linked polystyrene (*PSX*) beads were used, since it is comparatively easy to prepare such beads with different degrees of swelling (for example, by using various concentrations of the cross-linking agent, divinyl benzene) and thus gels with different mesh sizes. The beads were prepared by suspension polymerization[2] and the small quantities of soluble polymer, which these beads contain, were removed by packing a column with swollen beads and eluting with benzene until no further polymer could be detected in the eluant.

A sample of polystyrene, having a wide distribution of molecular weights[3], was fractionated by a typical chromatographic elution technique using *PSX* beads of different degrees of swelling (measured by observing the swollen volume of a known weight of beads in the presence of excess benzene). The fractions were recovered by freeze-drying the benzene solutions at the water pump followed by drying to constant weight at 60° C. and were characterized by measuring the specific viscosity ($\eta_{sp.}$) at one concentration (usually 0·4 gm./100 ml.) in toluene at 30° C.

In Fig. 1 the values of $\eta_{sp.}/c.$ are plotted against the cumulative weight together with two reference standards: (*a*) the horizontal line, which is $\eta_{sp.}/c.$ for the whole polymer and represents no fractionation; (*b*) a plot of the results obtained from a conventional fractionation using the solvent volatilization method[3].

It will be seen that whereas *PSX* beads which swell only 2·2 times give practically no fractionation, with beads having higher degrees of swelling fractionation appears in the lower molecular weight region. In the case of those that swell 51 times, the resolution in this region approaches that of the solvent volatilization method. However, the degree of fractionation in the high molecular weight region is much less pronounced, indicating that even with these beads the degree of cross-linking is not loose enough to allow the larger molecules to penetrate the network.

These preliminary experiments have established, therefore, that high polymeric materials, such as polystyrene, can be fractionated by this technique, and it is thought that, by preparing *PSX* beads

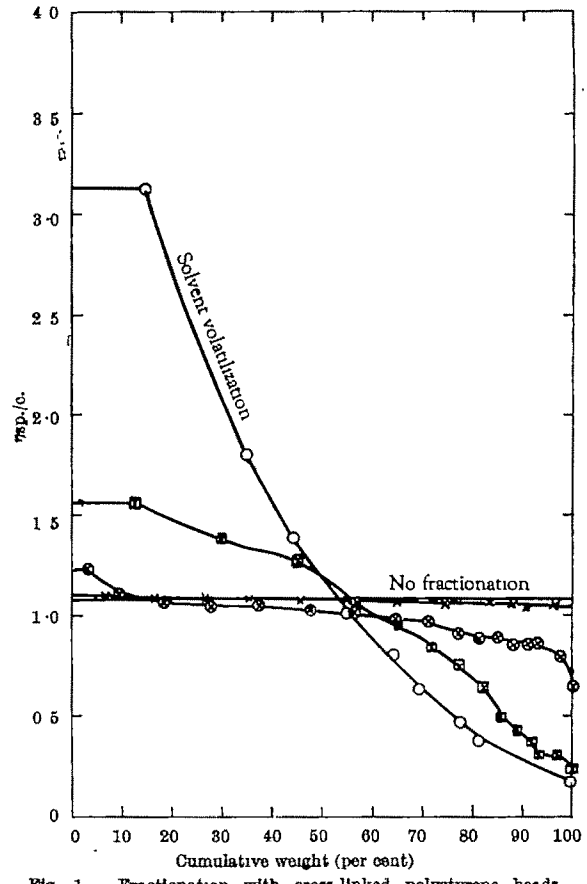

Fig. 1. Fractionation with cross-linked polystyrene beads. ×, *PSX* 524, degree of swelling 2·2, ⊗, *PSX* 509, degree of swelling 13; □, *PSX/S* 2, degree of swelling 51

having a higher degree of swelling and/or by modifying the column technique, the efficiency can be improved to approach that of the conventional fractionation methods. The possibility arises, therefore, of developing a simple method of polymer fractionation in which the fractions can be collected automatically and which is economical in the use of solvents, since most of the benzene can be recovered during the freeze-drying.

A further possible development could be in the separation of very low molecular weight materials (cf. Porath and Flodin, who cite the separation of glucose from dextran fractions of $\overline{M}_n$ 1,000 and 20,000), since although practically no fractionation took place with the *PSX* beads which swell 2·2 times, a little did, in fact, occur, suggesting that the smallest polystyrene molecules enter the *PSX* beads.

I wish to thank Miss S. A. Monksfield and Miss H. M. Sankey for assistance with the experimental work and Mr. D. Reichenberg for supplying the *PSX* beads 509 and 524, and also for his advice on the column procedure. This work is published by permission of the Director of the National Chemical Laboratory.

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Nitric Oxide Reduction in Methyl Nitrite Pyrolysis and the Transition from Isothermal Decomposition to Adiabatic Flame

WHEN the lower alkyl nitrite and nitrate esters[1,2] ($RONO$ and $RONO_2$) decompose isothermally, they do so by initial fission of the O–N bond yielding an alkoxyl radical $RO\cdot$ and the appropriate oxide of nitrogen. This step commonly controls the rate of isothermal decomposition; the subsequent reactions of the initial products[2] determine the stoichiometry. It has generally been assumed that the greater extent of decomposition of nitrates reflects the superior reactivity of nitrogen dioxide, while in the nitrites[1] isothermal decomposition scarcely involves nitric oxide at all:

$$CH_3ONO(g) \rightarrow NO(g) + 0{\cdot}5\ CH_3OH(g) + 0{\cdot}5\ CH_2O(g) \quad \Delta H\ c.\ \text{zero} \qquad (1)$$

Views on the inertness of nitric oxide in the methyl nitrite system, first challenged by Carter and Travers[3], had to be further revised when the methyl nitrite self-decomposition flame was discovered[4] in 1955; this flame depends on nitric oxide reduction for its existence.

Two questions arise: (1) How are the adiabatic flame and the isothermal decomposition related?, and (2) How is the transition from decomposition to exothermic flame accomplished?, for if normal decomposition does not proceed beyond nitric oxide and is genuinely thermoneutral, this transition can be induced only by external agencies. The investigation of these questions has thrown new light on the true course of isothermal decomposition.

The adiabatic flame. It has been found that the overall stoichiometry of the decomposition flame lies between the extremes predicted[4]. The products are basically the same as those reported earlier[5,6] and reaction may be written:

$$CH_3ONO \rightarrow 0{\cdot}72\ CO + 0{\cdot}56\ H_2 + 0{\cdot}54\ NO + 0{\cdot}42\ H_2O + 0{\cdot}14\ N_2 + 0{\cdot}13\ CH_3OH + 0{\cdot}10\ CH_2O + 0{\cdot}06\ NH_3 + 0{\cdot}05\ N_2O + 0{\cdot}02\ \text{'}CH_2NOH\text{'} + 0{\cdot}02\ CH_4 + 0{\cdot}01\ CO_2 \qquad (2)$$

The overall change in enthalpy thus resulting in the flame is $-27{\cdot}0$ kcal.mole^{-1} and this corresponds to a theoretical adiabatic flame temperature of 1,110° C., which agrees very closely with the experimental[5,7] value of 1,100° C.

Thermal decomposition and flame. Thermal decomposition of the pure vapour at 1 atm. was first studied in a flow system to simulate conditions of the stationary methyl nitrite flame. Even at 250° C., nitric oxide is reduced and water is formed. Reaction is correspondingly exothermic and thermocouple measurements show a 50 deg. rise in temperature. Thus a path is open by which methyl nitrite pyrolysis may become self-supporting; its potentialities are enhanced by the flexibility of a complex reaction mechanism; as the temperature rises so the stoichiometry alters and more heat is released. Equation 3 adequately represents the decomposition products up to about 500° C. where the self-heating is even more marked.

$$CH_3ONO \rightarrow 0{\cdot}76\ NO + 0{\cdot}46\ CH_2O + 0{\cdot}24\ CH_3OH + 0{\cdot}19\ H_2O + 0{\cdot}12\ N_2O + \text{some polymeric product} \quad \Delta H = c.\ -7\ \text{kcal.mole}^{-1} \qquad (3)$$

In the neighbourhood of 590° C. the change in stoichiometry is particularly rapid, and thereafter differs very little from that of the flame. By 700° C., a degree of self-heating of nearly 300° C. is achieved; equation 4 summarizes the course of reaction:

$$CH_3ONO \rightarrow 0{\cdot}536\ NO + 0{\cdot}10\ CH_2O + 0{\cdot}11\ CH_3OH + 0{\cdot}42\ H_2O + 0{\cdot}75\ CO + 0{\cdot}04\ N_2O + 0{\cdot}151\ N_2 + 0{\cdot}06\ NH_3 + 0{\cdot}01\ CO_2 + 0{\cdot}01\ CH_4 + 0{\cdot}02\ \text{'}CH_2NOH\text{'} \quad \Delta H = c.\ -26\ \text{kcal.mole}^{-1}. \qquad (4)$$

Isothermal decomposition. To establish whether the nitric oxide reduction discovered previously is merely a consequence of self-heating, the low-temperature pyrolysis of methyl nitrite has been examined under conditions of constant temperature.

Decompositions were carried out in aged 'Pyrex' reaction vessels using static systems (178–310° C.) and flow systems (235–315° C.). Velocity constants and the mean activation energy (36,400 cal.mole^{-1}) agree with old measurements[1]. Nitrous oxide is always formed, the yield never dropping far from 0·13 mole N_2O per mole nitrite decomposed. This figure is independent of temperature (from 235 to 315°), of reactant partial pressure (from 10 to 60 mm. mercury), and of percentage decomposition (from 7·7 to 100). Thus, nitrous oxide is a normal product of isothermal methyl nitrite decomposition:

$$CH_3ONO \rightarrow 0{\cdot}74\ NO + 0{\cdot}13\ N_2O + 0{\cdot}66\ CH_2O + 0{\cdot}30\ CH_3OH + 0{\cdot}12\ H_2O \qquad (5)$$

The mechanism of nitrous oxide formation proposed by Levy[8] in work on ethyl nitrite seems attractive here. Nitric oxide abstracts hydrogen from free methoxyl and the nitroxyl formed is the source of nitrous oxide. Added nitric oxide (molecular ratio $NO : CH_3ONO$ is 12 : 1) doubles the nitrous oxide yield without sensibly affecting the rate of reaction:

$$CH_3ONO \rightarrow CH_3O\cdot + NO;$$
$$CH_3O + NO \rightarrow CH_2O + HNO;$$
$$2\ HNO \rightarrow H_2O + N_2O$$

At low temperatures, nitrogen is never found. It arises only at elevated temperatures, where it may be a product of secondary reactions undergone by nitrous oxide.

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Esterification of Fatty Acids with Glycerol

SINCE Berthelot's classical work on the esterification of fatty acids with glycerol, in the last century, considerable work has been done on the topic[1–4]. The presence of 2-monoglyceride in technical products of glycerolysis has been reported recently[5]; this was not noticed by Feuge *et al.*[4] or by Becker *et al.*[6] on the ground that 2-monoglyceride is prone to be quickly isomerized to the more stable 1-monoglyceride at the high temperature of the reaction. The present

Table 1. ESTERIFICATION OF FATTY ACIDS BY GLYCEROL

Temperature, 180 ± 1° C., 0·1 per cent catalyst; relation in nitrogen atmosphere

Time (min.)	Lauric		Myristic		Palmitic		Stearic		Oleic		Linoleic	
	1-MG*	2-MG	1-MG	2-MG	1-MG	2-MG	1-MG	2-MG	1-MG	2-MG	1-MG	2-MG
40	39 53	7 04	55 1	4 80	43·24	4·86	42 50	6 89	57·45	0 33	70·39	2 21
60	44 50	5 85	55 16	4 64	47 5	8 22	45 08	9 68	58 05	0 15	60 58	8 11
120	39 66	5 06	46 29	3 72	43 66	11·41	43 01	6 78	47 28	0 92	49 14	6 41
180	35 97	3 92	40 84	nil	38 88	5 94	36 46	9 84	39 18	1 97	44 00	1·01
225	32 51	5 08	33 37	nil	35·23	6 14	33 07	9 09	34 16	0 04	33 94	1 08

* MG represents monoglyceride.

work on the esterification of lauric, myristic, palmitic, stearic, oleic and linoleic acids with glycerol was undertaken to clarify the question of the formation of 2-monoglyceride in the esterification reaction mixture.

Fatty acid, purified by low-temperature fractionation, was made to react with an equimolar quantity of glycerol at a temperature of 180 ± 1° C., in an inert atmosphere of nitrogen, in the presence of potassium carbonate (0·1 per cent on the weight of fatty acid) as catalyst. Stirring was continued throughout the reaction.

Samples of 1–2 gm. were drawn at intervals of 40, 60, 120, 180 and 225 min. and these were at once treated with 2 drops of 85 per cent phosphoric acid which 'killed' the potash soap catalyst. The mass was dissolved in excess ether and the ethereal extract of the fatty matter washed with cold saturated sodium sulphate solution several times, 5 per cent potassium carbonate solution and finally with water. The washed ethereal solutions were dried overnight with anhydrous sodium sulphate, filtered and evaporated to yield the purified glycerolysed product.

1-Monoglyceride and total monoglyceride content of the samples were determined by Pohle, Mehlenbacher and Cook's method[7], as modified by Handschumaker and Linteris[8], and Martin's perchloric acid isomerization procedure[9] respectively; the difference between total- and 1-monoglyceride content represented the 2-monoglyceride content. In a separate set of samples drawn simultaneously from the esterification mixture, the percentage of free fatty acid was determined. The results are given in terms of the particular fatty acid with which the experiment was performed. Expressing the percentage of free fatty acid in the mixture at a time t as A_t ($A_0 = A_t$, where $t = 0$, A_0 corresponds to 0 5 mole-fraction) and denoting $\frac{A_t}{A_0} \times 100$ by B, the decrease in the values of A_t and B with time (as also a plot of log B versus log t) would indicate extent of esterification at any particular time. The observations are noted in Table 1 and Fig. 1.

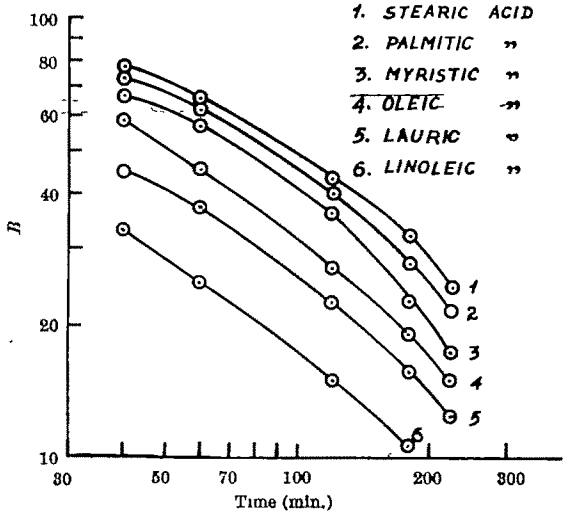

Fig. 1

The results clearly show that 2-monoglyceride constitutes a considerable proportion in the reaction products at various stages. Although it may be true, as suggested by previous workers[4,6], that 2-monoglyceride is prone to complete isomerization to 1-monoglyceride at higher temperature, this certainly does not hold good at or below 180° C. It would, therefore, be erroneous to report 1-monoglyceride as total monoglyceride, especially in esterification or glycerolysis reactions (as has been done in the current literature). Ignoring the presence of even a small amount of 2-monoglyceride would lead to wrong computation of the diglyceride content (the hydroxyl value being contributed not only by 1-monoglyceride and diglyceride but also by 2-monoglyceride); and hence also of the triglyceride content in the product obtained from esterification or glycerolysis reaction.

The rate of decrease of free fatty acid in the mixture indicates that the reactivity of fatty acids is greater with low molecular weight and unsaturated fatty acids. This reactivity is apparent, however, as the entire amount of fatty acid is not in a homogeneous phase with glycerol; low molecular weight and unsaturated fatty acids being relatively more miscible in glycerol[10], these react more quickly than the rest. The results obtained are not in full agreement with the observations of Toyama *et al.*[1], but they agree with those of Bhattacharyya and Hilditch[2].

We are indebted to Sri B. K. Mukherji, of the University College of Science and Technology, University of Calcutta, for his interest in this work.

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BIOCHEMISTRY

A Metabolite of 'Carbromal'

'CARBROMAL' (α-bromo diethylacetyl urea) is in widespread use as a sedative and hypnotic. None of its metabolites has, as yet, been fully characterized.

I recently isolated diethylacetyl urea from the intestine contents of a woman who was taking a proprietary drug containing 'Carbromal' 240 mgm. and 'Bromvaletone' 80 mgm. The method of isolation was that using acid ammonium sulphate, described by Nickolls[1]; 5 mgm. of the ureide crystallized readily from the neutral, ether-soluble fraction. Purification was by sublimation at 10^{-3} mm. at 100° C. It was at first thought that the product was α-ethyl crotonyl carbamate, which was noted as a product of the reaction of sodium hydroxide on 'Carbromal' by Newberry[2]. Both these compounds and their mixture melted within 5 deg. (200–205°); but because of their rapid sublimation these determinations were inadequate. Infra-red spectroscopy clearly differentiated the compound from α-ethyl crotonyl carbamate and from 'Sedormid' (allyl *iso*propyl, acetylurea). As a result of an examination of the spectra of several compounds in the series a specimen of diethylacetyl urea was prepared by hydrogenation of α-ethylcrotonylcarbamate (Dr. S. Trippett). After sublimation its spectrum in 'Nujol' was identical with that of the compound isolated from the intestines (Fig. 1). It seems probable that this is the compound observed by Turner[3].

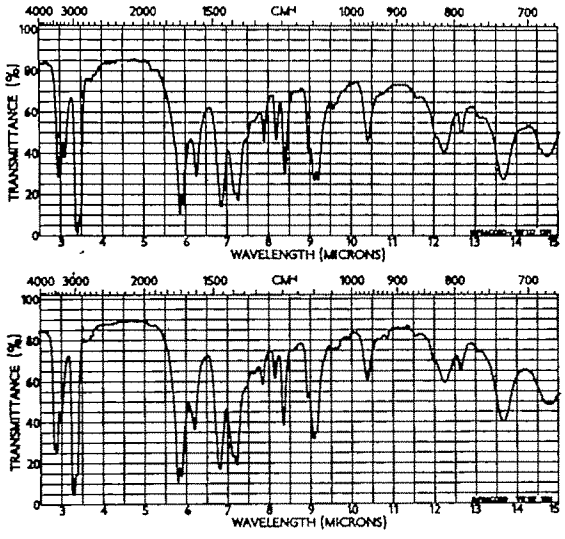

Fig. 1. The top curve shows the spectra of diethyl acetyl urea; the bottom curve is that of the crystals from the intestines

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Synthesis of Nicotinic Acid Nucleotides

NICOTINIC acid nucleotide (5′-phospho-β-D-ribofuranosylpyridinium-3-carboxylate) and its adenylyl derivative, adenine-nicotinic acid dinucleotide, have recently been identified as intermediates in the biosynthesis of pyridine nucleotide coenzymes[1]. These compounds have been found in fungi[2,3], and the mononucleotide has been isolated in small amounts from yeast[4]. Both nucleotides have also been obtained in very low yields by enzymic modification of adenine-nicotinamide dinucleotide (coenzyme I)[2,3,5].

It has now been found that nicotinamide nucleotides, which are commercially available, may be conveniently converted into nicotinic acid nucleotides by treatment with nitrous anhydride. Preliminary work showed that nitrous acid or hydrogen chloride in amyl nitrite deaminates adenine nucleotides to hypoxanthine nucleotides, but does not liberate the amide nitrogen from nicotinamide nucleotides.

β-Nicotinamide nucleotide was suspended in dry acetic acid (10 ml. per millimole) and kept at −10° while an equal volume of nitrous anhydride[6] was condensed in the reaction vessel. The suspension was then kept at 10–15° for 1 hr. After removal of volatile material in a stream of dry air, the reaction products were applied to a column of 'Dowex-1-formate' and the nicotinic acid nucleotide was recovered by elution with formic acid[1]. The nucleotide was identified by electrophoresis, ion-exchange chromatography and paper chromatography, and by spectrophotometry in the presence and absence of cyanide[1,2,4].

When coenzyme I was treated with nitrous anhydride in acetic acid both amide and amine nitrogens were displaced, and hypoxanthine-nicotinic acid dinucleotide was obtained. This dinucleotide was quantitatively hydrolysed to nicotinic acid nucleotide and hypoxanthine nucleotide (inosine-5′-phosphate) by nucleotide pyrophosphatase from potato.

With adenosine triphosphate and magnesium ion at *p*H 7·6 in the presence of highly purified nicotinamide nucleotide-adenylyl transferase (coenzyme I pyrophosphorylase) from pig liver nuclei the nicotinic acid nucleotide was quantitatively converted into its adenylyl derivative. This derivative was likewise identified by the physical methods described above, and further by its conversion into coenzyme I in the presence of glutamine, adenosine triphosphate, magnesium ion and coenzyme I synthetase from pig liver cytoplasm. The coenzyme I was identified by reduction with ethanol and alcohol dehydrogenase from yeast.

Nicotinic acid nucleotide obtained in this way is a competitive inhibitor of enzymic adenylyl transfer from adenosine triphosphate to β-nicotinamide nucleotide, and is evidently identical with the natural coenzyme precursor.

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Proteolysis in Stored Serum and its Possible Significance in Cell Culture

ALMOST all the mammalian cell lines grown in continuous culture require the presence of a small amount of serum protein, usually supplied as whole or dialysed serum. The role of that protein, in an otherwise chemically defined medium[1], is not yet known. It is used to an insignificant degree for the synthesis of cell protein[2]; and although it is reported to be necessary for the adhesion and flattening of the cells on the glass surface[3,4], it is no less essential in suspension cultures. It is here shown that serum protein, presumably because of associated enzymes[5], undergoes proteolysis on storage at 5° C. or during incubation to yield free amino-acids at a rate which may be significant in certain types of experiments. The amino-acids released are themselves not growth-stimulating since they are already supplied in the medium or are formed from glucose and glutamine. However, other breakdown products of the serum protein, or compounds bound to it and released by its degradation, may be the essential growth factors supplied by serum.

Pooled human serum protein was freed of small molecules by two different procedures. Dialysed serum was prepared by dialysis of serum on a rocking dialyser against running water at 5° C. for 24 hr.; sodium chloride was then added to give a concentration of 0·85 per cent. Gel-filtered serum was prepared by the methods developed by Porath and Flodin[6]. A 3·5 cm. × 40 cm. column (400 ml.) of dextran gel ('Sephadex *G*–50') was poured and washed with 500 ml. of 0·85 per cent sodium chloride. 100 ml. of serum was allowed to pass into the column and elution was continued with 0 85 per cent sodium chloride. The first 100 ml. of effluent was discarded. The following 120 ml., which contained all the protein, was collected. Small molecules from the serum did not appear in the effluent until another 80 ml. of effluent (300 ml. total) had passed. The column was washed with an additional 500 ml. of salt solution before being re-used.

The dialysed and gel-filtered serum preparations were sterilized by filtration through sintered-glass filters and stored at −20°, 5°, or 37° C. for various times. The free amino-acids were determined on samples which were deproteinized with picric acid[7] and lyophilized. Portions of the dissolved residue representing 2–4 ml. of serum were analysed on an automatic amino-acid analyser[8].

The results are presented in Table 1. An analysis of the free amino-acids in a pooled sample of fresh whole serum is included for comparison (column 1). It is apparent from these results that dialysed serum undergoes proteolysis at an appreciable rate even when stored at 5° C. (column 2). After 11 days the amino-acid levels in some cases were as high as those found in fresh whole serum, averaging about 30 per cent. Gel-filtered serum was considerably more stable. After 30 days at 5° C. (column 5), the amino-acid concentrations averaged about a third those observed in dialysed serum after 11 days at the same temperature. The higher stability of the gel-filtered serum was even more evident at 37° C. In an experiment employing one sample of pooled serum (columns 3, 4, 6, and 7), the free amino-acid level in dialysed serum after 5 days was more than half that in whole serum, while in gel-filtered serum it averaged only a tenth. After 28 days the amino-acid levels in dialysed serum had increased on average by nearly 60-fold, but less than 4-fold in gel-filtered serum. At −20° C. only negligible increases were observed in serum prepared by either procedure.

Repeat experiments gave essentially the same results as those reported in Table 1 with some variation between individual lots of serum. In some instances the occurrence of other reactions in addition to proteolysis was indicated by the appearance of amino-acids not present in proteins. The concentrations of citrulline, α-aminobutyric acid, and ornithine which were found in stored or incubated serum are listed in Table 1. The presence of other unidentified ninhydrin-reacting compounds was also indicated by the chromatograms.

It is abundantly clear that dialysed serum stored in the refrigerator cannot be considered to be free of amino-acids. The problem is less serious with gel-filtered serum. The reason for the more rapid breakdown of dialysed serum protein is not clear. It may be related to more efficient removal by the gel-filtration procedure of small molecules necessary as co-factors.

In order to examine the rate of proteolysis under cell culture conditions, dialysed and gel-filtered serums were incorporated at the 10 per cent level

Table 1. CONCENTRATION OF FREE AMINO-ACIDS IN SERUM (μM)

Amino-acid	Whole serum	Dialysed serum*			Gel-filtered serum†			10 per cent serum‡ 37°, 3 *d.*	
		5° 11 *d.*	37° 5 *d.*	37° 28 *d.*	5°. 30 *d.*	37° 5 *d.*	37° 28 *d.*	Dialysed	Gel-filtered
Aspartic acid	0 017	0 019	0 045	2·11	0·018	0·004	0 048	0 055	0·005
Threonine	0 156	0 064	0 083	0·24	0 017	0 016	0 059	0·031	0 005
Serine	0·149	0·051	0 132	0·01	0 057	0·031	0 092	0 062	0·010
Glutamic acid	0·076	0·071	0 220	9·43	0 023	0 028	0 109	0·083	0·010
Citrulline	0 034	0 019	0	0·87	0	0	0	0	0
Proline	0·273	0·029	0 080	7 42	0	0 014	0 040	0 029	0
Glycine	0 246	0·063	0·129	4 97	0 027	0·019	0·054	0·064	0 010
Alanine	0·413	0 078	0·256	11·96	0 030	0 038	0 102	0 068	0 019
Cystine	0·053	0	0	2·52	0	0	0	0 010	0·005
α-Aminobutyric acid	0 011	0	0	0·29	0	0	0	0	0
Valine	0 254	0 029	0·088	9·50	0	0 014	0 056	0 023	0·005
Methionine	0 021	0 002	0·029	2 92	0	0 006	0 017	0·010	0
isoLeucine	0 071	0·005	0·022	2·25	0 031	0·007	0 017	0 015	0·005
Leucine	0 132	0·062	0·180	11·66	0 039	0·032	0·108	0·057	0·015
Tyrosine	0 046	0·010	0 036	4·07	0	0·007	0 029	0 015	0
Phenylalanine	0·057	0·029	0·059	7 92	0 018	0·007	0 040	0 038	0
Ornithine	0 111	0 015	0·014	4 97	§	0 014	0·053	0	0
Lysine	0 174	0 048	0·112	15·75	§	0 020	0 078	0 044	0·010
Histidine	0·096	0 024	0 043	0 52	§	0·007	0 023	0·024	0·005
Arginine	0·075	0·088	0 106	0 17	§	0 011	0 023	0·053	0 015

* Dialysed 24 hr. against running water. †, Small molecules removed by filtration through 'Sephadex *G*-50' (ref. 6). ‡ Serum added to a medium (ref. 1), which was complete except for free amino-acids; concentrations calculated for undiluted serum. § Not analysed.

into a medium[1] which was complete except for the essential amino-acids and which was then incubated at 37° C. for 3 days. Free amino-acids appeared at about the same rate as in whole serum. With gel-filtered serum the final amino-acid concentrations were all less than 0 02 m*M* and averaged about 0·005 m*M*, calculated for undiluted serum. Dialysed serum released amino-acids at about six times this level.

In experiments in which the essential amino-acids are added to the medium in concentrations greater than about 0 05 m*M*, the additional amounts released by proteolysis would probably not be significant. At lower levels, however, the free amino-acids contributed by serum protein could have an appreciable effect, particularly in the case of dialysed serum. In one experiment, when cells were grown in a presumably valine-free medium supplemented with 5 per cent dialysed serum and 0·002 m*M* valine labelled with carbon-14, the specific activity of the valine residues in the cell protein was only 23 per cent that of the precursor amino-acid, the rest deriving from the protein (Eagle, H., and Piez, K. A., unpublished work). Similarly, in the case of the nutritionally non-essential amino-acids, which are synthesized by the cell from glucose and glutamine, the contaminating amino-acids derived from serum proteolysis may introduce a large error in isotope labelling experiments.

Although we have analysed only the free amino-acids formed by proteolysis, it is evident that large numbers of various-sized polypeptides must also be formed, and that some of these may be utilized by cells in culture[9]. Work is in progress in an attempt to evaluate this aspect of serum proteolysis. It is possible that such peptides may be an important and perhaps necessary contribution by serum protein, particularly in the light of the demonstration[10] that dialysable substances formed by the action of a dialysed pancreatic extract or crystalline proteolytic enzymes on serum protein can be substituted for the native serum protein in cell growth.

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Distribution of Guanylic Acid Residues in Tobacco Mosaic Virus Nucleic Acid

THE mode of arrangement of purine and pyrimidine nucleotides in tobacco mosaic virus nucleic acid was studied using the actions of pancreatic ribonuclease and micrococcal phosphodiesterase. This work showed that in tobacco mosaic virus nucleic acid the purine nucleotides and pyrimidine nucleotides occur in 'clusters' of two or more and also 'singly' alternating with each other. The extension of these studies to nucleic acids of three viral strains (*TMV*, *HR* and *M*) revealed for the first time significant differences in the arrangement of nucleotides in each of their molecules[1–5]. Additional information on the distribution of guanylic acid residues in tobacco mosaic virus nucleic acid, obtained by the action of an enzyme specific to secondary phosphate esters of guanosine 3′-phosphates, is given in the present communication.

Sato and Egami[6] recently reported the isolation and properties of a ribonuclease, present in taka diastase, which specifically cleaves the secondary phosphate esters of guanosine 3′-phosphates. This important discovery provided a much-desired additional tool for structural studies in ribonucleic acids. This enzyme has been purified in this laboratory using a modified procedure, the details of which will be reported at a later date. My preparations have properties similar to those described by the above investigators. The *p*H optimum in 0·1 *M tris* buffer was found to be at 7·4. When assayed according to the procedure described earlier[7] my preparations were found to contain 6×10^6 units of enzyme per mgm. of protein. This enzyme is specific in that it slowly converts guanosine 2′ : 3′-cyclic phosphate to guanosine 3′-phosphate exclusively. It degrades ribonucleic acid giving rise to monoguanylic acid (guanosine 2′ : 3′-cyclic phosphate, Gp! and guanosine 3′-phosphate, Gp) and oligonucleotides terminated by guanylic acid (Gp! and Gp). From these results it can be concluded that this enzyme cleaves the ribonucleic acid via transphosphorylation giving rise to guanosine 2′ : 3′-cyclic phosphates and oligonucleotides terminated by them and these are slowly converted to guanosine 3′-phosphates. Its mechanism of cleavage via transphosphorylation is reminiscent of that of leaf ribonuclease[8] even though the specificities of the two enzymes are different. This enzyme will be referred to here as taka ribonuclease-I.

The occurrence of polyguanylic acid segments in tobacco mosaic virus nucleic acid was established using the action of taka ribonuclease-I. 2 mgm. of tobacco mosaic virus nucleic acid, prepared according to the heat denaturation procedure[9], was dissolved in 0·4 ml. of 0·2 *M tris* buffer at *p*H 7·4 containing 4×10^{-3} *M* ethylenediamine tetraacetic acid. To this was added 0·1 ml. of taka ribonuclease-I (about 1,000 units, a large excess to ensure complete digestion) and a drop of chloroform to prevent microbial growth. The mixture was incubated at 37° for 18 hr. In the complete digest monoguanylic acid (Gp! and Gp) was found to an extent of 26·9 per cent of total guanylic acid residues in tobacco mosaic virus nucleic acid. This was calculated using the base composition data reported earlier[10]. Since the enzyme is specific to guanosine 3′-phosphate linkages, the minimum requirement for a monoguanylic acid to appear in the digest is the occurrence of at least two guanylic acid residues linked together. From this it can be concluded that about 26·9 per cent of total guanylic acid residues in tobacco mosaic virus nucleic acid occur in 'clusters' of two or more, $Gp(Gp)_n$, where $n = 1$ or more.

The average length of the larger fragments produced by the digestion of tobacco mosaic virus nucleic acid with taka ribonuclease-I was determined as follows: 9·2 mgm. tobacco mosaic virus nucleic acid, prepared according to heat denaturation procedure[9], were dissolved in 1 ml. of 0·04 *M tris* buffer at *p*H 7·4 containing 10^{-3} *M* ethylenediamine tetraacetic acid and to this was added 0·1 ml. of taka ribonuclease-I (10,000 units) and a drop of chloroform. The mixture

was incubated at 37° for 18 hr. At the end of the reaction time, the digest was transferred to an ice-bath and to this was added with mixing cold 50 per cent trichloroacetic acid. The final concentration of this acid in the mixture was 6 per cent. This was held at 0° for 30 min. and centrifuged at 4° for 15 min. at 2,500 r.p.m. The precipitate was washed with 0·1 ml. cold 6 per cent trichloroacetic acid and this was followed by one washing with 0·5 ml. of cold absolute alcohol. The washed precipitate was dissolved in 2 ml. of 0·02 *M* borate buffer at *p*H 8·6. This was then transferred to a dialysis bag and dialysed at 4° C. against 0·02 *M* borate buffer at *p*H 8·6 for 8 hr. with continuous stirring. The purine and pyrimidine composition[11] of the dialysed preparation was found to be as follows: guanine, 1·00; adenine, 2·17; cytosine, 1·34 and uracil, 1·53. The amount of guanylic acid present in the entire dialysed material was about 29·3 per cent of the total guanylic acid residues in tobacco mosaic virus nucleic acid. This preparation is a heterogeneous mixture of several polynucleotides terminated by guanylic acid. From the purine and pyrimidine composition and the specificity of the enzyme used, it can be suggested that they average about six nucleotides in length, $(Xp)_5Gp$ (where *X* is adenosine, cytidine and uridine), and these are all preceded by a guanylic acid residue in the intact tobacco mosaic virus nucleic acid.

In addition to monoguanylic acid in the complete digest of tobacco mosaic virus nucleic acid, three dinucleotides, cytidylyl-guanylic acid, uridylyl-guanylic acid and adenylyl-guanylic acid and several tri-, tetra-, etc., nucleotides terminated by guanylic acid were isolated. Full details of this investigation will be published elsewhere.

I am indebted to Dr. W. M. Stanley for his encouragement and support of this research.

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Note added in proof. Guanylic acid residues in a nucleic acid, in addition to occurring in 'clusters' of two or more, $(Gp)_nGp$, can also occur distributed in two other ways: preceded by pyrimidine nucleotides, cytidylic and uridylic acids, $(Pyp)_nGp$; and preceded by adenylic acid, $(Ap)_nGp$. Evidence for this type of distribution in tobacco mosaic virus nucleic acid was obtained by exhaustively digesting the nucleic acid with both pancreatic ribonuclease and taka ribonuclease-I[12]. About 46·4 per cent and 28·4 per cent of total guanylic acid residues in tobacco mosaic virus nucleic acid were found to occur as $(Pyp)_nGp$ and $(Ap)_nGp$ respectively.

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Biosynthesis of Damascenine in *Nigella damascena* L.

DAMASCENINE is present in the seeds of *Nigella damascena* L. to the extent of about 0·1–0·3 per cent (dry weight). The majority of the alkaloid is present in the testas. The seeds of other *Nigella* species hitherto investigated possess only traces of the base.

In the past few years Tyler[1] as well as Leete, Marion and Spenser[2] have dealt with the physiology and biosynthesis of damascenine. In order to clarify further the problem of the origin of damascenine in the plant we have studied its ontogenesis and its site of formation; experiments involving the feeding of labelled precursors have also been undertaken.

Damascenine was isolated from the plant material in the usual way and characterized by paper chromatography: circular paper-chromatographic technique was employed using Schleicher and Schüll chromatographic paper 2043 *b*, which was impregnated with phosphate buffer (*p*H 8); methanol served as the mobile phase; detection of damascenine (R_F 0·79) was achieved by its characteristic blue fluorescent property under filtered ultra-violet light. While with the help of Dragendorff's reagent (modified after Munier) quantities of more than 30 μgm. of damascenine could be identified on the filter, it required only as low as 1–2 μgm. of the alkaloid to be readily detected under ultra-violet light. Damascenine loses its fluorescing property in acid medium. In order to determine it quantitatively, the base was eluted from the filter with 96 per cent alcohol and with the aid of a reference curve the alcoholic solution was fluorometrically assayed for its damascenine content.

During the course of natural development of the cultivated plants, the damascenine content of different organs of a large number of *Nigella damascena* plants was determined at definite intervals. The seedlings, which were grown in sand, were found to be free from damascenine. This confirms the observations already made by Tyler[1]. In the earlier stages of development a very low damascenine content was found in the roots, stems, leaves and flowers; but this gradually increased with the progressive growth of the plants. Beginning with the ripening of the seeds, an enormous increase of damascenine content was noted, and this attained its maximum when the seeds reached maturity. At this stage of development the following values for damascenine content (dry weight) were determined: seeds 0·15 per cent, leaves 0·013 per cent, stems 0·0001 per cent and roots 0·0002 per cent.

In order to locate the site of damascenine synthesis in the plant, excised roots were grown under sterile conditions. Robbins's culture medium was employed, which consisted of 1·5 per cent sucrose, inorganic salts and vitamins, supplemented by the addition of 7 mgm. of arginine per litre (all dissolved in three-times distilled water). The roots were grown in Erlenmeyer flasks, each of which contained 20 ml. of the culture medium. The roots exhibited good growth when they were incubated in dark at 25° C. After an incubation period of 40 days there was on the average 12 mgm. of dried root mass found in each flask. Both the roots and the culture medium were at the end of the incubation period deep yellow in colour. The yellow colouring matter could be readily extracted from the culture medium by shaking it with chloroform (yield: 16 μgm. per

ml. culture solution). Paper-chromatographic investigations of the colouring matter in different solvent systems showed that it consisted of at least two different components, one of which exhibited a yellow, and the other a greenish-yellow, fluorescence in ultra-violet light. Further characterization of these compounds is in progress. Damascenine was present neither in the excised roots nor in the culture medium. Hence it is inferred that the isolated roots are not capable of biosynthesizing damascenine.

Grafting experiments were undertaken to identify the site of the biosynthesis of damascenine in the plant; and to this effect *Nigella damascena* L. was reciprocally grafted on to *Nigella sativa* L. and *Nigella arvensis* L., which are practically free of damascenine. The heteroplastically grafted specimens showed a comparatively smaller longitudinal growth than the ungrafted plants. However, they flowered and developed fruits and ripe seeds in the normal manner. By considering the results derived from a number of analyses carried out on these grafts, it can be established that the roots of *Nigella damascena* do not represent the site of biosynthesis of damascenine. This is in close agreement with the results of the investigations on sterile root cultures described here. It has been found instead that the shoot of *Nigella damascena* is capable of independently synthesizing the alkaloid. It is, however, not known whether the occurrence of damascenine in traces in *Nigella arvensis* as well as in *Nigella sativa* is somehow connected with degradation of damascenine in the plant. Investigations on this problem employing the use of suitably labelled damascenine are under way.

Young leaves of *Nigella damascena*, the stalks of which were dipped in water, were allowed to assimilate in light in an atmosphere of carbon-14 labelled carbon dioxide for a week. 31·2 per cent of the total activity used in the experiment was taken up by the leaves. Damascenine isolated from the dried leaves was purified by paper-chromatographic technique and with the help of radioautography it was found to be radioactive. The isolated damascenine contained 0·256 per cent of the activity taken up by the leaves. In a similar experiment using excised unripe fruits there was no trace of radioactive damascenine to be detected in the fruits chromatographically after having allowed them to stay for two weeks in an atmosphere of labelled carbon dioxide. It may be mentioned here that this is the stage at which the intact plants begin to biosynthesize damascenine at a rapid rate. Hence it can be concluded from these surprising results that the leaves are capable of participating in the biogenesis of damascenine.

As damascenine is a derivative of anthranilic acid, we therefore undertook feeding experiments with labelled anthranilic acid ($-^{14}COOH$). For this purpose the plants of *Nigella damascena* were aseptically grown in a culture solution containing inorganic salts. With the appearance of fruits on the plants the labelled anthranilic acid was fed (*a*) by injection into the stem, and (*b*) to the roots by adding it to the culture solution. After having fed the labelled compound, the test plants were further allowed to grow aseptically for about four weeks, at the termination of which they possessed ripe fruits and seeds; the plants were harvested at this stage and damascenine extracted from different organs was found to be inactive. This means that ^{14}C-carboxyl-labelled anthranilic acid, under these experimental conditions, was not utilized by *Nigella damascena* plants as a precursor for the biosynthesis of damascenine, or it might have been used up only after the loss of the activity by decarboxylation. Further work in this direction is being continued. The full details of the results obtained will be published elsewhere.

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Severe Distortion by 5-Bromouracil of the Sequence Characteristics of a Bacterial Deoxyribonucleic Acid

THE statement is often encountered in the literature that one or another purine or pyrimidine analogue, not found in the cell normally, can, when it is incorporated into a deoxy- or ribo-nucleic acid, partly replace one of the natural nucleic acid constituents. For example, 5-bromouracil is said to replace some of the thymine in deoxyribonucleic acid, or 5-fluorouracil some of the uracil of ribonucleic acid; and this view is even applied to minor constituents occurring in Nature, 5-methylcytosine replacing some of the cytosine, pseudouridine some of the uridine. Such statements are derived, implicitly, from the complementariness principles formulated in this laboratory for deoxyribonucleic acid[1] and ribonucleic acid[2]. But what actually is meant by replacement? If, as is the case, the molar sum of the 6-aminopyrimidines cytosine and 5-methylcytosine equals the molar concentration of the 6-ketopurine guanine in the deoxyribonucleic acid of rye germ[3], does this signify that every cytosine molecule along the polymer chain has an equal chance of being 'replaced' by a methylcytosine molecule? We have recently discussed the evidence for this not being the case[3].

The procedure for the study of the pyrimidine distribution in deoxyribonucleic acids, which in previous instances permitted differentiation between otherwise indistinguishable nucleic acid preparations from different cellular sources[4,5], has again been applied in the present investigation. In a previously studied case, the deoxyribonucleic acid of rye germ, it could be shown that a normal minor constituent, 5-methylcytidylic acid, does not replace the related 6-amino nucleotide cytidylic acid in a random fashion[3]. One of the notable features was, in fact, the much greater tendency of methylcytidylic than of cytidylic acid to be interjacent between purine nucleotides, that is, to occur as what we have termed a solitary unit[5].

It was, consequently, of interest to study the nucleotide pattern of a deoxyribonucleic acid that

had been forced to admit a minor, abnormal component, 5-bromouracil[6], ostensibly in the place of thymine[7,8]. In such systems, no obvious cellular mechanism of regulation, except death itself, can be discerned that would limit the extent of incorporation of the halogenated pyrimidine, whereas the complement of methylcytosine, and presumably also of other natural satellites, appears to be fixed rigidly by the cell[3,9].

The purpose of the present work was to ascertain whether, in the deoxyribonucleic acid of an *E. coli* strain requiring thymine, bromouracil really replaces thymine or whether the cell possesses a selection mechanism capable of distinguishing, to some extent, between two 6-ketopyrimidines, the normal thymine and the fraudulent bromouracil; a distinction demonstrated before in the case of the two normal 6-aminopyrimidine constituents of rye germ nucleic acid.

The thymine auxotroph of *E. coli* strain I employed in previous studies[8] was grown for 18 hr. at 37° on a slightly modified synthetic medium[10] to which 2 μgm./ml. of thymine had been added either alone (prep. 1) or together with 10 μgm./ml. of 5-bromouracil (prep. 2). The deoxyribonucleic acid specimens were isolated by a modification of a procedure employing the treatment of the cells with a buffered phenol–water system[11].

Table 1. COMPOSITION OF DEOXYRIBONUCLEIC ACID OF *E. coli* GROWN IN THE ABSENCE AND PRESENCE OF 5-BROMOURACIL

Preparation No.	Growth supplements	Moles constituent per 100 moles total					Molar ratios	
		A	*G*	*C*	*T*	*B*	$\frac{6\text{-}Am}{6\text{-}K}$	$\frac{A}{T}$ or $\frac{A}{T+B}$
1	*T*	24 8	25 0	25 5	24·8	—	1 01	1 00
2	*T* + *B*	25 3	24·3	25 1	16 4	9 0	1 01	1 00

A, adenine; *G*, guanine; *C*, cytosine; *T*, thymine; *B*, 5-bromouracil.

The composition of the nucleic acid preparations is shown in Table 1. It will be seen that, in a formal sense and as regards its total abundance, bromouracil can indeed be said to have occupied more than one-third of the places originally held by thymine.

Table 2. FREQUENCY OF SOLITARY AND COUPLED PYRIMIDINE NUCLEOTIDE UNITS

Preparation No.	Moles per 100 gm. atoms of total nucleic acid phosphorus				
	pTp	*pBp*	*pCp*	*pCpCp*	*pCpTp*
1	3 82	—	1·78	0 37	1·13
2	3 01	2 96	3 60	0 58	1·38

pTp, *pBp* and *pCp* designate the nucleoside 3′,5′-diphosphates indicative of solitary units, *pCpCp* and *pCpTp* the dinucleoside triphosphates. Compare Table 1 for other explanations and a previous paper (ref. 3) for the description of designations and techniques.

An entirely different aspect emerges, however, when individual positions of the pyrimidine nucleotides within the polymer chains are examined. The findings summarized in Table 2 were obtained by employing stage I of a previously described hydrolysis procedure (30 mgm. deoxyribonucleic acid treated with 1·5 ml. 0·1 *M* sulphuric acid at 100° for 30 min.)[4]. The separation and estimation of the fragments followed, essentially, the methods using chromatography on exchange resins and filter paper that have been described before[3]. In this manner, a fairly complete account can so far be given of the solitary pyrimidine nucleotides, isolated in the form of the corresponding nucleoside 3′,5′-diphosphates, and of some of the 'coupled' units, that is, two adjacent pyrimidine nucleotides flanked on both sides by purine nucleotides.

Had an unspecific replacement or displacement of thymine by bromouracil occurred, this would have been reflected in an equal relative utilization of both pyrimidines for common sequences, such as purine—thymine—purine and purine—bromouracil—purine. A glance at Table 2 will show that this is not at all the case. The reorganization of the nucleotide pattern of the deoxyribonucleic acid, brought about by the intrusion of the bromouracil, is so drastic that one receives the impression of dealing with two largely different populations of polymers[12]. In the cells grown in the presence of the halopyrimidine, the nucleic acid contains almost twice as many solitary pyrimidine units as does the normal preparation; the frequency of purine—cytosine—purine sequences has doubled and even the relative contribution of thymine to the corresponding units has increased; moreover, nearly one-third of the incorporated bromouracil has been segregated between purines in the form of solitary units. On the other hand, the concentration of the coupled unit purine—cytosine—thymine—purine has been comparatively little disturbed.

A fuller account of this and related work will be submitted later. For the time being, one must conclude that it cannot be stated that thymine has, in a specific sense, been 'replaced' by 5-bromouracil. One gains the impression that, after the selection of equal numbers of 6-aminopurines and 6-ketopyrimidines, on one hand, and of 6-ketopurines and 6-aminopyrimidines on the other, a second mechanism—an exclusion principle, as it were—comes into play, so that certain neighbours are tolerated and others not, or rarely.

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[12] The total deoxyribonucleic acid of *E. coli* grown in the presence of 5-bromouracil has been reported to be heterogeneous with respect to the incorporation of this pyrimidine (Bendich, A., Pahl, H. B., and Brown, G. B., in "The Chemical Basis of Heredity", 378 (Johns Hopkins Press, Baltimore, 1957)).

A Method for studying Amino-Acid Activation in Crude Tissue Extracts

THERE is now considerable evidence that the first step in protein synthesis involves amino-acid activation[1]. Using the methods of pyrophosphate exchange into adenosine triphosphate, and of hydroxamate formation, activation of all the common amino-acids, added singly, has been demonstrated in plant[2], animal[3] and bacterial[4] extracts, although the entire complement of activities is not usually detectable in most preparations[3]. Both these assay methods depend on differences observed in the presence and absence of added amino-acid, and difficulties in interpretation of results arise when applied to crude preparations in which the endogenous level of amino-acids is high. On the other hand, because of the lability of amino-acid-activating enzymes to procedures such as dialysis[5], any purification procedure to overcome this difficulty carries with it the danger of inactivating part of the enzyme systems being investigated.

In connexion with work on protein synthesis being carried out here, the need was felt for a method of analysing the amino-acid activation pattern in crude cell extracts, and, furthermore, it seemed advantageous that this should be done in the presence of the complex mixture of amino-acids necessary for protein synthesis. The latter consideration seemed especially important in view of the reported competition effects between structurally related amino-acids for the amino-acid-activating enzymes[4]. This communication describes a method for the quantitative measurement of the total amino acyl hydroxamates formed in the presence of a complex mixture of amino-acids and a further chromatographic procedure for the identification of at least 15 of the individual amino acyl hydroxamates. The procedure is unaffected by the endogenous level of amino-acids in the extracts. The application of the method to crude rat liver preparations as a test system is described here.

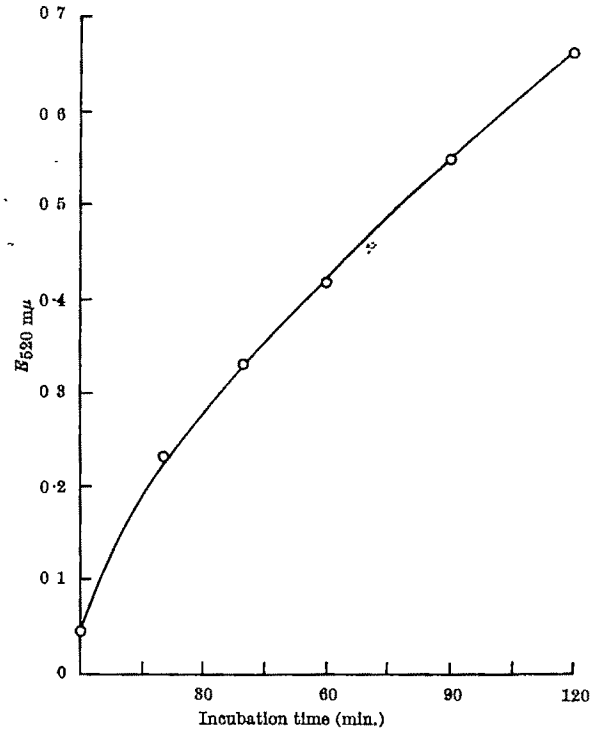

Fig. 1. Progress curve for amino acyl hydroxamate formation by crude 105,000*g* supernatant fraction of a rat liver homogenate. The complete system contained 25 μmoles K_2.adenosine triphosphate, 50 μmoles magnesium chloride, 6,000 μmoles 'low salt' hydroxylamine, 75 μmoles L-amino-acid (mixture containing equimolar concentrations of the 15 amino-acids, alanine, arginine, glycine, histidine, *iso*-leucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine and valine), 250 μmoles potassium phosphorylcreatine, 100 μgm. crystalline creatine phosphorylransferase, and 1·5 ml. 105,000*g* supernatant. The volume of the reaction mixture was 5·0 ml. and the *p*H 7 5. Incubations were carried out at 37°

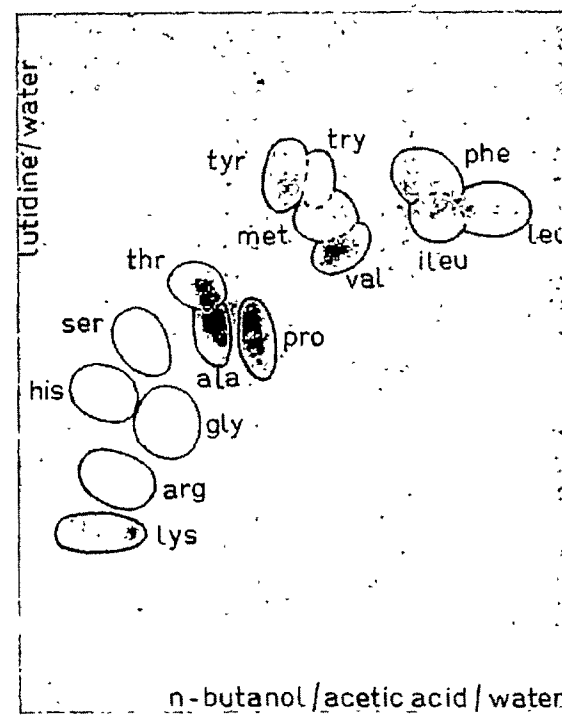

Fig. 2. Two-dimensional chromatogram of a mixture of 15 synthetic amino acyl hydroxamates

Rat liver was homogenized in a Potter–Elvehjem apparatus with 1·5 vol. of ice-cold 0 05 *M* potassium chloride and centrifuged at 105,000*g* for 60 min. Samples of the supernatant fraction were then added to reaction mixtures containing 15 amino-acids, 'low-salt' hydroxylamine, magnesium chloride, adenosine triphosphate and an adenosine triphosphate-generating system in a volume of 5·0 ml. After incubation, the reaction was stopped by the addition of 1·0 ml. of 60 per cent perchloric acid, and diluted with 6·0 ml. of water. The supernatant was collected by centrifugation and the residue washed with water. The combined supernatant and washings were adjusted to *p*H 7·5 with 3 *N* potassium hydroxide and the precipitate of potassium perchlorate filtered off. The filtrate was evaporated to dryness under reduced pressure at 37° and the residue stored overnight in a desiccator over concentrated sulphuric acid to remove residual hydroxylamine. The residue was extracted with 10 ml. of water and the extract adjusted to *p*H 5·0 with acetic acid. This solution was then passed through a column of 'Amberlite *IRC*-50', equilibrated at *p*H 5·0 with ammonium acetate buffer. After exhaustive washing with water, the column was eluted with 30 ml. of 2 *N* ammonium hydroxide and the eluate evaporated to dryness under reduced pressure at 37°. The residue was dissolved in 5·0 ml. of water and amino acyl hydroxamates determined by the method of

Schweet[6]. Control experiments showed that the column gave consistent 80 per cent recovery values with a mixture of 15 chemically prepared amino acyl hydroxamates. The incomplete recovery is not due to a loss of specific components, since material eluted from the column gave the same loss on recycling. The procedure does not permit the estimation of the hydroxamic acid derivatives of the dicarboxylic amino-acids but does have the advantage of eliminating aspartic and glutamic-ω-hydroxamates, both of which may be formed enzymically[7,8].

Fig. 1 shows a progress curve of amino acyl hydroxamate formation by a crude rat liver soluble fraction.

For the identification of the amino acyl hydroxamates present, the dried eluate from '*IRC*-50' columns, obtained as above, was extracted with a minimum amount of 90 per cent ethanol. The hydroxamate solution obtained was chromatographed in two dimensions on acid-washed Whatman No. 3 papers, run first in water-saturated 2 : 4-lutidine, followed by *n*-butanol–acetic acid–water (4 : 1 : 1). The spots were detected by spraying with 6 per cent ferric chloride in 0·2 *N* hydrochloric acid. For satisfactory results care must be taken that both ion exchange columns and chromatographic papers are metal-free. The resin was given a preliminary wash with ammonium versenate before use, and the papers were washed in 50 per cent acetic acid and then with water until acid-free[9]. In Fig. 2 the separation of a mixture of 15 synthetic amino acyl hydroxamates is shown. Fig. 3 shows the separation of the mixture of hydroxamates formed by rat liver. The identity of the hydroxamates of glycine, lysine, proline, serine and tyrosine was confirmed by the addition of reinforcing markers. The spots designated methionine and tryptophan were very faint and could not be identified with certainty. The separation is susceptible to overloading and this has been shown to be the reason for the distortion of the proline hydroxamate spot. In heavily loaded chromatograms a faint spot corresponding in position to the hydroxamate of histidine has also been observed.

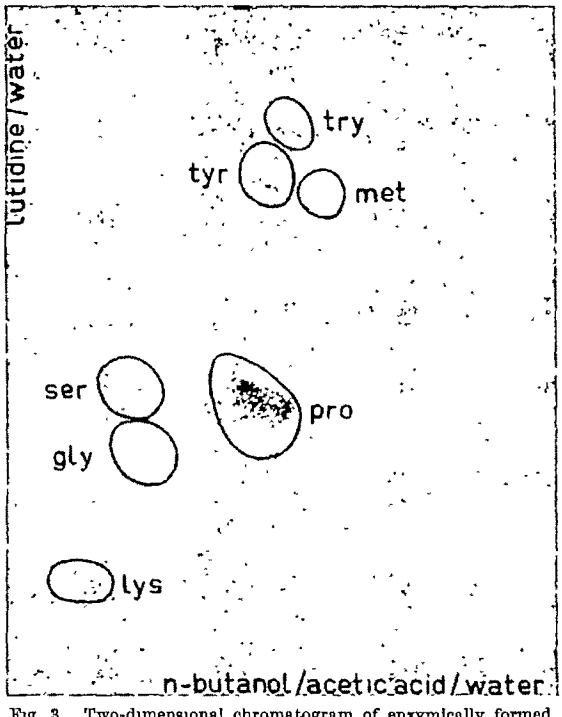

Fig. 3. Two-dimensional chromatogram of enzymically formed amino acyl hydroxamates. The hydroxamates were formed and isolated as described in the text

The procedure described here enables identification of at least 15 amino acyl hydroxamates formed simultaneously as a result of amino-acid activation in crude enzyme preparations. With suitable use of labelled amino-acids and carrier marker spots, the sensitivity could doubtlessly be considerably refined. It is also hoped that it may prove possible to apply quantitative methods of estimation to the individual components of the chromatograms.

Full details of this work will be reported later.

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Quantitative Isolation of Alkaloids from Plant Materials

The common methods of isolation of alkaloids in relatively pure forms from plant materials now available involve extraction by solvent partition and/or column chromatography. These methods are very cumbersome, emulsions usually occur, large volumes of solvents are required and the final products are very often impure.

The fact that ammonium reineckate forms insoluble derivatives with alkaloids is well known. The mechanism of the reaction between organic bases and ammonium reineckate has been studied, and the regeneration of the conjugate bases from their reineckates using ion-exchange resins has also been reported[1]. This suggests a method for the isolation of plant alkaloids as their insoluble reineckates from which the free alkaloids can later be regenerated by passing an acetone solution of these reineckates through an ion-exchange column. A detailed study of this method was undertaken in order to evaluate it as a means of recovering and determining alkaloids in both opium and nux vomica. The procedure yielded crystalline alkaloids even from opium, and the quantitative results obtained indicated a high degree of accuracy and precision. The basic technique can be applied to the isolation of alkaloids from other plant materials provided these alkaloids do not decompose on the ion-exchange column. This simple procedure promises to offer the first method known for the quantitative determination of the absolute amounts of the various alkaloids in opium. The quantitative results obtained for strychnine in nux vomica are very satisfactory, and a detailed report of this investigation will be published elsewhere.

Isolation of Opium Alkaloids. About 1 gm. of opium is treated with 50 ml. of 10 per cent hydro-

chloric acid for ½ hr. over a water-bath. The solution is filtered through a Whatman No. 1 filter paper and the residue washed with 3 ml. portions of warm dilute hydrochloric acid until the filtrate gave no precipitate with Mayer's reagent. 50 ml. of 2 per cent ammonium reineckate solution is added to the acid solution, cooled to 0° C. and filtered through a sintered-glass crucible with the aid of gentle suction. The precipitate is dissolved in acetone and calcium oxide is added to the acetone solution. A considerable amount of impurities is removed by the calcium oxide in this manner. This solution is filtered through a sintered-glass crucible, and the calcium oxide washed with acetone until the filtrate is colourless. The bright red-coloured acetone solution is then passed through an ion-exchange column of 'De-Acidite *FF*' which has previously been activated by passing a solution of 5 per cent sodium hydroxide and then washed with water until the eluate has a *p*H of 7–8. The colourless acetone eluate contains codeine, thebaine, papaverine and narcotine and the morphine is held back in the column. About 20 ml. of water is added to the acetone solution and concentrated to about 10 ml. The solution is made alkaline by the addition of sodium hydroxide and the alkaloids extracted from this solution with chloroform. Crystalline products are obtained on evaporation of the chloroform solution and tituration of the residue with 50 per cent ethanol.

The morphine is recovered from the column by first washing the column with water to remove the acetone and then with 10 per cent acetic acid solution. The acetic acid solution is concentrated to about 10 ml. and ammonium hydroxide is added until the solution is alkaline. The ammoniacal solution is extracted with 3 : 1 chloroform-*iso*butanol mixture and morphine is obtained upon evaporation of this solvent mixture.

Quantitative Determination of Papaverine in Opium. The chloroform extract containing codeine, thebaine, narcotine and papaverine is not evaporated but is extracted with 3 portions of 20 ml. of *N*/5 hydrochloric acid which removes the codeine and thebaine from the organic layer. The chloroform layer is transferred to a separating funnel and 50 ml. of *N*/5 hydrochloric acid is added to it. This mixture is shaken thoroughly and 30 ml. of 2 per cent ammonium reineckate solution is then added. The papaverine is determined by the method according to Lee and Farmilo[2,3]. The results are shown in Table 1. Satisfactory results were also obtained for narcotine. The procedures for the determination of codeine, thebaine and morphine are still under study.

Table 1. DETERMINATION OF PAPAVERINE IN OPIUM

Amount of opium used (gm.)	Amount of papaverine obtained (mgm.)	Percentage present
1 082	15·1	1 40
1 084	15·4	1 42
1 160	16·0	1 38
1 070 and 10 mgm. papaverine	24·9	1·30

Isolation of Strychnine and Brucine from Nux Vomica. 20 ml. of 10 per cent hydrochloric acid is added to 20 ml. of ethanolic extract of nux vomica and heated on the water-bath until the ethanol is removed. The acid solution is filtered through a Whatman No. 1 filter paper and the residue is washed with dilute hydrochloric acid until the filtrate gave no precipitate with Mayer's reagent. The strychnine and brucine are precipitated as their reineckates and the free alkaloids are obtained in crystalline forms using the same procedure as described earlier. Strychnine is determined quantitatively first by treating the alkaloidal mixture with nitric acid and sodium nitrite followed by the extraction of strychnine from an alkaline solution with chloroform. The strychnine is back-extracted from the chloroform solution with acid and afterwards precipitated and determined as its reineckate. The results obtained are shown in Table 2.

Table 2. DETERMINATION OF STRYCHNINE IN NUX VOMICA

Volume of Nux Vomica extract used (ml.)	Amount of strychnine obtained (mgm.)	Percentage present
20	74 2	3 71
20	73·0	3 65
20	75 3	3·76
20 and 20 mgm. strychnine	93·7	3·68

I thank the chief chemist, Mr. Chia Chwee Leong, for his interest in this work and for his permission to publish these results.

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Action on Some Synthetic Peptides of a Protease from Rabbit Spleen

SOME of the enzymes of bovine spleen have been studied in detail and classified as cathepsin *A*, *B* and *C* according to their specificity for certain synthetic peptides[1]. Examination of the action of rabbit spleen extracts on human serum albumin has shown the existence of a proteolytic activity having an optimal *p*H at 3·0–3·5 (ref. 2). It was shown that this activity was not due to an enzyme analogous with cathepsin *B* or *C* but could have been due to a cathepsin *A* (ref. 3). Recently we have demonstrated that this activity was due to a single protease which we have purified by chromatography on modified cellulose[4].

This communication deals with the action of the crude rabbit spleen extract and the purified protease on the synthetic peptides specific for the cathepsins *A*, *B* and *C* and carboxypeptidase of bovine spleen. The crude extract and purified protease were prepared from rabbit spleens as described previously[4]. The proteolytic activity of the two enzyme preparations was measured using human serum albumin as substrate[4]. The two preparations were employed in quantities such that their final concentration expressed in arbitrary proteolytic units was 35 U.P. in both cases. The final concentration of the substrates was 0·05 *M* in citrate buffer 0·1 *M*, *p*H 5·0. Cysteine, at a final concentration of 4 m*M*, was added to the different substrates with the exception of carbobenzoxy-L-glutamyl-L-tyrosine. The reaction media were incubated at 37° C. for 19 hr. except in the case of the hydrolysis of carbobenzoxy-L-glutamyl-L-tyrosine, by the crude extract, when the incubation time was 5 hr. The moles of carboxylic groups

Table 1. PERCENTAGE HYDROLYSIS OF THE DIFFERENT SYNTHETIC SUBSTRATES

Enzyme \ Substrate	CGluT	BAA	GPA	CGP
Crude extract, 4·2 mgm./ml	38	60	116	45
Purified protease, 0 60 mgm./ml.	0	0	10	0

CGluT, Carbobenzoxy-L-glutamyl-L-tyrosine: substrate for cathepsin *A*; BAA, benzoyl-L-argininamide-hydrochloride: substrate for cathepsin *B*; GPA, glycyl-L-phenylalaninamide-acetate: substrate for cathepsin *C*; CGP, carbobenzoxyglycyl-L-phenylalanine: substrate for carboxypeptidase.

liberated during the reaction were measured by the method of Grassmann and Heyde[5] and the percentage of hydrolysis is given by the relation:

$$\frac{\text{Moles carboxylic groups liberated} \times 100}{\text{Moles substrate employed}}$$

As can be seen in Table 1 the four substrates were hydrolysed by the crude extract, thus demonstrating the existence in rabbit spleen of enzymatic activities analogous with those of cathepsin *A*, *B*, *C* and carboxypeptidase of bovine spleen.

With the purified protease there is no hydrolysis of the substrates specific for cathepsins *A*, *B* or carboxypeptidase. There is hydrolysis of the substrate for cathepsin *C*, but it is minimal and is most probably due to the presence of traces of cathepsin *C*. These results show that the protease from rabbit spleen is different from cathepsin *A*, *B*, *C* and carboxypeptidase.

The inactivity of the rabbit spleen protease toward the specific substrates of cathepsin *A*, *B* and *C* is an additional property in common between this enzyme and a protease recently isolated from bovine spleen by Press, Porter and Cebra[6].

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Immuno-Electrophoresis of Insulin-binding Antibodies

THE presence of insulin-binding antibodies in the sera of insulin-resistant diabetics has been shown by a large number of investigators[1]. It has also been shown by Berson *et al.*[2] and Kalant *et al.*[3] that using paper electrophoresis the binding was mainly in the γ-globulin, while using free-boundary electrophoresis the binding was mainly in the β-globulin. The disadvantage of using paper as a supporting medium is discussed in work now in course of publication[4]. In view of the differences of opinion as to which of the serum proteins is responsible for the binding of insulin it was decided to apply the techniques of immuno-electrophoresis with subsequent autoradiography to the study of diabetic sera.

The insulin was labelled with iodine-131, using iodine monochloride as the carrier by the technique described by McFarlane[5], and had a specific activity of 3·2 mc. per mgm. insulin. A 1 per cent solution of 'Ionagar' (Oxo, Ltd.) was prepared in a 0·5-μ concentration of barbitone buffer[4]. 15 ml. of this was poured on to glass plates 6 in. × 2½ in., and holes approximately 1·5 mm. diameter were cut at regular intervals along the centre line. Each hole was filled with a serum sample to which had been added about one-tenth of its volume of the tagged insulin solution. The serum samples therefore contained approximately 30 μgm. of tagged insulin per ml. The volume of sera in each hole was approximately 0·003 ml.

Immuno-electrophoretic controls of bromphenol blue and nitroaniline were used to mark the movement of the albumin and γ-globulin respectively, as suggested by Wunderly[7]. Electrical contact was made through Whatman No. 3 filter paper and a current of 15 m.amp. passed. Small strips of filter paper soaked in the appropriate anti-sera were placed between adjacent holes (Pasteur horse anti-human serum, and anti-*S*7 γ-globulin–Soothill). The patterns were allowed to develop for 1 week in a moist chamber. The glass plates were then taken out, covered with filter paper to remove the excess protein and salts, and allowed to dry at room temperature. The precipitation pattern was developed in 0·1 per cent nigrosin in 2 per cent acetic acid overnight and then washed in 2 per cent acetic acid to which a little 'Teepol' had been added to remove the excess stain. They were then put on end to dry.

Autoradiography was performed by placing the agar plate in contact with 'Ilfex' double-coated X-ray

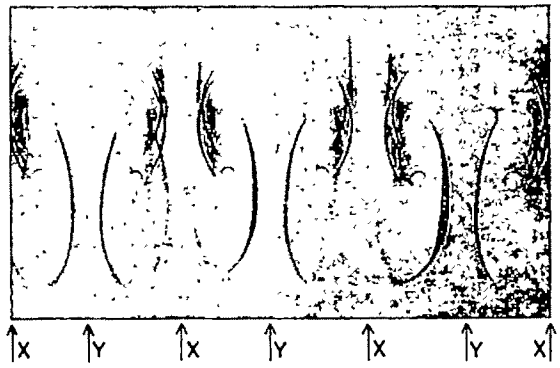

Fig. 1. Stained lines on agar plate. Arrows mark positions of strips of antisera. *X*, Pasteur horse anti-human serum; *Y*, anti-*S*7 γ-globulin

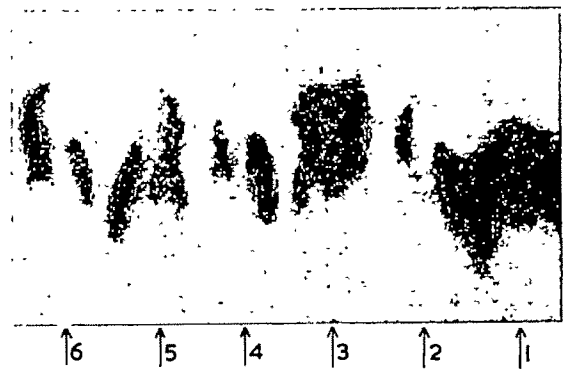

Fig. 2. Autoradiograph. Arrows mark positions of serum samples. Note serum sample 2 is the same serum as sample 1, but one-third of the concentration of active insulin used in all the other samples

film. Figs. 1 and 2 show the result of this technique. Fig. 1 is a photograph of a section of the stained and dried agar plate showing the results on 6 serum samples; Fig. 2 is the corresponding autoradiograph. In this case with an activity of approximately 0·04 μc. per sample an exposure of 12 days showed the result illustrated.

It will be seen that in the binding of the insulin two anti-bodies are responsible, one of which corresponds to the *S7* γ-globulin and the other to a globulin corresponding in mobility to β-globulin.

It is hoped to report the results more fully shortly and to investigate the binding quantitatively by examination of the density distribution in the appropriate areas of the autoradiograph.

We wish to thank Dr. Soothill for a generous gift of immuno-electrophoretically pure anti-*S7* γ-globulin, and Dr. John Bodman for much help with the immuno-electrophoresis.

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Regeneration of Visual Pigments from their Low-temperature Photoproducts

UNDER the above title Bridges has recently published an article which describes experiments said to be "in marked disagreement with the picture of the bleaching process" we have proposed[1]. We should like to comment briefly.

It has been known for many years that the bleaching of rhodopsin to yellow products—retinene, or indicator yellow—involves a sequence of photochemical and thermal reactions[2,3]. We have analysed these as follows[4–6]. Rhodopsin contains 11-*cis* retinene attached as chromophore to a protein, opsin. Light isomerizes the 11-*cis* chromophore to the all-*trans* configuration, yielding a first, highly coloured (red-to-violet) all-*trans* chromoprotein, called lumirhodopsin. All further reactions proceed in the dark, that is, they are thermal reactions. There are at least two of these. First, lumirhodopsin is transformed to another, orange-to-red, all-*trans* chromoprotein, metarhodopsin, by what is probably a configurational rearrangement of the opsin. Metarhodopsin is then hydrolysed to the yellow mixture of all-*trans* retinene and opsin (indicator yellow), and this is probably accompanied by further configurational changes of the opsin.

The synthesis of rhodopsin also can involve both photochemical and thermal reactions. If one mixes 11-*cis* retinene and opsin in the dark, the two join to form rhodopsin by a thermal process[7]. However, if one starts with the products of bleaching in solution —all-*trans* retinene and opsin—the retinene must be stereoisomerized before it can combine with opsin; and this can be done with light[8]. In this case, therefore, the formation of rhodopsin involves the photochemical stereoisomerization of retinene, followed by the thermal condensation of the appropriate isomer with opsin. Light can also regenerate visual pigments directly from the lumi- or meta-pigments by isomerizing the all-*trans* chromophore to the 11-*cis* configuration[4–6,9].

This is not a complete description of the bleaching and synthesis of visual pigments. The presence of further intermediates is implied by other observations, made under different experimental conditions in our own and other laboratories (cf. refs. 10, 11). However, we believe these to be the salient features: (1) photo-chemical stereoisomerization of the chromophore; (2) configurational re-arrangements of opsin; (3) combination of retinene and opsin by a Schiff base linkage, and its hydrolysis during bleaching. This scheme, first developed on the basis of observations with squid and cattle rhodopsins[4,9], has been confirmed with rhodopsins from five other species[5] (including two of the three used by Bridges), and with the chicken cone pigment, iodopsin[6].

In view of the number of reactions involved, it is evident that the analysis of the bleaching and regeneration of visual pigments is best performed under conditions such that the partial reactions take place one at a time, or as nearly so as possible. Bridges's experiments do not fulfil this condition, since they are performed in circumstances in which photochemical and thermal processes take place side by side. This is shown by the fact that in his experiments rhodopsin bleaches in the light to "orange products" and indicator yellow. The latter is always a product of thermal reactions, as has been shown repeatedly by lowering the temperature sufficiently during the irradiation (thus allowing only photochemical reactions to take place), and then warming in the dark[2–6,12].

It must be clear that this overlapping of reactions makes Bridges's attempt to analyse the bleaching and regeneration of rhodopsin into partial reactions exceedingly difficult. After close examination of his results, we see no present need to revise our interpretation of the mechanism of these reactions.

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Hubbard and Kropf's explanation of my results is based on the statement that the experiments were "performed in circumstances in which photochemical and thermal processes take place side by side". The implication here is that irradiation converted the parent visual pigment to an orange photoproduct, and that this photoproduct was unstable and decayed to indicator yellow. This is not so. It was explicitly stated that the orange photoproduct produced by irradiating frog rhodopsin at − 5° C. was thermally stable.

Thus irradiation for 1 hr. of frog rhodopsin at − 5° C. "generates a mixture of indicator yellow and a stable product with $\lambda_{max.}$ displaced about 20 mμ towards the blue. . . . At this temperature the photoproduct is stable (measurements at 20 mμ intervals from 380 to 620 mμ interlacing with return measurements from 610 to 390 mμ give a check of stability)"[1]. The whole spectrum was measured over the course of 1 hr., that is, the same period of time as for the bleaching operation. In the experiments carried out with conger eel and rhesus rhodopsins, the return measurements were actually slightly higher than the outward ones; far from decaying thermally to indicator yellow, the orange photoproduct was being regenerated from this substance.

It was shown experimentally that the rhesus photoproduct was photosensitive, yielding indicator yellow or retinene by a photochemical reaction. As was stated, the probable explanation for the presence of indicator yellow together with thermally stable orange photoproducts in the frog and conger eel experiments is that it was the product of photochemically bleaching these substances.

The use of light of long wave-length in the experiments reported (dominant wave-lengths of 550 and 580 mμ obtained from a Hilger–Barfit monochromator) makes it unlikely that regeneration from photoisomerized indicator yellow was involved in the thermal regeneration of rhodopsin. Even in the acid solutions used, indicator yellow has $\lambda_{max.}$ no higher than 440 mμ, and later experiments at *p*H 9·0, where indicator yellow has $\lambda_{max.}$ at 380 mμ, have yielded identical results.

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BIOPHYSICS

Plasticity of Wool

THE quality of a wool is not determined solely by the dimensional characteristics of the fibres, such as fineness, length and crimp. Differences in the nature of the substance govern the selection of wools for particular purposes, and it has been shown that these differences can be measured by determining the plasticity of the fibres[1]. The measurements are made by observing the rate of creep of the fibres in distilled water at 22·2° C., usually under a constant load of 6 kgm./mm.^{2}. When log $(E - E_t)$ is graphed against t, where E_t is the percentage extension at time t (min.), and E is an arbitrarily chosen limiting extension, a linear relationship is obtained in the later stages of extension; the slope (k) of this line gives a simple measure of plasticity.

Because plasticity measurements are tedious, there have been several attempts to devise more rapid methods of characterizing the substance of different wools, and le Roux[2] has suggested that there is a simple direct relationship between the plasticity of a wool and its urea-bisulphite solubility[3]. This possibility had been examined in these laboratories before the publication of le Roux's note, and as the two sets of results were found to be contradictory, further experiments have since been carried out. Most of the wools in the new group were from South Africa, because le Roux's work was confined to such wools. Plasticity measurements were made under the conditions defined above, and the rigidly defined conditions of Dusenbury were adopted for determinations of urea-bisulphite solubility[4]. Both sets of results are given in Table 1.

Table 1

Wool	Plasticity (k)	Urea-bisulphite solubility (%)
64*s* Port Elizabeth Grassveld	91·4	55·0
60*s* Port Elizabeth Grassveld	86·2	41·2
66*s* East London	77·6	63·0
70*s* Cape Town	70·3	48·0
64*s* Cape Town	75·8	57·6
Cape Town	95·3	53·4
Queensland	42·6	47·3
70*s* Durban	92·6	60·3
64*s* Durban	73·1	56·2
60*s* Durban	112·8	57·9

These results, like the earlier ones, indicate that there is no simple relationship between the plasticity of wool and its urea-bisulphite solubility.

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Orientation of Cockchafers

A PAPER by Dr. F. Schneider published in 1957[1] suggested that cockchafers can orientate themselves in the magnetic field of the Earth. I have therefore carried out some experiments to detect the possible existence of permanent magnetic material in the body of cockchafers.

Two methods were used. First, I suspended parts of dead cockchafers at the end of a thin glass wire (length 1 metre, diameter 25μ) and in a magnetic field up to 20 gauss. It was found that no magnet could be present of such strength that in a field of 0·2 gauss it would experience a torque of more than 2×10^{-6} dyne cm. In the second method I used very sensitive magnetometers of the Royal Netherlands Meteorological Institute, De Bilt, which enabled me to make measurements on living animals. These measurements showed that in a field of 0·2 gauss the torque exerted on the supposed magnet must be smaller than 2×10^{-7} dyne cm.

If the supposed magnet were 0·01 cm. long, the mechanical force exerted by one pole of the magnet would have to be 2×10^{-5} dyne to produce a torque

of 2×10^{-7} dyne cm. If we suppose that the sense cells are stimulated by the pulling of a hair, then it is reasonable (assuming that elongation of a hair of about $1 \cdot 4 \times 10^{-10}$ cm. is detectable and Brownian motion limits the natural sensitivity of sense cells) to accept the threshold for the perceptible force as about 0·1 dyne (according to Hl. de Vries). Therefore I conclude that, if the cockchafer has permanent magnetic material at all, it cannot exert a mechanical force in the Earth's magnetic field greater than 2×10^{-5} dyne, which is much too small to be perceived by the sense organs of the cockchafer.

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PHYSIOLOGY

Hypoglycæmic Response to Leucine in a Leucine-sensitive Man

IT has been reported previously[1,2] that certain individuals show a profound lowering of the blood glucose-level following ingestion of leucine or *iso*-valeric acid and that this is a familial trait.

We have studied the mechanism of this hypoglycæmic response in a fasting leucine-sensitive male aged 29 years (case 3[1]) using methods previously described to follow peripheral glucose metabolism in the forearm[3,4] and plasma insulin activity[5]. Following successive infusions into the brachial artery at rates of 7 mgm./min. for 20 min. of L-leucine and commercial *iso*valeric acid neutralized in saline, 10·5 gm. L-leucine was taken by mouth.

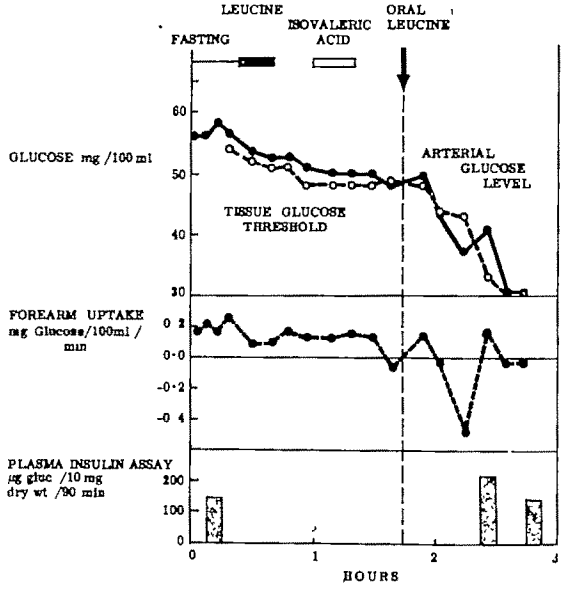

Fig. 1. Above, arterial blood glucose concentration ● --- ●, and glucose threshold ○——○; middle, glucose uptake by the tissues of the fore-arm (mgm. glucose removed from the arterial blood per 100 ml. tissue per min); below, arterial plasma insulin activity (µgm. glucose taken up per 10 mgm. dry weight of rat hemi-diaphragm)

Fig. 1 shows the arterial blood glucose-level and plasma insulin activity, the glucose uptake and calculated glucose threshold of the fore-arm tissues. Neither leucine nor *iso*valeric acid, when continuously infused, affected the glucose uptake or glucose threshold of the fore-arm tissues. The oral dose of leucine, however, lowered the blood glucose-level and the tissue glucose threshold. The arterial plasma insulin activity increased significantly ($P < 0 \cdot 05$) from 139 ± 20 to 212 ± 19 µgm. glucose/10 mgm. dry weight rat hemi-diaphragm/90 min. incubation, but this increase was only transient, results in accord with those published recently by Yalow and Berson[6].

The subsequent fall in the glucose threshold of the fore-arm tissues resembled that observed in normal individuals after injections of insulin[4]. It may be noted that the systemic fall of blood sugar was not accompanied by an increase of glucose uptake by the fore-arm tissues; this has also been observed in other subjects after intravenous insulin.

We conclude that: (1) it is unlikely that the peripheral tissues take up more glucose as a direct response to circulating leucine or *iso*valeric acid; (2) the hypoglycæmic effect of leucine in sensitive subjects is due to a transient rise in the plasma insulin activity.

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Effect of Strophanthin G on Oxidative Metabolism in Cardiac Muscle

PREVIOUS results published from this laboratory indicate that the increased mechanical efficiency (ratio of work output to energy input) apparent after the administration of non-toxic doses of cardiac glycosides to isolated spontaneously beating hearts is invariably associated with raised levels of oxidative metabolism[1,2]. Hajdu and Leonard[3] recently directed attention to the possibility that such an increased rate of oxygen consumption could be due to the increased mechanical work output associated with the positive inotropic response rather than to the fundamental metabolic action of the glycosides themselves.

An attempt has been made to investigate this possibility by comparing the effect of strophanthin *G* ('Ouabain' (Arnaud): Laboratoire Nativelle product) on the rate of oxygen uptake in actively beating hearts with that on hearts in systolic and diastolic arrest.

Experiments were carried out at 25·0° C. on hearts isolated from unselected summer toads (*Bufo*

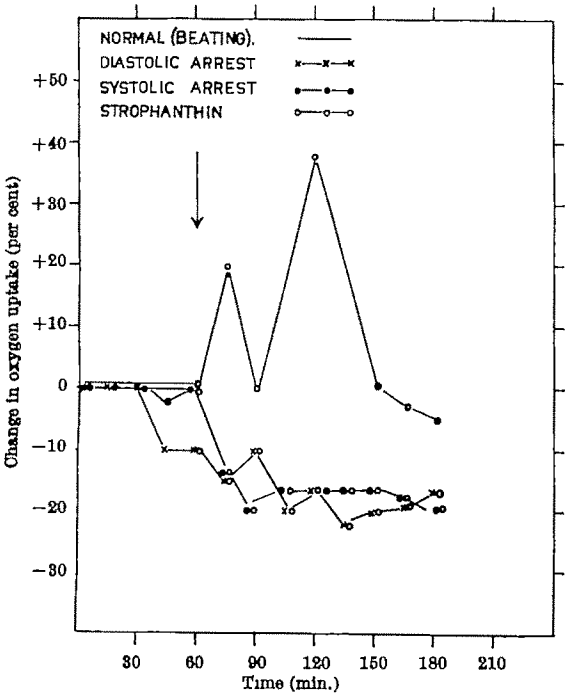

Fig. 1. Effect of strophanthin *G* (10 μgm./ml.) on the rate of oxygen consumption of actively beating hearts (mean 12 exp.) and hearts arrested in diastole (mean 6 exp.) and systole (mean 6 exp.). The drug was added at the arrow

marinus), using the perfusion apparatus and fluid previously described[4]. In six preparations isolated hearts were initially arrested in diastole by the addition of neutralized potassium chloride solution (minimal concentration). The rate of oxygen uptake was recorded at 15-min. intervals both during an initial control period of 1 hr. and throughout the 2 hr. following the addition of strophanthin *G* (final concentration 10 μgm./ml.). In a similar series hearts were arrested in systole by the administration of calcium chloride (neutralized), and the effect of strophanthin *G* on the oxygen consumption recorded as above. These results were compared with those previously recorded following the administration of strophanthin *G* at this same concentration to a series of actively beating hearts. The necessary control experiments were also carried out.

The results recorded are summarized in Fig. 1, from which it is evident that strophanthin *G*, at a concentration sufficient to produce a positive inotropic response[4], stimulated oxidative metabolism in actively beating hearts but failed to do so in those arrested either in diastole or systole. Similar observations were made in other experiments in which lanatoside *C* ('Cedilanide', Sandoz Ltd. product) was used (20 μgm./ml. final concentration). The rate of oxygen utilization in both the diastolic and systolic arrested control experiments gradually fell throughout the 3-hr. experimental period, while that of the control series of actively beating hearts remained relatively constant.

During the initial hour's perfusion, hearts arrested by potassium averaged an oxygen consumption of 1·59 ml./min./100 gm. wet weight (mean 12 exp.) compared with that of 4·233 ml./min./100 gm. wet weight (mean 10 exp.) recorded in the calcium arrested series.

These results demonstrate that, whereas the glycosides stimulate oxidative metabolism in actively beating hearts, they fail to do so in hearts which have been arrested. It may be argued that the increased rate of oxygen utilization recorded in the active series resulted from an effect of the glycosides on a specific stage during contraction or relaxation. Alternatively, as suggested by Hajdu and Leonard, the effect may be due primarily to the raised work output associated with the positive inotropic response in the active series. It seems unlikely that a gross metabolic effect could be involved.

In part these results explain the contradictory reports in the literature relating to the effect of non-toxic doses of glycosides on oxidative metabolism[3,5], since results from physiologically active preparations have been compared with those from inactive homogenate studies.

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Inhibition of Active Sodium Transport by Cholera Toxin

ACTIVE transport of sodium across cell membranes is now established as one of the fundamental physiological processes of most vertebrate cells. This process probably requires some sort of carrier molecule which binds sodium and which is coupled to a source of energy, the whole being designated for simplicity as a 'pump'. Failure of sodium transport may occur because of failure of energy supply, as, for example, in ischæmic skin and muscle after injury[1]. Certain drugs, such as cardiac glycosides, inhibit active transport by competing with sodium for the carrier[2]. One might also expect to find instances of failure or abnormalities of the pump itself, particularly in disease, but no examples of this are known.

Recent work[3] shows that in rat small intestine and colon, sodium is transported actively from lumen to blood, but that water transfer depends upon gradients of water activity and is a passive process. Net absorption of water, therefore, is dependent on active sodium absorption. If active sodium transport across the intestinal mucosa were decreased or abolished, one would predict the excretion of abnormally large amounts of water and sodium from the intestine, that is, diarrhœa.

This hypothesis could be tested by determining the effect on active sodium transport of crude extracts or toxins from micro-organisms which produce disease accompanied by diarrhœa. Cholera is an obvious example, and the preliminary results of such an investigation are reported here.

Experiments were carried out on abdominal skin and gastric mucosa from the European brown frog, *Rana temporaria*, and on skin from the American grass frog, *Rana pipiens*. The skin, or gastric mucosa, was fixed between two conical compartments filled with frog Ringer solution which was mixed by an air

pump. The potential difference across the tissue was measured, and in many experiments an external potential, applied through agar electrodes, was adjusted to maintain the potential difference at zero. The current produced by the untreated frog skin at zero potential (the 'short-circuit' current) has been shown by Ussing and Zerahn[4] to be equal to the net sodium flux. Therefore this current served in preliminary experiments to indicate changes in active sodium transport. In other experiments either the influx or efflux of sodium across the skin was measured with sodium-22, while the potential difference was held at zero, as described previously[5]. The flux in either direction could then be calculated from the relationship: net flux = influx − efflux.

All experiments reported here were performed with 'Cholera Filtrate Duphar' (N.V. Philips-Roxane, Amsterdam). The material was supplied freeze-dried in ampoules. The concentrations given are μgm. per ml. of Ringer solution in contact with the skin.

Fig. 1 shows a typical effect produced by the addition of cholera filtrate to both sides of the frog skin (725 μgm./ml.) Both short-circuit current and potential difference (measured by momentarily disconnecting the external electromotive force) decreased rapidly after addition of the cholera filtrate, a result characteristic of inhibition of active sodium transport. Fig. 1 also shows the effect of the same concentration of cholera filtrate on the potential difference and short-circuit current of the frog gastric mucosa. In this tissue only a transient increase in both occurred (possibly the effect of protein). Since the frog gastric mucosa does not actively transport sodium, this experiment indicates that the toxin is rather specific. In other experiments, similar to those

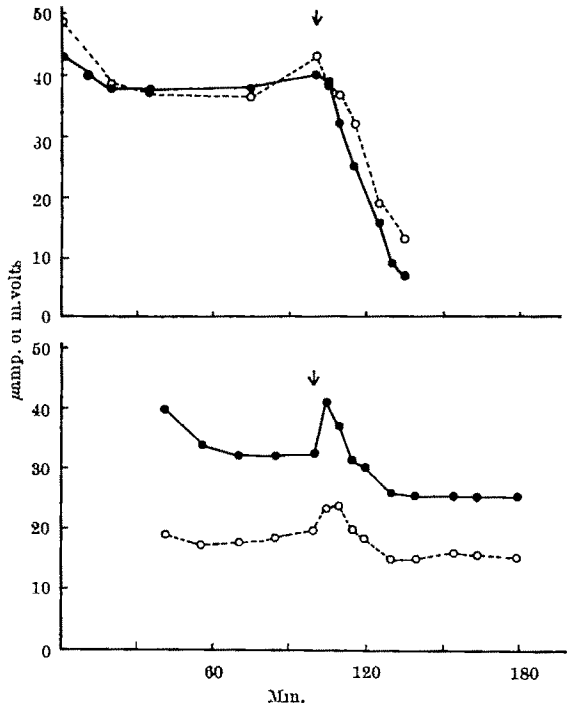

Fig 1. The effect of cholera filtrate on the short-circuit current in μamp. per cm.² (solid lines) and the potential difference (broken lines) across the skin (above) and gastric mucosa (below) of the frog. The arrows indicate the time of addition of the cholera filtrate

shown in Fig. 1, it was established that the minimal effective concentration of the cholera filtrate used was about 60 μgm./ml. The same effect was produced by adding the toxin to the solution on the anatomical outside of the skin only. Adding the toxin to the solution on the inside of the skin did not decrease the current or potential difference, indicating a possible effect on permeability of the outward-facing membrane.

Further experiments with skin from *R. pipiens* were made using sodium-22 as a tracer to prove that after addition of cholera toxin the decrease in short-circuit current was actually caused by decreased net sodium flux. Results from two representative experiments are given in Table 1. The influx of sodium was measured by addition of sodium-22 to the outside solution; net sodium flux was calculated from measurements of the short-circuit current; sodium outflux was calculated by difference. Cholera filtrate clearly decreased net sodium flux and sodium influx, that is, active sodium transport.

Table 1. EFFECT OF CHOLERA FILTRATE ON SODIUM FLUX ACROSS THE FROG SKIN

	Time (min.)	Influx	Efflux	Net flux
Experiment 1				
Control	0–30	1 10	0 19	0 91
	30–60	1 10	0 25	0 85
Cholera filtrate	60–90	0 92	0 22	0 70
	90–120	0 44	0 12	0 32
Experiment 2				
Control	0–30	2 44	0 42	2 02
	30–60	1 99	0 27	1 72
Cholera filtrate	60–90	1·88	0 25	1·63
	90–120	1 11	0 05	1 06
	120–150	0 49	−0 09	0 58

Sodium fluxes are given in μmole/cm.²/hr. for successive 30-min. periods. Cholera filtrate (550 μgm./ml.) was added to the solution on the outside of the skin.

Only a few experiments have been performed to attempt to determine the nature of the component of cholera filtrate which inhibits active sodium transport. After dialysis through 'Cellophane' the active material is present in the dialysate. The activity is not measurably decreased by heating for 1 hr. at 80° C. Its properties therefore resemble those of the cholera endotoxin described by Burrows[6], and differ markedly from those of receptor destroying enzyme[7] (neuraminidase). Further experiments are in progress to determine the nature of the active material. The effect on sodium transport is consistent with our hypothesis for the diarrhœa of cholera.

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PATHOLOGY

Influence of Hyperthyroidism and of Thyroidectomy on Induced Mammary Cancer

It has been found[1] that the intragastric administration of optimal quantities of 3-methylcholanthrene induces mammary cancer with great rapidity in females of a susceptible strain of rats under standardized conditions; all the animals have invariably developed multiple mammary cancers within two months. Sex hormones are of critical significance[2] in the induction of mammary cancer by aromatic hydrocarbons. The effects of hyperthyroidism and of thyroidectomy were investigated in the present work.

Female rats of the Sprague–Dawley strain were received from a dealer at age 42 days, and certain groups were subjected to ovariectomy or thyroparathyroidectomy on the same day under ether anæsthesia. The thyroidectomized rats were supplied 1 per cent calcium lactate as drinking fluid thereafter. At age 63 days all the animals were fed 3-methylcholanthrene 10 mgm., dissolved in sesame oil (1 ml.) by gastric intubation, and this was repeated semi-weekly for 7 weeks. In addition, 3-methylcholanthrene was administered similarly to a group of intact rats for purposes of control, and to two groups receiving l-thyroxine 0·5 mgm., or 1·0 mgm., respectively, beginning at age 63 days. l-Thyroxine was freshly prepared daily and administered intraperitoneally 6 days each week for 7 weeks. The rats were examined daily for palpable mammary cancer and each tumour was confirmed histologically. The cytology of the vagina was studied frequently by preparing vaginal smears.

Among criteria for completeness of thyroidectomy were a profound depression of body-growth (Fig. 1) and the findings at necropsy of small adrenal glands (41·1 ± 8 mgm.) and a small spleen. The spleen was approximately one-third the size of that of intact rats; the adrenal glands of the intact control rats weighed 84·6 ± 10·8 mgm. Ten of the thyroidectomized rats had regular 5-day œstrous cycles, while two animals had irregular cycles. l-Thyroxine (0·5 mgm.) did not modify the rate of body growth. Rats receiving l-thyroxine (1 mgm.) grew at a normal rate for 3 weeks, but body growth was retarded significantly thereafter (Fig. 1).

All normal control female rats, and those receiving l-thyroxine (0·5 mgm.), developed multiple mammary cancer (Table 1), which grew rapidly to a large size. Frequently the tumours attained a weight of 15 gm. by the ninetieth day of the experiment.

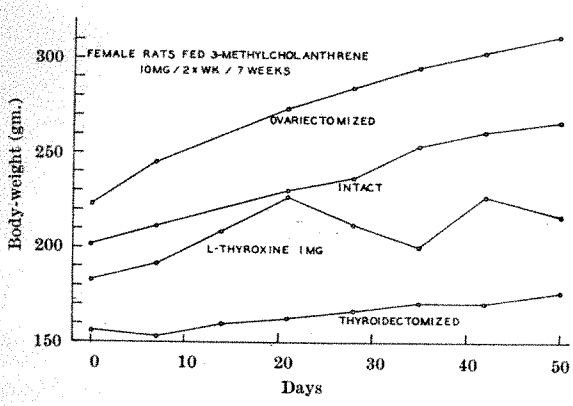

Fig. 1. Mean growth-rates of rats receiving 3-methylcholanthrene and other treatments

Table 1. Influence of Ovariectomy, Thyroidectomy and Thyroxine on Incidence of Mammary Cancer in Female Rats fed 3-Methylcholanthrene

	No. of rats	Rats with tumours	Appearance of palpable tumours (days) Range	Median	Mean
Intact, controls	10	10	40–78	57	60·5 ± 12·1
Ovariectomized	10	3	66–127	—	—
Thyroidectomized	12	7	52–134	119	106 ± 28·5
l-Thyroxine (0·5 mgm.)	10	10	35–69	43	49·5 ± 11·6
l-Thyroxine (1 mgm.)	11	4	64–119	—	—

Ovariectomized or thyroidectomized rats and animals receiving l-thyroxine (1 mgm.) had a significant decrease in the incidence of mammary cancer and a delay in their development. Only solitary cancers developed, and these remained small during observation for 6 months; the weight of the largest tumours was less than 100 mgm.

The decrease in incidence of mammary cancer in ovariectomized rats is certainly due to the deficiency of ovarian hormones. The decrease in the incidence of breast cancer in the thyroidectomized rats can be attributed to the influence of the consequent smaller calorie intake, which has been shown to have marked effects on the genesis of spontaneous and induced tumours[3,4]. In the case of rats receiving large amounts of l-thyroxine some other mechanism is more likely. It was of interest that ovarian function was preserved in most of the thyroidectomized rats despite the depression of the rate of body-growth.

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Myxomatosis in a Californian Brush Rabbit (*Sylvilagus bachmani*)

Since myxomatosis was first reported near San Diego in 1930[1,2] there have been sporadic outbreaks of the disease in commercial rabbitries along the coast at least as far north as San Francisco. Sharp outbreaks of a disease highly lethal for European rabbits (*Oryctolagus cuniculus*) have been interspersed with long quiescent periods; a pattern which suggests that the disease is maintained elsewhere than in European rabbits used for commercial purposes. Although it has been suggested[2,3] that wild rabbits (*Sylvilagus* spp.) might be the reservoir, this has never been demonstrated.

Two simultaneous outbreaks of myxomatosis were reported in California during August 1959. One of these was at Palo Alto, 40 miles south of San Francisco, and the other was in commercial rabbitries between Vista and San Luis Rey, near San Diego.

The outbreak at Palo Alto was confined to one group of eight pet European rabbits, and a single rabbit in a group of seven on a neighbouring property. There are no commercial rabbitries in this semi-rural residential area, although there are several small colonies of pet rabbits scattered through the district. There appeared to be no connexion between this outbreak and the larger one in southern California.

Three brush rabbits (*Sylvilagus bachmani*) were trapped in the immediate vicinity of the affected colony at Palo Alto. One of these had a small and rather dry tumour on its left foreleg. This was removed aseptically and stored in sterile 50 per cent glycerol. Afterwards it was ground in a chilled mortar and suspended in calf serum saline containing antibiotics. An aliquot of 0·8 ml. of the approximately 10 per cent suspension was inoculated intradermally at several sites on the plucked flank of a domestic rabbit (*Oryctolagus cuniculus*). Small palpable nodules were detectable at the sites of inoculation on day 3, and these had merged into a flat plate-like tumour by day 5. The rabbit died on day 9 displaying typical but subdued symptoms of myxomatosis; a syndrome characteristic of the disease produced by the Californian prototype strain[3].

The sera of all three brush rabbits contained complement-fixing antibodies against myxoma antigen; the serum of the infected rabbit having a titre of 1/320. The antigen used in these tests was prepared with a strain of myxoma virus recently recovered during an outbreak in laboratory rabbits in Panama. This strain causes symptoms similar to the classical South American strains (for example, Brazil/Campinas/1949/1-Lausanne)[3]. The sera of sixteen brush rabbits trapped several miles from the outbreak area were negative.

This demonstration of the occurrence of infection with myxoma virus in wild *Sylvilagus bachmani* lends considerable support to the view that myxomatosis is enzootic in the wild rabbits of California, and it seems likely that the sporadic outbreaks of the disease in commercial rabbitries are due to transmission by mosquitoes from this reservoir. It will be recalled that this pattern is similar to that demonstrated by Aragao[4] for myxomatosis in South America, where the reservoir host is the tapeti (*Sylvilagus braziliensis*).

Observations made at both outbreak areas and results of current experiments on transmission and immunology of myxomatosis in brush rabbits are being prepared for publication elsewhere.

These investigations were aided by a grant from the Wool Research Committee of the Commonwealth of Australia.

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BACTERIOLOGY

Brucella Bacteriophage

PARNAS *et al.*[1,2] obtained 14 samples of *Brucella* bacteriophage from old cultures of *Brucella abortus* and compared with these a *Brucella* phage originally isolated from manure in the U.S.S.R. The phages were described as being round, elementary bodies 60–80 mμ in diameter but with no tail. Cultures of *Br. abortus* were lysed by the phage, but cultures of *Br. suis*, *Br. melitensis* and a non-typical *Br. abortus* strains were not lysed. These observations have been confirmed by other workers[3,4].

A sample of the bacteriophage was received from Poland (through the courtesy of Dr. M. Kaplan, World Health Organization, Geneva). Originally, the phage was propagated by addition to young, actively growing cultures of *Br. abortus* strain 544 in Albimi broth but, later, a preparation with a much higher titre was prepared by the double layer method[5]. The phage was suspended in 0·033 *M* phosphate buffer containing 0·002 *M* magnesium, 0·00025 *M* calcium and 1/10,000 albumin[6]. Assay of this material on *Br. abortus* 544 gave a value of $2 \cdot 8 \times 10^{10}$ plaque-forming particles/ml. Two kinds of plaques were found, one being 2·5 mm. in diameter and the others being 0·1–0·5 mm. in diameter (Fig. 1). Repeated subculture of single small and large plaques still gave rise to a mixture of small and large plaques.

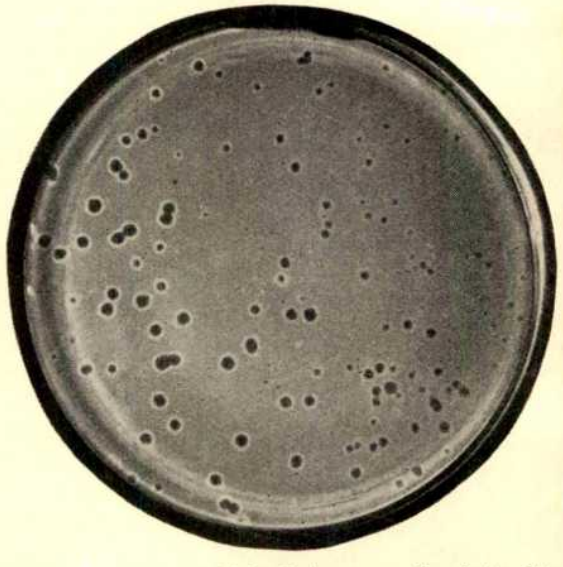

Fig. 1. The different kinds of plaques on *Br. abortus* 544

For phage typing, *Brucella* cultures were grown on serum dextrose agar for 24–36 hr. and the growth suspended in buffered saline. A loopful of the suspension was cultured on well-dried, serum dextrose agar plates and 0·02 ml. of the phage preparation, at the routine test dilution of 10^{-3}, spotted on the culture. Readings were taken after 24 and 48 hr. of incubation. All cultures of *Br. abortus* (including those of type II Wilson) were lysed but none of 4 cultures of *suis*. However, of 33 cultures of *Br. melitensis* studied, 24 were lysed by the phage preparation. All the *melitensis* cultures that were lysed had been isolated in Great Britain—mostly from bovine milk samples.

In another experiment, the phage preparation was titrated using *Br. abortus* strain 544 and *Br. melitensis* strain *H* (isolated in Britain) as host cultures. The value against *abortus* was $2 \cdot 8 \times 10^{10}$ plaque-forming particles/ml. and against *melitensis* 9×10^{9} plaque-forming particles/ml. Therefore the *Brucella* phage is able to lyse not only *Br. abortus* but also some strains of *Br. melitensis* as well.

For electron microscopy, the phage was washed in 0·033 *M* phosphate buffer containing 0·00025 *M* calcium chloride and examined by the negative contrast method[7]. The phage particles were polyhedral, 65 mμ across, hexagonal in plan view and bore a wedge-shaped tail, 14 mμ long, attached to one corner (Fig. 2). They are indistinguishable from *coli* phage *T*3 (Bradley, D. E., and Kay, D., unpublished work) and are believed to be the first example of this morphological type outside the *coli–typhoid* group of phages.

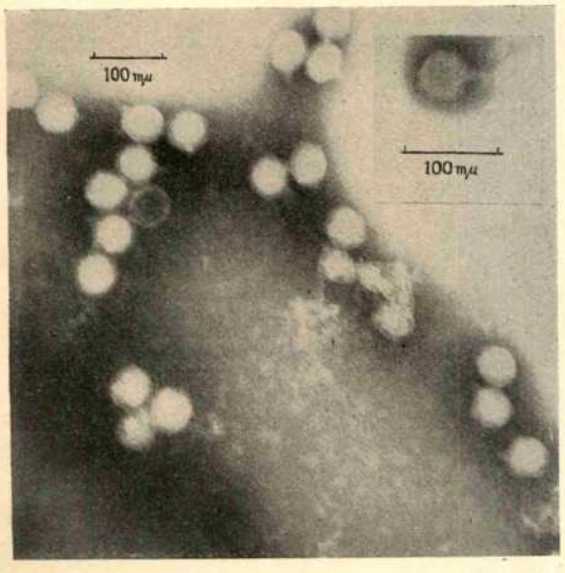

Fig. 2. *Brucella* bacteriophage. Negative contrast preparation with phosphotungstic acid

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Sensitivity to Dihydrostreptomycin of Enterobacteriaceae Strains on Media containing Ammonium

In the course of investigations of the fertility of some strains of Enterobacteriaceae, it was observed that *Citrobacter* (*E. freundii*) strains grew well on minimal medium plates supplemented with galactose 1 per cent and dihydrostreptomycin 100 μgm./ml. On the same medium, *E. coli* strains showed no growth. The *Citrobacter* strains were isolated during 1942–43 before the 'streptomycin era'. On complete medium with the same amount of dihydrostreptomycin, both *Citrobacter* and *E. coli* strains were completely inhibited. Even though an explanation of this phenomenon has not been reached as yet, a brief report on the results obtained so far will be given here.

The minimal medium was 'EMS', which contains ammonium sulphate as nitrogen source, magnesium sulphate, sodium chloride, dipotassium hydrogen phosphate, succinate, eosin methylene blue as indicator, and in this case galactose 1 per cent in addition. 'EMB', which was the complete medium used, contains peptone 1 per cent, dipotassium hydrogen phosphate, indicator and galactose 1 per cent. Plates were inoculated with one drop of a suspension (about 10^8 cells/ml.) in saline of a 20-hr. broth agar plate culture. The plates were read after 48 hr. at 37° C.

Table 1 shows the results of sensitivity tests on 'EMS' and 'EMB' medium supplemented with 100 μgm./ml. dihydrostreptomycin. A number of Enterobacteriaceae strains belonging to the biochemically defined genera *Salmonella*, *Arizona*, *Klebsiella* and *Cloaca* are included. Some *Shigella*, *Proteus*, *Providence*, *Hafnia*, *Morganella* and *Rettgerella* strains were also examined, but, as many of these grew only poorly or not at all on minimal medium, results with these strains are not recorded in Table 1. It appears that almost all *E. coli*, *Klebsiella* (and *Cloaca*) strains were sensitive to 100 μgm./ml. dihydrostreptomycin on both complete and minimal media. In contrast, all the *Salmonella* and practically all the *Citrobacter* strains were resistant to dihydrostreptomycin when tested on 'EMS' (minimal) medium, while the same strains were sensitive on 'EMB' (complete) medium. Some of the few *Arizona* strains examined were resistant and some were sensitive on 'EMS' streptomycin medium. In this connexion, it should be noted that the four *Arizona* strains that were streptomycin-resistant on 'EMS' medium were diphasic. None of the six streptomycin-sensitive strains was diphasic.

As mentioned above, the suspensions used for inoculation were made in distilled water from broth agar plates incubated at 37° C. for 20 hr. The results were the same when the inoculation suspen-

Table 1. Resistance of Enterobacteriaceae Strains to Dihydrostreptomycin on Minimal and Complete Media

	No. of strains	'EMB'		'EMS'	
		R	*S*	*R*	*S*
Salmonella	25	0	25	25	0
Citrobacter	31	0	31	26	5
Arizona	10	0	10	4	6
E. coli	205	0	205	0	205
Klebsiella	63	0	63	0	63
Cloaca	7	0	7	0	7

All media contain dihydrostreptomycin 100 μgm./ml. *R*, Growth; *S*, no growth. Strains which were streptomycin-resistant were excluded.

sions were prepared from minimal medium plates ('EMS' galactose).

Table 2 gives the results of sensitivity tests on 'EMS' and 'EMB' media supplemented with galactose and varying concentrations of dihydrostreptomycin, using strains selected at random from different genera of Enterobacteriaceae. It will be seen that the phenomenon described above for *Citrobacter* strains seems to be common for bacteria belonging to Enterobacteriaceae, that is, when high resistance to dihydrostreptomycin is found on minimal medium, a comparatively high, but in absolute figures much lower, resistance is found on complete medium. This also means that it is possible for all genera of Enterobacteriaceae to find a concentration of dihydrostreptomycin which will inhibit all growth on 'EMB' medium, while the same concentration on 'EMS' medium will have no visible effect on the growth. The level at which inhibition occurs varies between the different genera, and is exceptionally high for *Salmonella* and *Citrobacter*.

Table 2. INHIBITORY CONCENTRATIONS OF DIHYDROSTREPTOMYCIN ON COMPLETE AND MINIMAL MEDIA

Genus	Strain	'EMB'	'EMS'
		Dihydro-streptomycin (μgm./ml.)	Dihydro-streptomycin (μgm./ml.)
Salmonella	4066*	128	8,192
Citrobacter	Ballerup 1	16	2,048
Arizona	Arizona origin	<2	32
E. coli	*K*1	<2	32
Klebsiella	*K*20	<2	16
Cloaca	8127/51	4	32

* *S. typhi murium.*
Tests were read after 48 hr. at 37° C. The figures indicate the plates with the lowest concentration of dihydrostreptomycin which showed no growth. The plates contained two-fold dilutions of dihydrostreptomycin from 2 μgm./ml. to 8,192 μgm./ml.

It should be mentioned briefly that the principle described could be used for differential diagnosis between genera of Enterobacteriaceae, provided that the results can be confirmed on a larger material. Furthermore, the minimal medium described seems to act as an excellent primary selective medium for *Salmonella* and *Citrobacter* strains.

In order to ascertain which factor(s) were responsible for the great difference in sensitivity on minimal medium and on complete medium, some new media were devised. Common to these was the following basic medium called *B*: sodium chloride 1 gm., magnesium sulphate 1 gm., dipotassium hydrogen sulphate 2 gm., glucose 10 gm., agar 20 gm., distilled water 1,000 ml. The following additions were made: *B*1 = *B* + peptone 'Orthana' 0·2 per cent, *B*2 = *B* + casamino-acid 'Difco' 0·2 per cent, *B*3 = *B* + ammonium sulphate 0·5 per cent, *B*4 = *B* + ammonium sulphate + peptone 'Orthana' 0·2 per cent, *B*5 = *B* + ammonium sulphate + casamino-acid 'Difco' 0·2 per cent.

These five media were supplemented with dihydrostreptomycin in two-fold dilutions from 0·07 μgm./ml. to 10,000 μgm./ml. One *coli* strain, the test strain for *O*-antigen 0100, and a *Salmonella typhi murium* strain *Br* 4066, were tested on these media. The plates were inoculated with suspensions from 20-hr. broth agar plates in amounts which would give about 500 colonies per plate on a complete medium without streptomycin. Table 3 shows the concentrations of dihydrostreptomycin which completely inhibit visible growth on the different media. It will be seen that the great difference in sensitivity found on *B*1 and *B*2 on one hand, and on *B*3, *B*4 and *B*5 on the other, can be explained by the presence of ammonium sulphate. Similar results were obtained when ammonium sulphate was substituted by ammonium chloride. It was further found that the use of 3–4-hr. broth cultures for inoculation did not change the results. The conclusion must be therefore that the presence of ammonium in the media will hinder the activity of dihydrostreptomycin to a very great extent, namely, 20–100 times more dihydrostreptomycin is necessary to inhibit growth on the minimal medium than on complete medium. This effect is not caused by differences in *p*H, as *p*H determination of the five different media just before pouring showed only variations from 6·8 to 7·1. In order to test whether dihydrostreptomycin inhibited the transport of amino-acids through the cell membrane, examination was made to see whether dihydrostreptomycin could hinder the growth of amino-acid-dependent mutants in media supplemented with the appropriate amino-acids. Three mutants of *E. coli* 0100, one histidine-dependent, one tryptophan-dependent and one leucine-dependent, were tested on *B*1 and *B*3 media supplemented by the amino-acids in question; dihydrostreptomycin concentration 2·35 μgm./ml. It was found that at least these mutants were able to utilize the amino-acids added to the media also when dihydrostreptomycin was present.

Table 3. INHIBITORY CONCENTRATIONS OF DIHYDROSTREPTOMYCIN ON MEDIA WITH AND WITHOUT AMMONIUM SULPHATE

	Media without ammonium sulphate		Media containing ammonium sulphate		
	*B*1	*B*2	*B*3	*B*4	*B*5
E. coli 0100	0·14	0·14	9·0	9·0	9·0
Salmonella 4066*	50	50	5,000	5,000	5,000

* *S. typhi murium.*
The experiment was carried out as plate dilution test. Figures indicate the lowest concentration of dihydrostreptomycin in μgm./ml. which will completely inhibit growth.

It would appear that dihydrostreptomycin interferes with the availability of nitrogen when this is present as amino-acids or more complex compounds. When the micro-organisms are able to utilize ammonia, the presence of ammonium salts will render the bacteria resistant to very high doses of dihydrostreptomycin.

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BIOLOGY

Cover on River Bottoms

IN a previous communication[1], C_v was defined as the area of bottom covered by stones in a given area of stream bed. It was also suggested that this concept could be expressed as the ratio of the covered bottom to the sample area and written as a fraction varying from 0 to 1. The same term cannot, however, be used for both measure of the area and the fraction, and it is therefore proposed to restrict the term C_v to the prior definition so that C_v is expressed as an area. The term C_{vf} is proposed for the fraction covered

bottom/sample area and could be conveniently referred to as the 'cover fraction'.

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Tolerance to Maternal Skin Grafts in Rabbits induced by Hyaluronidase

VASCULARIZED transplants are permanently successful only between identical twins or within a highly inbred strain. Even homografts from the mother to her litter are destroyed by the immunological process initiated by her transplant antigens[1]. However, tolerance for individual specific transplant antigens can be produced by the direct injection of donor cells into the fœtal or neo-natal animal[1]. These offspring accept grafts of normal tissue from the antigen donor. In contrast, uninjected control animals reject similar homologous transplants.

This report describes a biochemical method for the production of tolerance to maternal tissues by the intravenous injection of hyaluronidase into the pregnant rabbit. Presumably, the hyaluronidase alters permeability relationships so that the specific transplantation antigens pass from the pregnant rabbit to the litter.

Sixteen pregnant rabbits were given a single intravenous dose of 15–45 turbidity reducing units of hyaluronidase ('Infiltrase', Armour Laboratories, Chicago 11, Illinois). They were injected at 10–27 days after an observed coitus (Table 1). The gestation period in these outbred albino rabbits is 31 days. Nine litters from the injected mothers, a total of 44 progeny, were available for grafting when they were about 12 weeks old. Several rabbits failed to produce offspring, and some of the young died soon after birth.

Full-thickness skin grafts from the mother were applied to sites on the ears of the offspring. These transplants were about 3 cm. in diameter and were held in place with silk sutures. The grafts were observed daily. Rejection of a graft began with hyperæmia and œdema and was followed within 24 hr. by the formation of a hard dry scab. The initial hyperæmia was taken as the end-point of graft survival. All the control grafts were clearly devitalized by the fifth to the seventh day (Table 1). To eliminate the possibility that our sample of 10 controls might not adequately represent the total population we have assumed that only grafts remaining intact for more than 12 days demonstrate a significantly prolonged survival.

The experimental results (Table 1) indicate that intravenously injected hyaluronidase produces tolerance in the 11–19 day period of gestation. The progeny from animals injected on the tenth or after the twenty-second day of pregnancy failed to show a significant degree of tolerance to skin grafts. The best results thus far obtained are in the 11–15-day interval of fœtal development. Eight of the 15 young from pregnant mothers injected during the 11–15-day period of gestation showed significant prolongation of graft survival. One graft is still viable at 40 days and even shows some hair growth.

Of 44 experimental animals, 19 died during the course of these experiments. They are indicated by italicized numbers in the last column of Table 1. The cause of death has not been established. Only an occasional animal with stunted growth was observed.

Table 1. SURVIVAL OF SKIN GRAFTS FROM MOTHER TO OFFSPRING FOLLOWING THE INTRAVENOUS INJECTION OF HYALURONIDASE INTO THE PREGNANT RABBIT

Exp. No.	Days of pregnancy at injection	Dose of hyaluronidase (turbidity reducing units)	Graft survival* (days)
1	—	none	6, 6, 5, 5
2	—	none	7, 7, 7, 7, 6, 6
3	10	30	12, 11, 9, 9, 8, 7
4	11	30	>40, 15, 14, 10, 8, >*6*, 6
5	14	30	>*12*, >*11*, 8
6	15	15	>*21*, >*18*, 9
7	15	30	14, 14
8	18	45	10, 7, 7, 7, 5
9	19	45	>*11*, *16*, >11, 11, >*9*, >*9*, >*9*, >*8*
10	22	45	9, *8*, 8, 8, >*6*, *6*, *6*, *4*, *4*
11	27	45	7

* Each figure is for a single member of the litter. The italicized values are for animals that died within 24 hr. of their last observation. The > sign indicates that the graft was in good condition at the time of death.

The pregnant mothers appeared unharmed by the low dose of hyaluronidase, 15–45 turbidity reducing units. The injection of 150–450 turbidity reducing units did not produce toxic effects in a few acute experiments.

Fig. 1 shows a microscopic section of a graft taken from experiment 6. This graft has good survival of all cell layers at 21 days. There is a mild infiltrate of lymphocytes.

Billingham, Brent and Medawar[1] tested 29 rabbits from four litters with grafts from their untreated

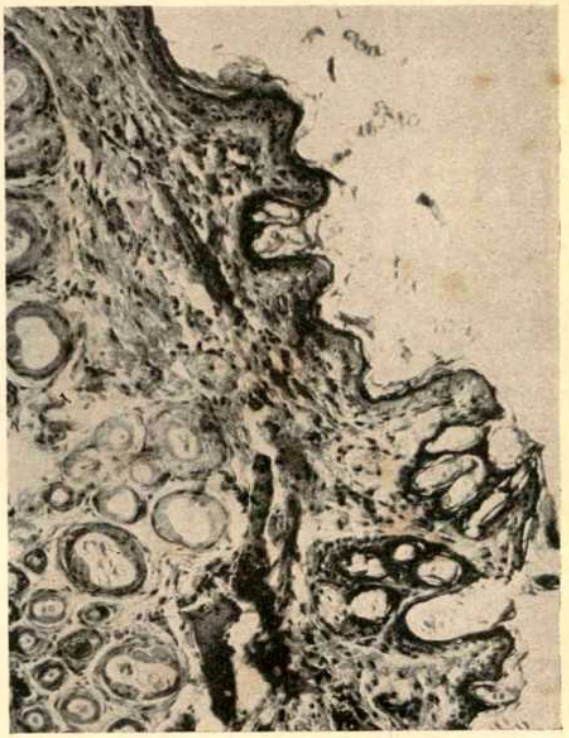

Fig. 1. Tissue section from a maternal skin graft 21 days after transplantation (Exp. 5, Table 1). All the cell layers are in good condition. A mild infiltrate of lymphocytes is present. (Hæmatoxylin and eosin, × 90)

mothers. None of the grafts survived for more than 12 days. These results, which we have confirmed in our control experiments (experiments 1 and 2), indicate that sufficient individual specific antigen to produce immunological tolerance normally does not pass from mother to fœtus. However, maternal tolerance has been produced in rats by Lengerova[2], who irradiated animals on the fifteenth day of their pregnancy. Despite many fœtal deaths, enough of the progeny survived to demonstrate immunological tolerance to their mother's tissues.

Porter[3] has recently demonstrated by direct injection that the twenty-second day of development in the fœtal rabbit represents the end of the period for production of tolerance. Our results also indicate that maternal tolerance terminates at this stage. The present preliminary results further show that maternal tolerance can be obtained by the intravenous injection of hyaluronidase as early as the eleventh day of fœtal development.

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A Gular Plate in *Albula vulpes* (L.)

THE Elopidae and Megalopidae are considered to be the most primitive families of teleosts chiefly for three reasons: (1) the presence of an unpaired gular plate; (2) the presence of a true ethmoidal commissure between the infra-orbital sensory lines of both sides[1]; (3) the conditions with regard to the skeleton of the caudal fin[2]. In addition it may be mentioned that the Elopidae still possess a bucco-hypophysial canal (in the parasphenoid)[3] and that in the Megalopidae there persists a conus arteriosus with two rows of valves. The latter primitive character is also encountered in *Albula vulpes* (L.), which has therefore also been regarded as a primitive teleost.

According to Ridewood[4] and statements in modern text-books (for example, Berg[5]) *Albula vulpes* lacks an unpaired gular plate. In order to examine this condition, I stained a head of the latter species (Grenada, West Indies, June 28, 1955) in alizarine. By removing the skin rostral to the branchiostegal rays I then found immediately below the corium a long, narrow, median bone plate (Fig. 1) which beyond question is a gular plate at a more advanced stage of reduction than the corresponding plate in *Elops* and *Megalops*. The detection of this plate naturally does not mean that *Albula vulpes* would have a closer relationship to the Elopidae and Megalopidae than what has so far been assumed, for as is clear from other facts, *Elops*, *Megalops*, and *Albula* all represent evolutional lineages of their own.

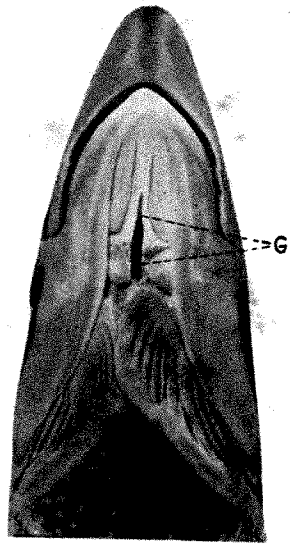

Fig. 1. *Albula vulpes* (L.). Head viewed from the ventral side. (2/3 nat. size)

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Variations in the Serum Specificities of Higher Primates detected by Two-Dimensional Starch-Gel Electrophoresis

THE proteins of human serum subjected to two-dimensional zone electrophoresis, a combination of filter-paper and starch-gel electrophoresis, can be resolved into at least 21 distinct components[1,2]. Some of these proteins, for example, haptoglobin and transferrin, were found to be made up of components which exhibit genetically controlled variations in the human population[1–3]. To enlarge our view of the evolutionary process underlying such variability in serum specificities, we began a comparative study of the distribution of protein components in the sera of the Primates. So far, sera from 13 chimpanzees, 19 cynomolgus monkeys, 17 rhesus monkeys, and several other macaques in addition to human sera have been analysed by two-dimensional zone electrophoresis in a discontinuous system of buffers[4,5]. This communication reports on the results gathered up to now which enable us to distinguish the four primate groups and which emphasize a taxonomic gradation in the differences among the sera examined.

Examples of the typical starch-gel patterns of human, chimpanzee, rhesus and cynomolgus sera are shown in Fig. 1. It can be noted that each pattern has its own characteristic constellation of components. The human and chimpanzee patterns show remarkable similarities in respect to prealbumin, albumin, α-1 globulins (especially the presence of orosomucoid in the chimpanzees) and the fast moving α-2 globulins.

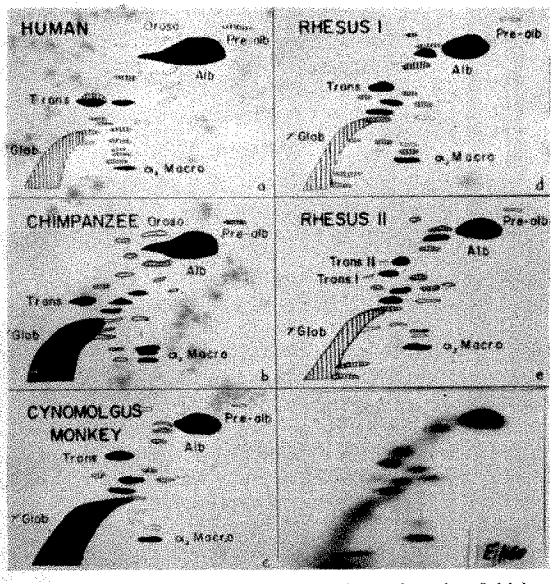

Fig. 1. Two-dimensional starch-gel electrophoresis of higher primate sera. The typical results in the four primate groups are represented diagrammatically. In addition, a photograph of the serum pattern of the rhesus monkey with the two transferrins is also presented

However, the two Hominoidea differ in the following way: the transferrin of the chimpanzees migrated more slowly on filter paper than the transferrin of the humans, and the α-2 macroglobulin ($S\alpha$-2) of the chimpanzees migrated more rapidly than the human protein. The amount of gamma globulin in the chimpanzees always exceeded the amount found in humans.

The starch-gel patterns of the macaques (cynomolgus and rhesus) could be distinguished from those of the humans and chimpanzees in several ways. For example, the prealbumin could barely be detected and the amount of albumin was not as large. Perhaps the clearest diagnostic feature of the macaque patterns was the absence of a fast-moving α-1 globulin of orosomucoid mobility, and the presence of a new component which has the filter paper mobility of a γ-1 globulin but in starch-gel migrates faster than gamma globulin and slower than transferrin.

The closer taxonomic relationship of the cynomolgus and rhesus monkeys to each other than to any of the other primates is clearly reflected in the starch-gel patterns. Whereas a number of features in the patterns distinguish the macaques from the higher anthropoids (as we have indicated above), very few features distinguish the sera of *Macaca* (cynomolgus) *irus* from *Macaca* (rhesus) *mulatta*. In respect to the intrageneric differences, we observed that the cynomolgus sera always had a much larger quantity of gamma globulin.

Furthermore, in our limited sampling, the rhesus monkeys showed more intraspecific variation in serum pattern than the cynomolgus monkeys. An example of this is presented in Fig. 1*e*, in which a second transferrin can be seen to be directly ahead of the first by both the filter paper and starch-gel separations. This result confirms the observation of Bangham and Tee, reported by Allison[6], of a β-globulin variation among rhesus monkeys. In our work 10 of the 17 rhesus sera showed the additional component in contrast to the 19 cynomolgus sera which only showed the one transferrin. It is of interest that the rhesus monkey occupies a broader ecological habitat than the cynomolgus, and because of this, one is tempted to speculate that between the two species the rhesus will show more examples of polymorphism. Obviously, extensive surveys in natural populations will have to be conducted before conclusions of this type in respect to the Primates can be arrived at.

The identity of the various components was established by immunochemical methods, of which immunoelectrophoresis[5] was particularly suitable. For this purpose, we employed rabbit antisera (supplied by the Behringwerke, Marburg, Germany) to human γ-globulin, transferrin, α-2 macroglobulin, albumin, and prealbumin[7]. We also employed chicken antisera against the same proteins and against orosomucoid[8]. The primate sera belonged to the collection gathered for a previous study[9]. It is again a pleasure to thank Drs. G. D. Brigham, Sidney Gaines, Albert B. Sabin, and George B. Rabb for providing these samples. The generosity of Prof. H. E. Schultze in having portions of his highly specific rabbit antisera sent to us is also appreciated. This research was supported by the National Institutes of Health, National Multiple Sclerosis Society (U.S.A.), and Children's Fund of Michigan.

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Metabolism of D-Xylose by Moulds

THE filamentous fungi have been called ubiquitous and omnivorous, and certainly they are widely distributed in Nature where they play a most important part in the decomposition of complex organic matter and as pathogens for many plants. Since much of the plant-derived organic matter in Nature contains a large amount of pentoses, mostly in the form of pentosans, a study of the pentose metabolism of the fungi which decompose this material is of interest not only because it is a basic phenomenon, but also, as we have found, because it is somewhat unique.

Early work on the fermentation of D-xylose-1-^{14}C by the resting cells of *Fusarium lini* Bolley suggested a dissimilation similar to that in *Lactobacillus pentosus*[1]; namely, the conversion of the D-xylose to equimolar quantities of carbon dioxide, ethanol and acetic acid presumably following a split of the molecule into a C_2 and a C_3 fragment. Another aspect of pentose metabolism in filamentous fungi is the formation of mycelial glucosan from pentoses labelled with carbon-14 by an unknown pathway in *Aspergillus niger*[2]. Indeed, there is but little information

on the enzymatic sequences and intermediates of pentose metabolism in any of the fungi. In contrast, recent intensive studies on the metabolism of pentoses by various bacteria have revealed two common features in the sequence of intermediates. Metabolism is initiated with the conversion, by the appropriate isomerase, of the aldopentose to the corresponding ketopentose; specifically D-xylose and L-arabinose are converted to D-xylulose and L-ribulose respectively[3-11]. The second feature common to the utilization of the pentoses is the conversion of the ketopentose to the important intermediate D-xylulose-5-phosphate. This is accomplished by the phosphorylation of the ketopentose followed by epimerization to D-xylulose-5-phosphate[12,13]. The latter intermediate is further metabolized by well-established pathways.

During the course of work in this laboratory on D-xylose metabolism by cell-free extracts of *Penicillium chrysogenum* an enzymatic sequence was found for the interconversion of pentoses which is quite different from that in the bacteria. Instead of being converted to the corresponding ketopentose, D-xylose is reduced rapidly to D-xylitol by a triphosphopyridine nucleotide-linked reductase, followed by oxidation of the D-xylitol to D-xylulose or L-xylulose with a diphosphopyridine-linked dehydrogenase. Whether D- or L-xylulose is formed depends upon whether the C_2 or C_4 carbon is oxidized, since xylitol is symmetrical[14,15]. When the mould is grown on L-arabinose a similar enzymatic mechanism converts this pentose to L-ribulose and L-xylulose with the formation of L-arabitol as an intermediate[16].

To determine how general this metabolic pattern is among micro-organisms a study was made on fourteen species of moulds and yeasts selected from nine genera according to their ability to grow on D-xylose as the only carbon source and their common occurrence in Nature. The cultures were transferred twice on a xylose-mineral salts-agar slant and spores from the second slant were inoculated into the same medium minus the agar[15]. This synthetic medium was not the best for all the fungi; however, sufficient growth occurred after 72 hr. on a rotary shaker so that the cells could be harvested for the preparation of cell-free extracts. The enzyme preparation from yeasts was made by breaking the cells with small glass beads in a 10 kc./s. sonic oscillator and from the moulds by grinding a washed sand–cell mixture in a chilled mortar. Table 1 gives the experimental details and the results of this general survey. The xylitol and xylulose produced by the fungi listed in Table 1 were further identified by paper chromatography.

It should be pointed out that no attempt has been made to obtain maximum activity for any of the organisms and that the specific activities cannot be associated with the amount of growth on D-xylose in this particular medium. All the *Aspergillus* species grew luxuriantly on D-xylose and showed low specific activity for xylose reductase, whereas *Myrothecium verrucaria* grew comparatively less and showed the highest specific activity. A possible explanation of the variation in xylose reductase activity is that the glucose-6-phosphate is susceptible to phosphatases and consequently the triphosphopyridine nucleotide reducing system is destroyed. This was quite apparent with the *Neurospora crassa* experiments where considerable free glucose was evident on the paper chromatograms that were used to separate D-xylose and xylitol. With the exception of *Neurospora crassa* and *Myrothecium verrucaria*, the rate of reduced diphosphopyridine nucleotide oxidation in a mixture of D- and L-xylulose was equal to the sum of the rates on each isomer alone, indicating the stereospecificity of two enzymes; this may not be true with the exceptions mentioned.

The fourteen fungi listed in Table 1 as possessing this unique method of D-xylose metabolism were the ones in the twenty which were tested that grew on D-xylose. *Escherichia coli*, *Aerobacter aerogenes*, *Bacillus subtilis*, *Bacillus cereus*, and *Pseudomonas aeruginosa* grew well in a medium with D-xylose as the only source of carbon, but their cell-free extracts were devoid of the reductase. It seems that this unique pathway for the metabolism of aldopentoses is confined to filamentous fungi and yeasts, thus

Table 1. SPECIFIC ACTIVITIES OF XYLOSE REDUCTASE AND XYLITOL DEHYDROGENASE IN CERTAIN FUNGI GROWN ON D-XYLOSE*

Fungi examined	Xylose reductase†	Xylitol dehydrogenase‡	Reduced diphosphopyridine nucleotide oxidation§		
			D-Xylulose	L-Xylulose	D-Xylulose and L-xylulose
Penicillium chrysogenum	2·32	0·217	1·61	1·61	3·23
Penicillium citrinum	2·33	0·261	4·58	2·68	7·20
Penicillium expansum	2·34	0·136	5·68	2·84	8·50
Aspergillus niger	0·65	0·100	1·98	2·05	3·98
Aspergillus oryzae	0·33	1·41	2·61	2·13	4·65
Aspergillus fumigatus	0·32	0·084	2·99	1·21	4·20
Aspergillus ochraceus	0·23	0·065	0·82	0·61	1·39
Rhizopus nigricans	1·53	0·088	3·08	1·63	4·61
Gliocladium roseum	1·71	0·198	3·39	1·61	5·16
Byssochlamys fulva	1·01	0·081	7·75	15·80	26·00
Myrothecium verrucaria	2·89	0·256	11·30	7·10	14·15
Neurospora crassa	0·40	0·079	21·00	7·26	22·60
Rhodotorula glutinis	1·02	0·071	13·70	7·43	20·93
Torulopsis utilis	1·39	0·112	22·10	18·55	40·15

* All the activities are corrected for endogenous reactions.

† The assay system contained 30 μmoles glucose-6-phosphate, 0·2 mgm. glucose-6-phosphate dehydrogenase, 1 μmole triphosphopyridine nucleotide, 10 μmoles magnesium chloride, 30 μmoles D-xylose and 10 mgm. protein in a total volume of 2·0 ml. of 0·05 *M* phosphate buffer at *p*H 7·2. Incubation was at 30° for 40 min. Aliquots were analysed simultaneously for xylose and xylitol by the orcinol and periodate oxidation procedures respectively after the reaction was stopped by zinc barium precipitation. The specific activity is expressed as μmoles xylose reduced per mgm. protein.

‡ The assay system contained 40 μmoles xylitol, 20 μmoles diphosphopyridine nucleotide, 10 μmoles magnesium chloride and 10 mgm. protein in a total volume of 2·0 ml. of 0·1 *M tris* buffer at *p*H 8·5. Incubation was at 30° for 1 hr. Aliquots were analysed for ketopentoses by the cysteine–carbazole colour test. The specific activity is expressed as μmoles ketopentose formed per mgm. protein.

§ The assays were made spectrophotometrically at 340 mμ. The system contained 0·16 μmole reduced diphosphopyridine nucleotide, 15 μmoles of either ketopentose or both and enough enzyme protein to give a 0·1 *O.D.* change per min., in a total volume of 0·1 ml. of 0·1 *M* phosphate buffer at *p*H 7·5. The readings were taken after a reaction time of 2 min. The specific activity is expressed as μmoles × 10^3 reduced diphosphopyridine nucleotide oxidized per min. per mgm. protein.

differentiating them biochemically from bacterial and animal cells.

A portion of this information was presented at a meeting of the Society of American Bacteriologists during May 1–5. The work was supported by grant *E*-1201 from the National Institutes of Health.

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Structure of *Acrocomia* Fruit

OF the palm kernels utilized as feeding materials, those of the coconut (*Cocos nucifera* L.) and palm nut (*Elaeis guineensis* L.) are best known. The differences in structure of the endosperm cells probably provide the most reliable means of distinguishing between the two species in meals or cakes. The endosperm cells of the coconut are more elongated than those of the palm nut and their walls are uniformly thickened, as opposed to the pitted walls of *Elaeis*[1].

Occasionally, commercial samples are obtained under the description of Paraguayan palm. The botanical name for this plant has been given as *Acrocomia totai*. This palm is an important oil plant in Paraguay[2] but no descriptions have been found of the histology of the fruit. Studies of the histology of fruits and seeds can be important in plant taxonomy and are also valuable in the identification of commercial plant products.

An investigation has been carried out into the histological structure of the commercial samples of Paraguayan palm with the view of establishing some

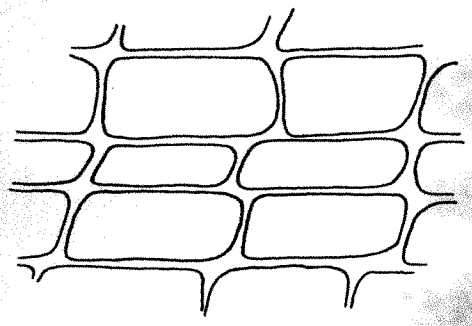

Fig. 1. Endosperm cells of *Acrocomia*. (× 200)

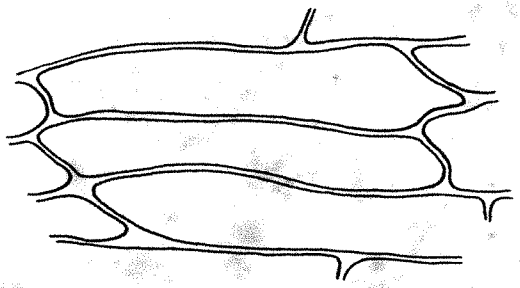

Fig. 2. Endosperm cells of *Cocos*. (× 200)

means of distinguishing between them and samples of coconut and palm nut. To augment this material, fruits of *Acrocomia sclerocarpa* Mart. have been obtained from Brazil. This species is very closely related to *totai*[2].

It has been found that, as in the case of *Cocos* and *Elaeis*, a consideration of the structure of the endosperm is most useful for the purposes of identification. Fig. 1 illustrates some typical endosperm cells of *Acrocomia* as they appear in a cleared preparation. The cells are brick-shaped, and their walls show no obvious pits. The absence of pits immediately distinguishes *Acrocomia* from *Elaeis*. In comparing the endosperm with that of *Cocos*, the shape of the cells provides the main distinguishing feature. Fig. 2 illustrates some typical *Cocos* endosperm cells. These cells are much more elongated than those of *Acrocomia*, a feature shown equally well in a longitudinal section of endosperm or a cleared preparation of a cake or meal.

It is intended to publish the details of this investigation elsewhere. I am indebted to Salamon and Seaber (consulting analytical chemists) for the supply of certain material used in this work.

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Changes in Sex in the Hop caused by Plant Growth Substances

DURING an experiment to test the effects of certain systemic chemicals on the hop plant (*Humulus lupulus* L.) the production of male flowers by a genetically female plant was noticed. This behaviour may occur naturally in some varieties; but the phenomenon has not been reported in the variety Fuggles which was used in the present experiments. These were designed originally to determine whether treatment with low concentrations of certain systemic chemicals would lead to changes in the chemical composition of the plant. For this purpose plants were sprayed with aqueous solutions of a number of phenoxy and phenylthio acids which, although similar in structure to plant growth substances, were either inactive or only weakly active[1].

Three levels of treatment were given, the plants being sprayed to run-off with 500 p.p.m. solutions of each of the acids as their sodium salts either once, twice or three times, with intervals of several days between sprayings. When flower parts appeared it was observed that male flowers had only developed

Fig. 1. Production of male organs on a genetically female plant following the application of α (2-chlorophenylthio)propionic acid

on those plants which had been sprayed with solutions of α (2-chlorophenylthio)propionic acid; three plants showed this effect, not all of which had received the maximum spray treatment.

In the following year an experiment was designed specifically to test whether the stage in growth of the plant at which the spray was applied was an important factor in relation to male flower development. The spraying was carried out as before with a 500 p.p.m. solution, and in a row of about 30 plants a different plant was sprayed at two-day intervals, beginning on July 2 and continuing until the beginning of August. The plants not sprayed were left as controls.

When the flowers developed it was seen that a large number of male flowers had developed on those plants sprayed on July 2 and 4; there were fewer on the plant sprayed on July 6, and practically none on those which were sprayed afterwards. The plants sprayed on July 8 and 10 showed slight deformities of the cones, but those plants which had received the later sprayings showed no abnormal effects and could not be distinguished from the controls.

Heslop-Harrison, in reviews of conditions governing sex expression in flowering plants[2,3], describes changes of sex resulting from treatments with the plant growth substance 2:4-dichlorophenoxyacetic acid or with the plant growth hormone indoleacetic acid. It seems possible that the weak growth properties of α (2-chlorophenylthio)propionic acid may operate in inducing the responses reported here. In this connexion, however, it is important to note that in all cases reported previously, growth substance treatment caused a change from male to female flowering whereas the changes reported here have been from female to male.

It is of interest that the experiments quoted in the literature where sex changes appeared were carried out with short-day flowering plants; the suggestion has been made, however, that long-day plants may not follow the same pattern[5], it having been observed that spinach tended to produce male flowers under short-day conditions.

Heslop-Harrison has suggested that photoperiodism may be related to natural auxin concentration; if this is the case with spinach, then either auxin concentration is lowered under short-day conditions or the initiation of male flowers arises from high auxin-levels. While the former possibility is unlikely, the latter supposition is difficult to correlate with the findings that with other plants, application of growth substances leads to the formation of female flowers.

The present experimental results with hop plants throw light on this problem if it be assumed that, as long-day plants, the hop and spinach behave similarly with respect to both day-length and applications of growth substances. A distinction may then be drawn between a long-day and a short-day flowering plant; in the former, high auxin-levels might promote the growth of staminate structures whereas in the latter, high auxin levels might promote pistillate structures.

I wish to thank Prof. R. L. Wain for his guidance and encouragement, the Hop Research Department for facilities, and Mr. R. A. Neve for his valuable help.

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STATISTICS

Structural Relations in Component Analysis

IN a recent communication, Hey and Hey[1] have described Berkson's postulate of the 'controlled variable' as unjustified and his mode of analysis as invalid. After correspondence with Hey and Hey, we feel that it is their criticisms that are not valid; had they been, they would have applied equally to the whole of regression theory. In particular, they do not seem to attach sufficient weight to the need for a careful specification of the reference distribution with which the observations are to be compared.

In our communication[2] to which Hey and Hey refer, we included Berkson's method in a list of several which can be appropriate in various circumstances; we should perhaps have stated more clearly that differing experimental conditions necessitate differing analyses, and that no one method (not even that of least squares) has overall applicability. We did point out that in some versions of the structural relations problem, the method of least squares has been shown to lead to inconsistent estimates; so that in all but the simplest cases consistency and efficiency have to be justified *de novo*.

The problem considered by Hey and Hey[1] of fitting ν linear relations to a set of n-dimensional observations all subject to error is essentially equivalent to component analysis, for which see, for example, Girshick[3] or Kendall[4]; and has been treated explicitly in econometric contexts, for example, by Tintner[5].

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FORTHCOMING EVENTS

*(Meeting marked with an asterisk * is open to the public)*

Monday, October 3

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S.W.7), at 5 p.m.—Prof. W. B. Emery: "The Antiquities of Nubia and the High Dam".

BRITISH SOCIETY FOR THE PHILOSOPHY OF SCIENCE (in the Joint Staff Common Room, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. G. L. S. Shackle: "Time, Nature, and Decision".

SOCIETY OF ENGINEERS (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Mr. W. A. Crago: "Some Notes on Hovercraft".

Wednesday, October 5

INSTITUTE OF PETROLEUM (at 61 New Cavendish Street, London, W.1), at 5.30 p.m.—Mr. J. S. Elliott and Mr. E. D. Edwards: "Synthetic Lubricants for Gas Turbines".

INSTITUTE OF INFORMATION SCIENTISTS (at Swedenborg Hall, Barter Street, Bloomsbury Way, London, W.C.1), at 6.15 p.m.—Dr. G. Malcolm Dyson: "New Research at Chemical Abstracts".*

SOCIETY FOR ANALYTICAL CHEMISTRY (at the Chemical Society, Burlington House, Piccadilly, London, W.1), at 7 p.m.—Scientific Papers.

Thursday, October 6

ROYAL INSTITUTION OF NAVAL ARCHITECTS (at 10 Upper Belgrave Street, London, S.W.1), at 5.15 p.m.—Mr. R. N. Newton and Mr. H. P. Rader: "Performance Data of Propellers for High Speed Craft".

INSTITUTION OF ELECTRICAL ENGINEERS (at Savoy Place, London, W.C.2), at 5.30 p.m.—Sir Hamish D. Maclaren, K.B.E., C.B.: Inaugural Address as President.

SOCIETY OF CHEMICAL INDUSTRY, MICROBIOLOGY GROUP (at 14 Belgrave Square, London, S.W.1), at 6.15 p.m.—Prof. A. A. Eddy: "The Chemistry of the Cell Surface".

Friday, October 7

BRITISH MYCOLOGICAL SOCIETY (in the Large Physics Lecture Theatre, Birkbeck College, Malet Street, London, W.C.1), at 10.45 a.m.—Meeting on "The Cereal Rusts".

INSTITUTION OF ELECTRICAL ENGINEERS, MEDICAL ELECTRONICS DISCUSSION GROUP (at Savoy Place, London, W.C.2), at 6 p.m.—Discussion on "Nerve Endings" opened by Dr. O. C. J. Lippold and Dr. D. R. Wilkie.

SOCIETY OF DYERS AND COLOURISTS (at the Royal Society, Burlington House, Piccadilly, London, W.1), at 6 p.m.—Prof. C. F. Carter: "Science in Industry".

SOCIETY OF CHEMICAL INDUSTRY, FINE CHEMICALS GROUP (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Prof. D. H. Hey, F.R.S.: "Some Recent Developments in Heterocyclic Chemistry".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

ASSISTANT EXPERIMENTAL OFFICER (with at least G.C.E. in five subjects, including two (science or mathematics) at "A" level, or equivalent, and laboratory experience in chemistry or biochemistry) IN THE BIOCHEMISTRY DEPARTMENT—The Secretary, Institute of Animal Physiology, Babraham, Cambridge (October 8).

LECTURER or SENIOR LECTURER (with qualifications in educational psychology and/or history and philosophy of education, and teaching experience) IN EDUCATION at the University of Queensland, Australia—The Secretary Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, October 8).

SENIOR LECTURER IN PURE MATHEMATICS—The Registrar, The University, Leicester (October 8).

ASSISTANT LECTURER (with special qualifications in physical chemistry) IN CHEMISTRY—The Registrar, The University, Manchester (October 15).

ASSISTANT TECHNICAL OFFICER (with G.C.E. in at least five subjects, two of which at advanced level (preferably including biology), or equivalent Scottish or Northern Irish qualification), for work in biological electronics and construction of apparatus for physiological research—Head of the Department of Zoology and Comparative Physiology, The University, Birmingham 15 (October 15).

PRINCIPAL LECTURER IN PHARMACEUTICS—The Principal, College of Technology, Belfast (October 21).

CHAIR OF GEOLOGY in the University of Malaya, Kuala Lumpur—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Malaya and London, October 22).

LECTURER IN MATHEMATICS, to take the subject to pass degree standard—The Principal, Bede College, Durham (October 22).

LECTURERS or ASSISTANT LECTURERS (3) IN THE DEPARTMENT OF MATHEMATICS, University of Malaya, Kuala Lumpur—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Malaya and London, October 22).

SCIENTIFIC OFFICER/SENIOR SCIENTIFIC OFFICER (with a first- or second-class honours degree in chemistry or equivalent, and well acquainted with the application of modern techniques to the analysis of foods and feeding-stuffs including estimation of amino-acids, and preferably previous experience with tropical foods) at the Tropical Products Institute (D.S.I.R.), London, W.C.1, to take charge of the analytical work in the Food Section—The Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting Ref. F.658/0A (October 29).

SCIENTIFIC OFFICER (with a first- or second-class honours degree with physical or inorganic chemistry as the principal subject) IN THE DEPARTMENT OF PEDOLOGY, for work involving investigations upon soil formational processes with a physicochemical bias—The Secretary, Macaulay Institute for Soil Research, Craigiebuckler, Aberdeen (October 29).

SENIOR SCIENTIFIC OFFICER (with a first- or second-class honours degree in a science, preferably chemistry, or equivalent, at least three years appropriate postgraduate experience, a wide interest in general scientific matters, and an aptitude for administration and dealing with people) in the Information Division, D.S.I.R., H.Q., London, to assist a survey team preparing detailed reports on selected scientific subjects and to undertake comprehensive surveys of scientific and technological problems in co-operation with representative and national and international organizations—The Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting Ref. F.666/0A (October 29).

ASSISTANT LECTURER or LECTURER IN THE DEPARTMENT OF VETERINARY PATHOLOGY—The Registrar, The University, Liverpool, quoting Ref. CV/T (October 31)

LECTURER IN PHYSICS at the University of Western Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, October 31).

ASSISTANT LIBRARIAN (graduate with a professional qualification) at the University College of Sierra Leone (Fourah Bay College)—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (November 10).

LECTURER or ASSISTANT LECTURER IN GEOLOGY at the University of Otago, Dunedin, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand and London, November 10).

ASSOCIATE PROFESSOR OF STATISTICS IN THE FACULTY OF AGRICULTURAL ECONOMICS, University of New England, Armidale, New South Wales, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, November 11).

PHYSICISTS AND RESEARCH ENGINEERS (with a first- or second-class honours degree or corporate member of a senior engineering institution, or with equivalent qualifications), for research work in the Engineering Studies Branch of the Reactor Development Division; field of research covers a very wide range of basic engineering topics, with particular emphasis on methods of extracting heat from power-producing nuclear reactors, cooled by gases, liquids and two-phased coolants—The Personnel Branch (W.340/34), U.K.A.E.A., A.E.E., Winfrith, Dorchester, Dorset (November 13).

MAY READER IN MEDICINE—The Registrar, University Registry Oxford (December 2).

READER IN SOIL SCIENCE—The Registrar, University Registry, Oxford (December 2)

ASSISTANT EDITOR (with a physics degree and a knowledge of physics literature) for Section A (Physics) of the monthly publication *Science Abstracts*—The Secretary, Institution of Electrical Engineers, Savoy Place, London, W.C.2.

ASSISTANT LECTURER or LECTURER (with an interest in vertebrate physiology) IN BIOLOGY—The Principal, Derby Training College, Uttoxeter New Road, Derby.

FELLOW IN OZONE RESEARCH in the Division of Meteorological Physics, Commonwealth Scientific and Industrial Research Organization, Melbourne, Australia, to take charge of the programme of research into the measurement of ozone distribution and the meteorological applications thereof—Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2, quoting Appointment No. 420/161.

FEMALE SCIENCE ASSISTANT (preferably recent honours B.Sc. graduate), for a three-year post in bacteriology at the Dysentery Reference Laboratory—The Director, Central Public Health Laboratory, Colindale Avenue, London, N.W.9.

GRADE B ASSISTANT IN THE DEPARTMENT OF SCIENCE TO TEACH CHEMISTRY mainly to G.C.E. "A" level and in O.N.C. courses—The Principal, Reading Technical College, King's Road, Reading.

GRADUATE (metallurgy, chemistry or physics, and preferably some language knowledge) IN THE INFORMATION DEPARTMENT, for work including abstracting, production of the Association's monthly Bulletin, answering inquiries and related matters—The Secretary, British Non-Ferrous Metals Research Association, Euston Street, London, N.W.1.

GRADUATE RESEARCH ASSISTANT IN THE DEPARTMENT OF ZOOLOGY AND COMPARATIVE PHYSIOLOGY, to work on the physiology of tissue changes during metamorphosis in insects—The Registrar, The University, Edgbaston, Birmingham 15.

LABORATORY TECHNICIAN (with experience of working with scientific or technical apparatus), to assist in the Physics Laboratories—The Headmaster, Chatham House Grammar School, Ramsgate, Kent.

LECTURER IN ZOOLOGY; a LECTURER IN ORGANIC CHEMISTRY; and a LECTURER IN BACTERIOLOGY at the University of Queensland, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1, or The Registrar, University of Queensland, St. Lucia, Brisbane, Australia.

LECTURER (with practical experience and a good honours degree) IN FLUID MECHANICS—Prof. C. M. White, Imperial College of Science and Technology, London, S.W.7.

LINACRE PROFESSOR OF ZOOLOGY—The Registrar, University Registry, Oxford.

OFFICER, Assistant Experimental Officer grade (with a degree in science or horticulture, or a diploma in horticulture), to assist in

experimental work—The Secretary, National Vegetable Research Station, Wellesbourne, Warwick.

POSTDOCTORATE FELLOW IN THE DEPARTMENT OF PHYSICS, for work on electron resonance—The Registrar, University College of North Staffordshire, Keele, Staffs.

RESEARCH ASSISTANT (CHEMIST) IN THE DEPARTMENT OF CHEMICAL PATHOLOGY, for work on problems associated with steroid metabolism—The House Governor, St. Mary's Hospital, Paddington, London, W.2.

RESEARCH ASSISTANT (with a first- or second-class honours degree in chemistry with physiology in the final year of the honours degree) IN THE DEPARTMENT OF PHYSIOLOGY AND PHARMACOLOGY—Clerk to the Governors, Chelsea College of Advanced Technology, Manresa Road, London, S.W.3.

SENIOR LECTURER (qualified to direct research) IN PHYSICS; a LECTURER (preferably with an interest in mycology, ecology or cytogenetics) IN BOTANY; and a LECTURER (preferably with qualifications in research) IN MATHEMATICS—The Clerk, Northern Polytechnic, Holloway, London, N.7.

SENIOR RESEARCH ASSISTANT (with a Ph.D. or appropriate research experience) IN THE PHYSICS DEPARTMENT—Prof. J. G. Wilson, Department of Physics, The University, Leeds 2.

TIMBER OPERATIONS OFFICER (under 50 years of age, with a university degree in forestry with at least three years practical experience in the control of timber exploitation on a large scale) in the Southern Cameroons, for the administration and management of all timber operations—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BOD.61/603/02/T.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Ciba (A.R.L.), Limited. Technical Notes No. 210 (June, 1960) Strip Heating, Part 2 (Conclusion). Pp. 6. (Duxford: Ciba (A.R.L.), Limited, 1960.) [87

The Church Information Office. Both Old and New: Fourteenth Report of the Central Council for the Care of Churches. Pp. 7+14 plates. (London: Church Information Office, 1960.) 3s. 6d. [87

Ministry of Power. Reports of H.M. Inspectors of Mines and Quarries under the Mines and Quarries Act 1954, for 1959. Scottish Division. By H. Hyde. Pp. iv+47+3 plates. (London: H.M. Stationery Office, 1960.) 3s. 6d. net. [87

The Grassland Research Institute. Experiments in Progress No. 12: Annual Report for 1958–1959. Pp. 112. 7s. 6d. The Development and Work of the Grassland Research Institute. By William Davies. Pp. ii+31+4 plates. (Hurley, near Maidenhead: Grassland Research Institute, 1960.) [117

The Chemical Society. Special Publication No. 14: Handbook for Chemical Society Authors. Pp. vii+224. (London: Chemical Society, 1960.) 21s.; 3 dollars. [117

Annual Report of the Yorkshire Philosophical Society for the year 1959. Pp. 15. (York: Yorkshire Philosophical Society, 1960.) [117

Government of Northern Ireland: Ministry of Agriculture. Leaflet No. 145: Chemical Weed Control in Horticulture. Pp. 25. (Belfast: Ministry of Agriculture, 1960.) [117

Scotland. Western Regional Hospital Board: Regional Physics Department. Annual Report of the Regional Physicist for the year 1959. Pp. ii+52. (Glasgow: Western Regional Hospital Board, Physics Department, 1960.) [127

The Council for Nature. Nature and Conservation in East Anglia. Pp. 16. (London: The Council for Nature, 1960.) [127

Bulletin of the British Museum (Natural History). Botany. Vol. 2, No. 8: On the Geographical Relationships of the Angiosperm Flora of New Guinea. By Ronald Good. Pp. 203–226. 10s. Historical. Vol. 2, No. 4: Darwin's Notebooks on Transmutation of Species. Part 3: Third Notebook, July 15th 1838—October 2nd 1838. Edited with an Introduction and Notes by Sir Gavin de Beer. Pp. 119–150. 12s. (London: British Museum (Natural History), 1960.) [197

United Kingdom Atomic Energy Authority. Sixth Annual Report for the period 1st April, 1959—31st March, 1960. Pp. vi+72+4 plates. 5s. net. Atom 1960: an Illustrated Summary of the Sixth Annual Report from 1st April 1959 to 31st March 1960 of the United Kingdom Atomic Energy Authority, with some additional material to 1st July 1960. Pp. 34. 2s. 6d. net. (London: H.M. Stationery Office, 1960.) [197

Imperial College of Science and Technology. Telecommunication as a Social Science. Inaugural Lecture, 3 November 1959. By Dr. Colin Cherry. Pp. 105–124. 4s. 6d. Physiology Has No Frontiers. Inaugural Lecture, 1 December 1959. By Prof. H. K. Porter. Pp. 125–137. 5s. Superficial Chemistry and Solid Imperfections: Inaugural Lecture, 2 February 1960. By Prof. F. C. Tompkins. Pp. 139–148. 5s. (London: Imperial College of Science and Technology, 1960. Distributed by The Modern Book Co., Ltd., 19 Praed Street, London, W.2.) [197

Other Countries

Union of South Africa: Department of Commerce and Industries. Division of Fisheries Investigational Report No. 41: The Biology of Guano-Producing Sea-Birds—The Distribution, Abundance and Feeding Habits of the Cape Penguin, *Spheniscus demersus*, off the South-Western Coast of the Cape Province. By R. W. Rand. Pp. 28 (Reprint from *Commerce and Industry*). (Pretoria: Government Printer, 1960.) [117

European Productivity Agency, O.E.E.C. O.E.E.C. Standard Code and Test Bulletin for Agricultural Tractors. Pp. 37. (Documentation, 1959 Series, Food and Agriculture, No. 20.) (Project No. 251/4) (Paris: European Productivity Agency, Organization for European Economic Co-operation; London: H.M. Stationery Office, 1960.) 2 N.F.; 8s.; 0.50 dollars; 2 Swiss francs; 1.70 D.M. [117

Smithsonian Contributions to Astrophysics. Vol. 3, No. 9: Geodetic Users of Artificial Satellites. By George Veis. Pp. iv+95–161. 65 cents. Vol. 4, No. 1: Catalog of Hourly Meteor Rates. By Charles P. Olivier. Pp. ii+1–14. 15 cents. (Washington, D.C.: Government Printing Office, 1960.) [117

United States Department of Commerce: Weather Bureau. Technical Paper No. 38: Generalized Estimates of Probable Maximum Precipitation for the United States West of the 105th Meridian for Areas to 400 Square Miles and Durations to 24 Hours. Pp. iii+66. (Washington, D.C.: Government Printing Office, 1960.) 1 dollar. [117

Publications de l'Institut National pour l'Etude Agronomique du Congo Belge. Série Scientifique No. 85: Recherches Taxonomiques et Caryologiques chez quelques Espèces du Genre *Hevea*. Par J. Bouharmont. Pp. 64+13 photographs. (Bruxelles: Institut National pour l'Etude Agronomique du Congo Belge, 1960.) 100 francs. [117

Smithsonian Miscellaneous Collections. Vol. 139, No. 11: A Classification for the Birds of the World. By Alexander Wetmore. Pp. i+37. (Publication No. 4417). (Washington, D.C.: Smithsonian Institution, 1960.) [117

United States Department of the Interior: Fish and Wildlife Service. Bureau of Sport Fisheries and Wildlife. Statistical Digest No. 46: Propagation and Distribution of Food Fishes for the calendar years 1957 and 1958. Prepared by the Branch of Fish Hatcheries. Pp. ii+46. (Washington, D.C. Government Printing Office, 1960.) 20 cents. [117

Neue Physik, Doppelheft 4/5 (1959). Das Atommodell der Photronentheorie: Die Verhältnisse in der Elektronenhülle und die Spektralterme, Der Aufbau des Atomkerns und die Kernkräfte. Von K. Nowak. Pp. 113–176. (Wien: *Neue Physik*, Mollardgasse 8, 1960.) 24 schillings; 4 D.M. [127

Geological Society of South Africa. Transactions and Proceedings of the Geological Society of South Africa, Vol. 62, January-December 1959. Edited by E. Mendelssohn, H. J. Nel and D. J. L. Visser. Pp. iii+397+clxix+30 plates. Annexure to Vol. 62, 1959: Sand—Its Origin, Transportation, Abrasion and Accumulation. By Ph. H. Kuenen. (Alex L. du Toit Memorial Lectures, No. 6). Pp. i+38+8 plates. (Johannesburg: Geological Society of South Africa, 1959.) Transactions and Annexure. £5 5s. [197

World Power Conference Sixth Plenary Meeting, Melbourne, October 20th–26th, 1962—Technical Programme. Pp. 20. (Melbourne: Australian National Committee of the World Power Conference, 1960.) [197

United States Department of the Interior: Geological Survey. Bulletin 1058–B: Geology and Ore Deposits of Northwestern Chichagof Island, Alaska. By Darwin L. Rossman. Pp. iv+139–216+plates 12–16. Bulletin 1071–H: Igneous and Tectonic Structures of the Stillwater Complex, Montana. By W. R. Jones, J. W. Peoples, and A. L. Howland. Pp. iv+281–340+plates 23–31. Bulletin 1106–E: Index to Geophysical Abstracts, 176–179. By Dorothy B. Vitaliano and others. Pp. ii+533–621. 35 cents. Bulletin 1112–C: Some Geologic Features of the Pima Mining District, Pima County, Arizona. By John R. Cooper. Pp. iv+63–103+plates 1–5. (Washington, D.C.: Government Printing Office, 1960.) [197

United States Department of the Interior: Geological Survey. Water-Supply Paper 1312. Compilation of Records of Surface Waters of the United States through September 1950. Part 8: Western Gulf of Mexico Basins. Prepared under the direction of J. V. B. Wells. Pp. v+633+1 plate. Water-Supply Paper 1543–B: Storage and Flood Routing. By R. W. Carter and R. G. Godfrey. (Manual of Hydrology, Part 3. Flood-Flow Techniques). Pp. iv+81–104. 15 cents. Water-Supply Paper 1555: Surface Water Supply of the United States, 1958. Part 3–A: Ohio River Basin except Cumberland and Tennessee River Basins. Prepared under the direction of J. V. B. Wells. Pp. xii+574. Water-Supply Paper 1557: Surface Water Supply of the United States, 1958. Part 4: St. Lawrence River Basin. Prepared under the direction of J. V. B. Wells. Pp. x+394. Water Supply Paper 1565: Surface Water Supply of the United States, 1958. Part 11: Pacific Slope Basins in California. Prepared under the direction of J. V. B. Wells. Pp. xiv+681. 2.25 dollars. (Washington, D.C.: Government Printing Office, 1960.) [197

United States Department of Commerce: National Bureau of Standards. Monograph No. 14: Bibliography on Molecular and Crystal Structure Models. By Deane K. Smith. Pp. iv+7. (Washington, D.C.: Government Printing Office, 1960.) 15 cents. [197

United States Department of the Interior: Geological Survey. Professional Paper 315–D: Stratigraphy of Pennsylvanian and Lower Permian Rocks in Brown and Coleman Counties, Texas. By D. Hoye Eargle. Pp. iii+55–77+plates 25–30. Professional Paper 333: The Foraminiferal Genus *Orbitolina* in North America. By Raymond C. Douglass. Pp. iv+52+plates 1–14. 1.50 dollars. Professional Paper 334–C: Trilobites of the Upper Cambrian Dunderberg Shale, Eureka District, Nevada. By Allison R. Palmer. Pp. iii+53–109+plates 4–11. 65 cents. Professional Paper 351: Mode of Flow of Saskatchewan Glacier, Alberta, Canada. By Mark F. Meier. Pp. ix+70+9 plates. (Washington, D.C.: Government Printing Office, 1960.) [197

Bulletin of the American Museum of Natural History. Vol. 119, Article 4: Permian Gastropoda of the Southwestern United States, 3: Bellerophontacea and Patellacea. By Ellis L. Yochelson. Pp. 205–294+plates 46–57. (New York: American Museum of Natural History, 1960.) 8 dollars. [197

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GOVERNMENT SCIENTIFIC AND TECHNICAL ADVISORY COMMITTEES

IT is now some two years since the Prime Minister indicated in reply to a Parliamentary question that he proposed to inquire into the working of the present system of government in Britain from the point of view of easing the burden on Ministers and securing the more efficient working of Parliament. Although there have been several re-arrangements of Ministerial offices, including the appointment of a Minister for Science, no specific report or statement on the subject has yet been made to Parliament; though in reply to a Parliamentary question on November 30, 1958, it was stated that the Government is now advised by some 850 bodies of a central or national character. This is only one aspect of the problem, however, though it was discussed by Prof. K. C. Wheare in his book "Government by Committee" published in 1955, and received further attention in the wider survey by a study group of the Royal Institute of Public Administration entitled "The Organization of British Central Government 1914–1956" published in 1957.

Political and Economic Planning has now published a full-scale report on "Advisory Committees in British Government"*, based on a study made possible by a grant from the Leverhulme Trust. It is concerned solely with those advisory committees attached to departments of the central Government which are of a standing or permanent, rather than a temporary, character, and as local and regional committees are also excluded, it does not cover many of those included in the total given to Parliament in 1958. A table included in the report suggests that 484 is a more accurate figure for the purpose of this particular study, and a glance at this table should suffice to show how closely this aspect of government touches the scientist and technologist.

The assumption of new functions necessitated by broadening of the responsibilities of the Government mean that administration is no longer a self-contained system. A continuing need has developed for contact and consultation with people outside the Civil Service, and nowhere is this more important than in scientific and technical matters. This is one reason for the appointment of a Minister for Science, and the study of advisory committees is important, both for the light it throws on the means of developing effective contacts with professional groups and organized interests, and the provision of specialist and technical advice. Indeed, it is interesting to note that the Colonial Office, which appears to have led the way in setting up advisory committees of the modern type, had several such committees before the First World War, and they were all committees of experts and were concerned with scientific subjects, particularly with the development and use of scientific knowledge to improve the conditions of living in the territories with which they dealt. Such committees were appointed because the Colonial Office at that time lacked within itself scientific experts, and it emphasizes rather than otherwise the importance of the advisory committee in considering the place of the scientist in government and the means of presenting scientific and technical advice. The Haldane Report on the machinery of government in 1918, while making no recommendations regarding the organization of advisory bodies, foresaw an important place for such bodies and considered government administration was unlikely to retain public confidence unless "it was recognized as an obligation upon departments to avail themselves of the advice and assistance of advisory bodies so constituted as to make available the knowledge and experience of all sections of the community affected by the activities of the Department". Some two decades later, R. V. Vernon and N. S. Mansergh, in their study "Advisory Bodies", noted how the Haldane Committee's recommendation had reinforced the tendency to resort to external advice in this way, especially when the Government had to enter new spheres.

The survey prepared by Political and Economic Planning would be of great interest to the scientist and the technologist merely for the way in which it displays the extent to which scientific interests are affected by this tendency. It does not describe the operations of particular bodies, though the Advisory Council on Scientific Policy, the National Advisory Council on the Training and Supply of Teachers, the Colonial Research Council, the Engineering Advisory Council and the Advisory Council on Scientific Research and Technical Development of the Ministry of Aviation are among the fifteen major bodies the membership and functions of which are outlined in some detail by way of illustration, the last-named being of special interest in that no other account of its work appears to be available. More important, however, the survey reviews in succession just those aspects of the work of advisory bodies on which it is important that there should be public understanding not only in Parliament and among the specialist bodies whence the membership of such committees is often drawn but also in the country generally. Indeed, in the absence of such public understanding, the full advantages of such an advisory system are unlikely to be reached, because informed and intelligent discussion of public policy is hindered.

Beginning with a general review, in which the extent to which many committees are concerned with research, sometimes in an administrative rather than an advisory capacity, is duly stressed, and scientific committees as such receive a special note, Political and Economic Planning considers the problems of composition which may arise and their implications, the methods of work and the functions and influence

* Advisory Committees in British Government. Pp. xii+228. (London: Political and Economic Planning, and George Allen and Unwin, Ltd., 1960.) 25s. net.

of such committees. The difficulty of definition is frankly recognized, particularly that of differentiating between a committee responsible for advising on research programmes or policy, and one which is required to sponsor or organize research; but the research boards of the Department of Scientific and Industrial Research, the Medical Research Council, the Agricultural Research Council, the Nature Conservancy and the Overseas Research Council are regarded as possessing sufficient authority to be treated as administrative bodies, and as such are not discussed in the report, although the Scientific Advisory Council of the Ministry of Power is included. This limits to some extent the value of the survey as a discussion of the place of the scientific expert in administration, though here a major weakness is the failure of the report to make any reference to the need to have inside the Government, both at Ministerial level and in the Civil Service, those who are qualified to interpret and assess the scientific and technical advice presented to them.

This omission is the more striking in that, in the chapter on the functions and influence of committees, the nature of the problem is otherwise fairly stated, and the increasing reliance of a Government on advanced scientific knowledge, and hence on the specialists who are able to provide it, is fully admitted. Whether the need is met by employing scientific and professional staff inside the Civil Service, or by organizing the supply of knowledge from outside, there must be administrators and Ministers capable of assessing that advice in relation to other factors involved in matters of policy. This, of course, is largely a matter of education, but, while that point is overlooked, the report stresses the importance of education in the sense that it is effected by a sound public relations policy. The report takes a somewhat optimistic view of the influence of scientific committees, especially of the Advisory Council on Scientific Policy, and attributes the advantages of the advisory committee to its more systematic procedure, the more comprehensive personal contacts which it ensures, its general convenience and stability, and the more formal commitments it produces. The report questions seriously Prof. Wheare's suggestion that the development of advisory committees has strengthened Whitehall at the expense of Parliament; rather the view is held that the increased power of Ministers and their departments is counterbalanced by their dependence on independent organizations; and advisory committees are a feature of that dependence.

The report does not advocate unlimited publicity for the work of advisory committees; the risks of such publicity as well as those of excessive secrecy are both recognized. Indeed, this chapter of the report, with its clear discussion of the factors which assist or hinder the effectiveness of advisory bodies, deserves to be studied carefully both by the individual scientist and technologist and by his professional associations. One point in particular should be noted. The scientific community, the report comments, has not so far developed the unity and cohesion displayed by some trades and professions, nor do its political and social attitudes differ markedly from those of the rest of the populace. This may well explain the absence of professional associations of scientists or technologists from among the major nominating bodies listed as sending representatives or suggesting names for inclusion on the 484 advisory committees within the scope of the report. Even if the co-operation of scientists in the machinery of government does not become politically more important, this situation represents a serious weakness in some of the positions that may develop out of the present methods of recruitment of advisory committees.

The nature of that weakness is indicated by the title of a broadsheet "Government by Appointment" (No. 443, July 25, 1960), issued by Political and Economic Planning almost simultaneously with the report. This broadsheet reviews the practice and implications of the present system of appointments to a whole range of some 40,000 posts, from nationalized boards to regional and local bodies, many of which fall outside the scope of the report itself. Both the report and the broadsheet show that the need to secure people with particular qualities for particular jobs, and for Ministers to exercise some form of remote control over administrative bodies, has led to a new system of patronage which has come to stay, but appears to involve excessive plurality; this should be diminished if possible. The report only examines evidence of plurality from Home Office and Board of Trade committees, but there is no reason for regarding this evidence as atypical. Such plurality as exists is attributed mainly to the practice of nomination by outside organizations; and while it is not regarded as of serious proportions, it could with advantage be less.

The broadsheet suggests three principles that might guide policy in recruitment. The methods used should be, so far as possible, orderly and systematic, and should be widely known, so that nominations may come from all quarters. Within the limits imposed by the nature of the job, as great a variety of persons as possible should be appointed. Thirdly, plurality should be treated as a general problem and not considered merely in relation to a particular set of institutions. Until it has been fully examined on this basis, statements about the large numbers of people willing to give voluntary service should be treated with reserve.

Clearly, if this question of appointment to advisory committees is to be handled satisfactorily, so as to reduce plurality and establish public standards of propriety and good practice, professional associations of scientists and technologists have an important part to play. They might perhaps do more than at present to discover potential candidates among their membership, particularly in the younger age-groups, to arouse their interest in such work, possibly even to coach them or prepare them for participation. Moreover, there are other important matters to be discussed which bear alike on the effectiveness of advisory bodies and the willingness of professional men and women to serve on them; for example,

membership of any such committee may bring a scientist within the operation of the Official Secrets Act, with all its effects in his contacts and relations with professional colleagues outside the committee. Such issues are only just touched on in the report; but both report and broadsheet display a range of problems which touch the scientist and technologist closely indeed, and call for further study and independent thinking both by individuals and by their professional associations.

THEORETICAL HYDRODYNAMICS

Theoretical Hydrodynamics

By Prof. L. M. Milne-Thomson. Fourth edition. Pp. xxi+660+4 plates. (London: Macmillan and Co., Ltd.; New York: St. Martin's Press, Inc., 1960.) 65*s*. net.

THE book under review is the fourth edition of one which appeared for the first time in 1938. In the pages of *Nature* (142, 1136; 1938) I discussed a number of text-books on hydrodynamics before dealing specially with the first edition of Prof. Milne-Thomson's book. In that review I ventured to suggest that the mathematical approach to hydrodynamics followed in the book might well have been amplified by a more physical approach. That is still my view, but I must add that Prof. Milne-Thomson's book has had a resounding success during the twenty-two years that have elapsed since it first appeared. I have come across many experts, both in Britain and abroad, who have spoken very highly of "Theoretical Hydrodynamics" and of the approach adopted in the book. To that extent I misjudged the need for a comprehensive book of the kind planned and written by Prof. Milne-Thomson. Each successive edition has been amplified to some extent and has incorporated new material.

There is no unique road to the study of hydrodynamics. There is the approach of the physicist who treats the subject as a branch of physics in which there are discussed the forces which act on liquids, and which are exerted by them. There is also the approach of the engineer, who is concerned mainly with applications, though some of the modern applications of hydrodynamics to engineering are compelling experts to try to obtain a deeper insight into fundamental processes than appears to have been necessary in the past. Then there is the 'express route' to trans-sonic, supersonic and hypersonic flow, which appears to be much favoured nowadays, avoiding the gaps in our existing knowledge of subsonic hydrodynamics. Prof. Milne-Thomson has taken none of these paths—his is the road of the mathematician. Clear physical statements are transformed into mathematical assumptions, and the mathematics of hydrodynamics is developed with clarity and economy. The practical and theoretical sides of the subject are made to supplement each other, but the emphasis remains that of the mathematician. The virtue of this method is that as "a scientific theory becomes more exact, so does it of necessity tend to assume a more mathematical form", and Prof. Milne-Thomson's approach seems to have found considerable support. In 1938 his method, which is based consistently on vector methods and notation, was considered to be a departure from the traditional approach, but it is now generally accepted and is followed by many applied mathematicians.

Chapter 1 of the book is concerned mainly with inferences which may be drawn from the 'pressure theorem' of Daniel Bernoulli, who may justly be considered to be the father of hydrodynamics—the word 'hydrodynamica' was first used by him about 1780. Chapter 2 discusses those properties of vectors which are essential for the analysis of the motion of a fluid element and for the formulation of the equations of hydrodynamics. In Chapter 3 there are discussions of the general basic properties and equations of fluid motion. Chapter 4 is concerned with the mathematical properties of two-dimensional motion in so far as they can be treated without the complex variable. Chapter 5 introduces the complex variable, and conformal mappings are treated in some detail.

Chapters 6–14 treat two-dimensional motion from the unified point of view of the complex variable. In Chapter 6 there is a discussion of streaming motion followed, in Chapter 7, by a consideration of Joukowski aerofoils, while sources and sinks are dealt with in Chapter 8. In Chapter 9 the motion of a moving cylinder is treated in detail and Chapter 10 discusses specialized aspects of conformal mapping and their applications. Chapters 11 and 12 contain important applications to the discontinuous motion of jets, currents and cavities. Chapter 13 concerns itself with the motion of vortices, and the drag associated with a vortex wake. Chapter 14 deals with two-dimensional wave motion.

In Chapter 15 the Stokes stream function is introduced, and the general motion of spheres and ellipsoids is treated in Chapter 16. In Chapter 17 Milne-Thomson derives Kirchhoff's equations in vector form. Chapter 18 discusses vortex motion in general, with special application to aerofoils of finite span. Chapter 19 gives an outline of the application of vector methods to viscous fluids and a brief description of boundary layer theory. Chapter 20, the final chapter of the fourth edition, is designed as an introduction to the theory of flow of a compressible fluid at subsonic and supersonic speeds.

The presence of well-graded sets of exercises at the end of each chapter is much appreciated by many of those who teach hydrodynamics to mathematicians in British universities. The appearance of the book is clear and attractive, and the text is lavishly illustrated with line drawings and photographs which have been chosen with discretion.

Prof. Milne-Thomson's book has stood the test of time and has, in fact, been accorded increased recognition with each successive edition. Within the limitations which Prof. Milne-Thomson set himself, and which are clearly stated in the preface, his book on theoretical hydrodynamics may be described as being 'of the first water'.

L. ROSENHEAD

LOGIC AND SCIENCE

An Introduction to the Logic of the Sciences

By R. Harré. Pp. viii+180. (London: Macmillan and Co., Ltd.; New York: St. Martin's Press, Inc., 1960.) 21*s*. net.

THIS is a very welcome book. It should be said at the outset that the author's intention to write largely for undergraduates in science may prove a little on the modest side, since many students working for higher degrees would probably produce

substantially better theses if they could find time to read what Dr. Harré has to relate.

Part 1 deals with scientific discourse, and Part 2 with discovery and confirmation. Translated into working terms, this means a discussion on the place and understanding of 'models', followed by a thorough drilling in the reasons why laws and theories come to be accepted or rejected as the case may be. In the latter context, the author adopts a sound *via media* in his warning against premature jettisoning of a theory which may, indeed, be inadequate, but perhaps for instrumental reasons. Returning to the role of models in theoretical physics, the dangers of taking them too literally are partly due to giving excessive weight to what scientists say, rather than to what they do. In the light of history, the Rutherford–Bohr planetary atom served its generation well, and signified effectively what happened in the Cavendish Laboratory; but nobody could seriously have thought that the particular imagery would last. Yet, the grand point is that—from the aspect of discovery—disciplined insight came first, and the application of mathematical analysis afterwards. Essential as the latter is, momentous advances usually begin with remarkably simple premises. Incidentally, Max Planck is known to have fought hard and long in his mind against the consequences of his own quantum concept. The statistical and indiscriminate nature of much of modern physics was not to his liking. But that is the penalty of greatness. Questions like these are ably handled by Dr. Harré, and the moral is driven home.

Towards the end of the volume, some finer points of procedure are illustrated in the chapters dealing with "fitting the facts", and "non-factual criteria". In the first of these, the development of van der Waals' equation out of Boyle's law is treated epistemologically. It is highly important in showing the student that if he performs his experiment $pv =$ *constant* properly he ought to find discrepancies, and that these are due to his working with *real* gases.

The other matter is quasi-æsthetic, namely, the place of 'elegant' proofs in science. It is suggested that the inclusion of some ingenious device is needed for satisfaction of this kind. Maybe it is; but the most sublime thought can be 'symmetrical' and 'well-rounded' rather than 'angular', and this may have something to do with it. In the greatest minds, these qualities are undoubtedly revealed, and, fascinating as the subject is, we may well have to leave it at that.

F. I. G. Rawlins

A NEW LUNAR ATLAS

Moon Maps, with a Chart showing the Other Side of the Moon based upon Soviet Photographs

By H. P. Wilkins. Pp. 36+27 maps. (London: Faber and Faber, Ltd., 1960.) 30*s*. net.

When H. P. Wilkins died, on January 21, 1960, the astronomical world lost one of its most dedicated selenographers. His last undertaking was the preparation of a lunar atlas designed for use at the telescope. These new "Moon Maps" are based on an earlier set published in his volume "The Moon" (in collaboration with Patrick Moore, 1955), which is undoubtedly familiar to amateur lunar observers.

The accompanying text is limited to a gazetteer in which all named features, indexed alphabetically, are described briefly and keyed to the corresponding maps. The latter are reproduced on a scale of 55 4 miles to the inch and are therefore approximately 40 per cent larger than those in the 1955 volume. The entire visible surface of the Moon is covered in 25 sections. In addition, the area surrounding the walled plain of Ptolemaeus is shown on a larger scale, and a map of the far side has been prepared from the photographs obtained in October 1959 by means of *Lunik* III.

The most unusual feature of the atlas stems from its very imaginative binding. Whereas the pages of text are spiral-bound in the conventional way, the maps are attached to the outer edge of the back cover, thus allowing the reader to place side by side any page of the gazetteer and any chosen map.

It is unfortunate that the author's failing health evidently prevented him from giving the book a final critical review before it went to press; but the few obvious omissions are by no means irreparable. In particular, the enlarged map of Ptolemaeus (Plate XXVI) bears no title and the word Ptolemaeus itself does not appear anywhere on the page; since Plate XXVI is not indexed in the gazetteer and is mentioned only briefly (by the anglicized name Ptolemy) in the introduction, this very useful map is apt to be overlooked by the casual reader.

The key chart, which appears on p. 47 of "The Moon", is absent here and would be a welcome addition, especially because the co-ordinates of the new maps are printed in type so small as to be nearly illegible in the dim light of a telescope dome. The names of the features are rather inconspicuous, too. This is of course necessary for preserving the many fine details which otherwise would have been obliterated; but these formations could be located more easily if approximate co-ordinates had been included in the gazetteer.

In spite of these few shortcomings, "Moon Maps" should be nevertheless a valuable addition to the reference shelf of the amateur observer for its abundance of minute details not readily available elsewhere.

Simone Daro Gossner

NEW APPROACHES TO DYNAMICAL ASTRONOMY

Introduction to the Mechanics of the Solar System

By Rudolf Kurth. Pp. ix+177. (London and New York: Pergamon Press, 1959.) 42*s*. net.

The study of the dynamics of the solar system, which until a few years ago appeared to be almost in abeyance, has recently shown signs of a renewal of interest. This was in large measure initiated by the development of high-speed automatic computers, vastly accelerating the large amounts of numerical calculation intrinsically associated with the subject, and has been augmented by the launching of artificial satellites and space probes, which have brought new problems in dynamical astronomy with them. As a consequence there is a need for introductory books to the subject, one or two of which have appeared in the past few years, and it is into this category that this book falls.

The general approach of the book is empirical, and its simple and direct treatment (making use of vector notation throughout), as well as the inclusion of elementary explanatory material in the first chapter,

will make it of great value to those making their first acquaintance with the subject, even if they have little or no previous knowledge of the composition of the solar system, the planetary motions, or even of Newton's laws of motion and of gravitation. The first chapter shows how Kepler's laws of planetary motion may be arrived at inductively from the observations, and discusses the solution of Kepler's equation, with some analytical results. The second chapter examines the notion of force, laying down postulates for it, deriving the inverse square law, and obtaining the general solution to the general two-body problem. This chapter also contains a brief but clear description of the bases of Laplace's and Gauss's methods of orbit determination. Chapter 3 is concerned with the many-body problem, in several of its aspects. In Section 4 there is an unusual and instructive derivation of the time derivatives of the orbital elements in terms of the components of the disturbing force, based on Poisson's method of variation of parameters. (The fact that the expression for the acceleration is analytic in the time does not resolve the question of the convergence of the first-order perturbations, as suggested in Section 2·2, since the relevant radius of convergence may be very small, and in fact some modern work suggests that it is so.) Chapter 4 deals with the oblateness problem in broad principle, and Section 2 gives a lucid treatment of the precession and nutation, using vector and matrix notation, and deriving the major terms. At the end of each chapter there is a set of instructive examples for solution of varying difficulty, and some useful notes and references.

The study of orbital perturbations has given rise, in the past two centuries, to a vast edifice of mathematical developments and techniques (including the distinction of various classes of term in the expansion of the disturbing function, and the wide use of canonical transformations), and the author, in his wish to view the subject more directly from the point of view of the physical principles involved, betrays his impatience with some of these developments. This attitude is capable of leading to important new insights, and is not too much out of place in an introductory work; but it is a pity that the author expresses such especially violent lack of confidence in the Hamilton-Jacobi method (both in the Introduction and in the notes to Chapter 3), especially since he does not reach those problems where the method exhibits its power, as, for example, those related to the long-period features of orbital perturbations, or to the special conditions arising near small integer commensurabilities of period, or near the critical inclination in the artificial satellite problem.

P. J. MESSAGE

APPLIED MATHEMATICS

Mathematics in Physics and Engineering

By J. Irving and N. Mullineux. (Pure and Applied Physics: a Series of Monographs and Textbooks, Vol. 6). Pp. xvii+883. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1959.) 11.50 dollars.

THIS book presents a comprehensive account of those parts of mathematics which find application in the solution of problems in physics and engineering. The tone of the book is practical and 'down to earth', with emphasis on solutions carried to the numerical stage. It will be valued by the applied mathematician, at least as a reference book, because so much material is covered in its almost 900 pages of text. Each chapter is accompanied by a set of problems (with answers) and the text is copiously illustrated with problems worked out in detail. Thus the book is admirably suited to the needs of students, but it is not likely to help the research mathematician very much, since it is not a specialized text and the reference lists are not very extensive.

The first chapter deals with methods for solving partial differential equations, and includes a section on Cauchy's problem and the solution of hyperbolic, elliptic and parabolic equations. Chapter 2 is devoted to the solution of ordinary differential equations and it introduces a number of the special functions. On the other hand Bessel and Legendre functions receive amplified treatment in Chapter 3. Laplace and other transforms are introduced in Chapter 4, and some applications to problems of oscillation are discussed. Chapter 5 deals with matrix algebra, with emphasis on numerical work, such as solving equations or finding latent roots. Analytical methods in classical and wave mechanics are presented in Chapter 6, and these are illustrated by reference to the top and the linear harmonic oscillator.

Chapter 7 treats the calculus of variations. It covers the usual elementary problems and also isoperimetric problems and the Rayleigh-Ritz method. Some torsion and viscous-flow problems and some elastic plate problems are solved. There is a section on the binding energy of the helium-4 nucleus; but about twice the experimental value is obtained from a theoretical calculation, and then it is remarked that this shows that "the assumed interaction is not valid". It seems to me that it would have been better to omit this section, or, if the aim was to give an application of the variational calculus to theoretical physics, then an example where the result is more in accord with experiment might have been chosen.

Complex variable theory, the calculus of residues, and conformal transformations find widespread applications in physics and engineering; they are adequately covered in Chapters 8 and 9, which together occupy about 150 pages. General transform theory is dealt with in Chapter 10, and application is made to various problems of supersonic flow. Chapter 11 is on numerical methods, and Chapter 12 deals with integral equations, both analytical and numerical methods of solution being presented. The numerical treatment of integral equations deserves special mention. It goes further than that given in any other book known to me. There is an appendix of 80 pages on various topics in pure mathematics; it will mainly be of use for reference purposes.

The work should be of great assistance to senior undergraduates, and to physicists and engineers who move in the world of technology. If it is a matter of deciding, in a practical case, whether mathematics can help, this book will go a long way towards answering the question. So far as the actual printing is concerned, this is very clear. But the mathematical formulæ and equations are frequently displayed in such a way that space is not utilized very efficiently, such as on p. 527 or 579. Formulæ and prose might have been combined in some places, and in others the formulæ printed on several consecutive lines might have all been put on one line. In spite of this, however, it must be admitted that the Academic Press has produced the book at a reasonable price.

L. S. GODDARD

Annual Review of Physiology

Vol. 22. Edited by Victor E. Hall, in association with Frederick A. Fuhrman and Arthur C. Giese. Pp. viii+725. (Palo Alto, Calif.: Annual Reviews, Inc., 1960.) 7 dollars.

THE "Annual Review of Physiology" has appeared regularly since 1939. The new number is much like its predecessors: it provides a fairly complete, but not very critical, summary of the year's literature. There is an interesting prefatory chapter by Dr. Franklin D. McLean, who has seen great changes in physiology since he took his degree in 1910—the year when Abraham Flexner's report on medical education appeared. He has come in close contact with many famous men—A. J. Carlson, L. J. Henderson, Otto Loewi, A. E. Cohn, Baird Hastings and many others, and has done much to make medicine scientific.

The new volume contains a cumulative index of chapter titles for Volumes 11–22. Articles on the adrenal cortex, heart, peripheral circulation, digestive system, kidney, reproduction, respiration, and three or four articles on the nervous system appear each year. This year there are articles on the comparative physiology of muscle and blood pigments and there are articles on nuclear function, genetics, the alimentary tract, vision, and the thyroid. There are no more reviews of Russian physiology.

The preface directs especial attention to the article on the regulation of volume of the blood by E. B. Reeve, T. H. Allen and J. E. Roberts of Colorado. In this article, quantities such as the rate of uptake of water from the gut, the rate of flow to and from the interstitial space, and the intracellular space are defined algebraically in terms of various symbols. The relations between these quantities are then expressed as formulæ. The precise definitions given facilitate the discussion of the experimental papers reviewed, and will help to clarify thought in a complex field. This is a new departure for annual reviews; it is a constructive article and will provoke thought and criticism. It is hoped that more such reviews will appear in later volumes. J. H. GADDUM

Ancient Mexico

An Introduction to the Pre-Hispanic Cultures. By Frederick A. Peterson. Pp. 313+24 plates. (London: George Allen and Unwin, Ltd., 1959.) 35*s*. net.

AN up-to-date account of Mexican archæology is badly needed, and this book goes some way towards meeting that need. The author clearly knows his material, and he has had the advantage of long residence in Mexico, but these very qualifications may be responsible for his writing in some places in a way which will be understood better by the specialist than by the general public to which the book is directed. Rather a serious drawback is the way in which its general arrangement and tone obscure the differences between the Classic and Post-Classic Periods, particularly the introduction of large-scale war and violence with the arrival of the Tolteos at the beginning of the Post-Classic.

There are a number of points of detail which could be criticized; however, most of these will affect the general reader but little. Two only will be noted here because they will increase the natural difficulty which that reader may be expected to find in grasping the essentials of the Maya calendar and numerical system. One is a statement that "all the day names come 5 days later in the following year"; what is meant is that the day name in the 260-day cycle of the first day of a 365-day year falls 5 days later in that list of names than that of the first day of the preceding 365-day year, so the result is that a given day name will be shifted backwards by 5 days, not forwards. The other is a misprint of 2259 against a Maya number 2258.

The publication of this book raised hopes that it might take the place of Vaillant's "Aztecs of Mexico", which is out-of-date in some respects, though still very valuable in others. Although it is quite a useful work, by comparison with Vaillant's it is a dull production. G. H. S. BUSHNELL

Paper-Making Practice

By H. Hardman and E. J. Cole. Pp. xi+334. (Manchester: Manchester University Press, 1960.) 45*s*. net.

THOSE best qualified to write books on this subject seldom have the time or incentive to do so. This work was begun when the authors were lecturing at the Manchester College of Technology, and they have relied almost completely on the scientific literature and on machinery manufacturers' publications. It is therefore greatly to their credit that they have managed to assemble a remarkable amount of useful practical information, set out in simple language.

The book is a modified version of a series of articles which appeared in a trade journal, and it presupposes a fairly considerable knowledge of pulp and paper manufacture. Unfortunately, it is marred by some serious defects. Thus, the treatment of the subject is extremely un-even (wood pulping receives 74 pages, but rag and esparto pulping, of principal interest in Britain, are omitted); it is not particularly up to date (for example, in respect of methods of stock preparation, continuous pulping, fines removal, wire and felt construction); and of the approximately 110 literature references only two are subsequent to 1955. There are no index, no link-up between the body of the book and the bibliography, and no references to text-books (not even to "Clapperton"); and the text itself sorely needs editing.

Nevertheless, the book can profitably be read by the students and paper makers to whom it is addressed, and I hope that it will soon reach a second edition, when the above defects can be remedied and its value thereby greatly enhanced. J. GRANT

Biographical Memoirs of the National Academy of Sciences of the United States of America

Vol. 34. Pp. vii+368+15 plates. (New York: Columbia University Press; London: Oxford University Press, 1960. Published for the National Academy of Sciences of the United States of America.) 40*s*. net.

WITH the exception of those of J. U. Nef (1915), L. V. Pirsson (1919) and L. B. Stillwell (1941) all the subjects of these memoirs died within the last decade, and most within the last three years. The memoirs are characterized by the high standard which has come to be associated with this series, and they will be valued also for the comprehensive bibliography which accompanies each memoir. Apart from those names already mentioned, those best known to British scientists are probably W. E. Bachman, R. A. Daly, C. F. Kettering, M. S. Kharasch, O. Meyerhof and W. R. Whitney.

PRODUCTIVITY OF THE SEA AND FRESH WATER

IT was appropriate that Section D (Zoology) of the British Association meeting at Cardiff should devote a session to the "Productivity of the Sea and Fresh Water" when the subject of feeding humanity loomed large in the deliberations of the Association as a whole. Indeed it was all the more timely for, as Dr. C. E. Lucas pointed out in the course of the session, one could see no mention at all of the sea or its potential in the programme of the Association's whole-day general symposium on "World Food and Population Problems".

The session was opened by Sir Alister Hardy, who outlined the natural economy of the sea by way of introduction and then, after stressing the need for getting more food from the sea, proceeded to discuss various ways in which the yield might possibly be increased. Apart from the development of new fisheries, better conservation of stocks already fished and other such fishery problems which would be dealt with by Dr. Lucas, he sought to answer the question: "Can we come any nearer to actually farming the seas?".

The manuring or the fertilizing of the waters with phosphates and other chemicals which had been so successful in confined freshwater fish culture could scarcely be used in the sea, he thought, except in certain very limited areas. The late Dr. F. Gross and his colleagues during the Second World War had demonstrated that such chemicals could be so used, but only in the land-locked arms of a sea loch; the open sea itself is too big a place to be treated in such a way on any large scale.

Sir Alister then referred to recent experiments conducted by Mr. J. E. Shelbourne, of the Fishery Laboratory at Lowestoft, in the rearing of young plaice in large nursery tanks until they were past the delicate stage at which the greatest mortality occurs in the sea. A number of sea-fish hatcheries, he said, have been established in the past, but it has been very doubtful if they really contributed much to the increase in the stocks of fish because the fry were liberated at far too early a stage; now, through Mr. Shelbourne finding how to keep them successfully until much later in their development, there is a new and real hope of adding materially to the fish stocks by such means.

He then recalled the experiments of the late Prof. Walter Garstang in the transplantation of young two-year-old plaice from the over-crowded coastal banks of Holland to the Dogger Bank, where they were shown to grow so much more quickly. Prof. Garstang had worked out the cost of transplanting millions of such young fish in ships specially fitted with tanks for the purpose, and had shown that such enterprise could yield a handsome profit to the industry; such farming, however, has not yet been possible because no one nation would put in the capital when all others would be free to reap the benefit. The time, however, will come, Sir Alister believes, when the need to get more food from the sea will bring about closer international co-operation in such matters.

Sir Alister ended his contribution by discussing another possible way of farming the sea which, while admitting that it lay very much in the future, he believed would be most important and should be prepared for. His ideas for such farming, he said, arose from considering the researches of Dr. Gunnar Thorson, the distinguished Danish marine biologist, who has shown that there is a much heavier competition on the sea-bed, from various animals such as starfish, for the food available for fish, than was originally thought. In a recent paper Dr. Thorson has demonstrated that such invertebrate predators will actually eat about four times as much food as will a quantity of fish of the same total weight; this, Thorson says, leads to "the amazing fact that only 1 to 2 per cent of the (potential) fish food is actually eaten by the fish".

These findings present a great challenge to marine biologists. Will future farmers of the sea be able to eradicate some of these pests and so step up the quantity of fish which may be carried on a given area? asked Sir Alister Hardy, and he went on to express his belief that this will eventually come about. If Dr. Thorson's calculations are correct, and if we could eliminate just a quarter of the pests and so allow the fish to have some 20, instead of just 2, per cent of the potential food supply, then we could make an area support ten times the quantity of fish that it does to-day. How could they be eliminated? Just as we harrow and roll the land in addition to reaping our crops, Sir Alister believes that we will in time systematically drag some combing or other devices over the sea floor at intervals to weed out the creatures that take the food from the much more valuable fish; and the pests themselves may well be converted into poultry food. Looking to the still more distant future, he believes that the fishermen of a hundred years hence may be frogmen working tractor-driven trawls sent down from parent ships above and pulling starfish eradicators over the sea bed. But whatever the future holds, he stressed, any such farming of the sea will require much more pure ecological research to determine just which of the animals we can do with in smaller numbers.

The second speaker was Dr. C. E. Lucas, director of Scottish Fisheries Research. The sea, he reminded us, is still our major highway, the very active natural boundary of all our lands, and an almost incalculable natural source of power. As the envelope of a sea-bed covering 70 per cent of the Earth's surface, it must be as rich in minerals as the land, or even richer. In addition, it is the source of our valuable marine fisheries.

With rare exceptions, the problem of the fishermen in taking their catch is a very difficult one; both they and the scientists have to work in the dark. Just before the Second World War, science began to help with the adaptation of the echo-sounder for 'seeing' fish as well as the sea bed, and since then scientists have used it with the under-water camera and television; but the fisherman still needs all the aid he can get. What are we doing about it? Dr. Lucas

asked. The answer, he said, depends on how we view the problem. On one hand, the knowledge we already have of the seas and their resources is a tribute to the skill of the fishermen and the scientific progress already made. From another aspect, with the vastness of the oceans and their potential value in view, both the harvest and the scientific effort are small.

Except during the Wars, over the past fifty years, Britain has taken each year about a million tons of fish from the north-east Atlantic: its present value at first sale is about £50 million. During that time the European catch increased steadily, and it stood at some eight million tons in 1957, when the Food and Agriculture Organization estimated the world's marine catch at nearly 30 million tons, compared with 20 million in 1938. These figures are themselves impressive enough until we compare them with those for agriculture: for the world, around 1,000 million tons of vegetable produce and probably 50–100 million tons of animal protein. So, despite its size, the sea's present yield is not so impressive after all, and it is chiefly this fact that has limited our research and exploratory investment. There is, however, another way of looking at this marine harvest; in terms of the yield per fisherman, it can compare very favourably at times with the agricultural yield per man. Why is it, then, that we get so little from the seas compared with the land?

There are, of course, many reasons, among which the problem of distributing the catch to populations far from the sea is important; it is being slowly conquered by research designed both to improve the means of preserving and transporting fish over greater periods and distances, and to provide forms of fish-meal which shall be attractive for direct human consumption. Primarily, however, it is because we are still very old-fashioned and unscientific in our exploitation of the seas. This is neither a criticism of research work nor of the hard-working fishermen. The fisheries scientists must necessarily direct a large proportion of their effort to the problems of the industry as it exists, while the fishermen can only afford to fish for profitable markets. It is simply a statement of fact, for there are many more fish, and other animals, in the sea than ever came out.

The conventional fish stocks are based on the continental shelf. The fish fluctuate in abundance, largely in response to variations in the ocean currents and the plankton which 'supports' them and the animals of the sea-bed. But their abundance also depends on man himself, with his frequently wasteful fishing; success has usually led to ruthless exploitation until the stock has been unable to recruit and grow as fast as man has reaped. In slowly reproducing animals such as whales, this has led to near extinction; but fortunately most fish stocks are more resilient and respond rapidly to a reduction in fishing.

These matters are among the objects of study in marine laboratories and particularly fisheries laboratories. Here Dr. Lucas went on to review some of the important lines of fisheries research carried out at these laboratories; but as he said, viewed in relation to agricultural and industrial research, the whole is pathetically small. Yet it has given a general picture of the sea and its riches which demands further investigation and exploitation.

The seas occupy more than 70 per cent of the world's surface and have their own natural crop of plants and animals. While these vary considerably from place to place, we now know that their overall productivity, in terms of plant matter, is at least as great as that of the land, about 100,000 million tons (+) per annum. One of our problems at present is to know just how productive it is, and the final answer may be that, acre for acre, it beats the land. Here, however, comes one of the big differences. On the land, most of the basic production is in terms of grass, trees and other plants which are often directly usable. With the exception of the seaweeds, on which a not unimportant industry is now developing, production in the sea is based on countless myriads of unicellular plants, from which vast crops might be taken, except that they are individually so small that we do not know how to harvest them. At present we have to rely on the fish and whales to harvest them for us, mainly via the small animals which feed directly on the plants, and with them form the plankton. Only in a few instances do we know much of the food-chains in the sea; but we do know that there is a great loss in productive efficiency at each stage, that is, between the plants and the animals that feed on them, between these animals and the next larger ones, etc.—perhaps 80–90 per cent in each step. So that the original 100,000 million tons (+) of plant matter produced is probably reduced to about 1–2,000 million tons (+) in terms of animals of a size conventionally acceptable for food. Yet that is far greater than the 30 million tons caught at present. Not all these sizeable animals are fish, of course, but a large fraction of them are; of the others, many are molluscs or crustaceans such as have long been familiar to us as food, and many more are representatives of animal groups which already provide food in one part of the world or another.

Considered from this position, can we—either Britain or the world as a whole—afford to view the seas merely as a source of 30 or even 50 million tons of fish? Even in food terms alone, it is a potential source of protein too valuable to be taken in the present somewhat primitive way. But the oceans have other significance for us. Can we afford any longer to treat marine research as almost the Cinderella of the sciences? Does it not deserve a place among the major groups of investigation basic and applied? asked Dr. Lucas. He then discussed in more detail the further potential food supplies we can anticipate from the sea. He dealt with increases to be expected, on one hand through a better and international conversion of stocks already fished, and on the other through the exploitation of new stocks as yet untapped. He also considered new fisheries for smaller species of fish, at least for conversion to fish-meal, if not for direct human food; and this could free for man's consumption fish such as the herring which are being unnecessarily taxed for such uneconomic purposes as animal feeding. Then, after considering further some of the possible farming methods discussed by Sir Alister Hardy, he turned to the possible harvesting of plankton.

There are, Dr. Lucas said, the distant but enormous possibilities of the natural plankton itself. Even now the larger zooplankton is caught and eaten in some parts of the world where circumstances are particularly favourable. In general, however, we have not yet the means to harvest either the phytoplankton or the zooplankton; but, in the richer areas, such as the polar regions, the annual production presents a challenge which may some day be accepted. At present we can merely set against the difficulties and

the costs, and the fact that whales and fish harvest these for us freely, the loss we incur by taking less than 0·1 per cent of the total marine production. To acquire that fraction the world uses more than a million vessels of various sizes and probably more than 4,000,000 men. Some day, when the incentive is great enough, as for many 'miracles' it was during the War, some of us will see that in true perspective, and decide that such an effort deserves a greater return and therefore a major effort to see whether a solution cannot be found.

The sea, then, at present gives us some 30 million tons of animal protein, etc., and we can have every confidence in that being at least doubled by the simple application of present knowledge and techniques, and probably more cheaply in human effort than now.

Finally, Dr. Lucas said that in Britain, we are now spending about £1¼ million a year on marine research of all kinds, compared with about £7 million on agricultural research, to say nothing of medicine, defence and atomic energy. We are also talking of spending millions more on space research, and the Americans and Russians are thinking in terms of hundreds of millions a year. Yet there are vast unexplored spaces off our coasts which are intellectually and physically as exciting as any; we know less of the sea-bed than we do of the face of the Moon.

The two contributions on freshwater fisheries to the symposium which followed were concerned with tropical conditions and were more specialized. Dr. R. S. A. Beauchamp, until recently director of the Jinja Laboratory on Lake Victoria, dealt with the lake fisheries of East Africa. The abundant light and heat of the tropics, he said, provide ample energy, so that, other things being equal, tropical lakes should be more fertile and more productive than those in temperate regions. The abundance of fish and other animals (hippopotami, crocodiles, etc.) found when some of the East African lakes were first visited had seemed to provide proof of this, yet their exploitation has shown that they are not as productive as they seemed to be; research has given at least a partial explanation.

For a number of years the stocks provided all the fish required. With the increase in the human population, however, the demand for fish increased and the fishery was greatly developed; in consequence, in Lake Victoria the fish were reduced to about one fiftieth of what they were. This has not caused the alarm it should, because the gross annual yield has been maintained by increasing the fishing effort. The methods for investigating the productivity of these lakes are the same as those used for temperate ones; but only after a time does one realize how very different a tropical lake is. In a temperate-zone lake, the vital processes go on at a rate determined by the weather and the changing seasons; in the tropics these are constant or vary only slightly. This, he said, puts the question of what determines the rate of productivity in rather a new light, and it becomes apparent that in a tropical lake this is determined by its own characteristics; there are certain physical circumstances which limit production in any given lake, but within such limits it is determined by the biological processes themselves.

With this idea in mind, one is forced to consider what these lakes were like before they were heavily exploited: when they contained, according to the earliest records, very many more fish than they do now. These records have by some been discredited or considered as exaggerated. However, there are, in East and Central Africa, still a few lakes that have not been heavily exploited or have only been opened up recently, and all these provide evidence for the validity of the records regarding the number of fish originally found in lakes such as Lake Victoria.

It is generally recognized that any natural complex of plants and animals, if left to itself, will develop so as to produce and support the maximum number of living organisms. It is also fairly apparent that, almost without exception, man's interference in any such natural biological resource leads to its deterioration. The African lakes vividly illustrate these two contentions. Man has caused so much damage because he strikes at the most crucial link in the succession—where plant material is being converted into animal material. This conversion is brought about, not, as in other lakes, by the invertebrate animals, but directly by fish belonging to the genus *Tilapia*, which feed on phytoplankton.

With an excess of light and heat, a limit to plant growth is set by the rate at which nutrients become available. In Lake Victoria (and probably some other lakes) a primary deficiency has been shown to be a shortage of sulphate; and it was also found that the inflows contained little or none of this. However, the main supply of nutrients in a large lake is not from its inflows but from its bottom deposits. In Lake Victoria the organic content of the bottom muds was found to be extremely high, containing enormous quantities of organically combined sulphur. Here in contact with the water we have an abundance of the very substance that constitutes a deficiency. How this comes about is not yet fully explained, but the mud contains organisms which seem to prevent the usual processes of decomposition and decay; thus the nutrients in the plankton that falls to the bottom are largely removed from circulation. For this reason, it is very desirable that as much as possible of the plankton should be eaten in order to keep up the general level of fertility by the return of animal excretion; to this end considerable stocks of *Tilapia* should be maintained in the Lake. Unfortunately, these fishes form the basis of the commercial fisheries and suffer the severest exploitation. Twenty-five years ago an officer of the Sleeping Sickness Department who had spent most of his life on Lake Victoria said he thought it was becoming a watery desert; this is even more true to-day.

The concluding speaker was Dr. C. F. Hickling, fishery adviser to the Colonial Office, who described experiments on the effects of fertilizers on the fish yield at the new Fish Culture Research Station in Malacca. It is well known, he said, that the natural production of fish in a pond can be greatly increased by the use of fertilizers and the supply of supplementary foods. But fertilizers are cheap, both in cost and labour, whereas foods are by comparison expensive and tending to be more so. Therefore fish-pond economy demands that the maximum increase in fish production should be got by the use of fertilizers, with supplementary feeding as an extra.

Temperatures at Malacca are high and show little variation (27° C. at night; 32° C. by day), so growth is very rapid. Since earlier work suggested that a neutral or slightly alkaline reaction is essential for the successful use of fertilizers, the first series of trials tested the effects of graduated doses of calcium

carbonate, given as powdered limestone, on the water and the fish stocked in the ponds. All the experiments were done in 36 one-acre ponds arranged as a Latin square (6 × 6) and each stocked with 250 common carp and 200 *Tilapia mossambica*; after six months the ponds were drained and the fish crop weighed. It was shown that the yield of fish was not increased even though acidity was neutralized and alkalinity increased four-fold.

Next the same ponds were used to test the effect of 20 lb. of phosphate (P_2O_5), given as triple superphosphate, on the fish production at three different levels of limestone dosage, and also the effect of potash (K_2O) with and without phosphate, against an untreated control. The potash without phosphate gave no significant increase in yield over that of the control or of the former experiment; the phosphate, however, gave an important effect in every case: even in the unlimed ponds, it increased the fish crop from 93 to 217 lb., and in the limestone ponds it was increased to 344 lb. In a third series of experiments it was shown that the addition of nitrogen (as calcium nitrate) gave no significant increase over phosphate alone, and it also showed that the addition of 20 lb. of phosphate gave as good a crop of fish as nearly 7 tons of cowdung. 40 lb. of phosphate gave the highest yield of all—an average of 373 lb. with a maximum of 551 lb. In summing up, Dr. Hickling said the lessons to be learnt from these experiments are, first the paramount importance of phosphates, and secondly the rapid rate of turnover, which is to a large extent a function of temperature; this latter factor, he believes, accounts for the far better utilization of phosphates shown at Malacca as compared with earlier German experiments in colder temperate waters.

Both the marine and freshwater contributions gave rise to a good general discussion.

SCATTERING OF HIGH-ENERGY ELECTRONS BY PROTONS

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THE elastic scattering of electrons by protons is described[1] by the Rosenbluth formula (lengths will be expressed in fermis, and $\hbar = c = 1$. For momenta $1 f^{-1} = 197$ MeV./c.):

$$\frac{d\sigma}{d\Omega} = \frac{\alpha^2}{4E^2}\frac{\cos^2\theta/2}{\sin^4\theta/2}\left[1 + \left(\frac{2E}{M}\right)\sin^2\theta/2\right]^{-1}$$

$$\left\{F_1^2 + \frac{q^2}{4M^2}\left[2(F_1 + \varkappa F_2)^2\tan^2\frac{\theta}{2} + \varkappa^2 F_2^2\right]\right\} \qquad (1)$$

where $\frac{d\sigma}{d\Omega}$ is the laboratory differential cross-section, α is the fine structure constant, E is the laboratory energy of the incident electron, θ is the laboratory angle of scattering, M is the proton mass, $q^2 = 4E^2\sin^2\theta/2[1 + (2E/M)\sin^2\theta/2]^{-1}$ is the square of the four-momentum transfer, and $\varkappa = 1{\cdot}79$ is the anomalous magnetic moment of the proton in nuclear magnetons. The form factors F_1 and F_2 are associated respectively with the Dirac and Pauli interactions of the proton with an electromagnetic field.

The formula, of course, relies on the validity of conventional quantum electrodynamics, and also on the absence of fourth-order processes in which two photons are exchanged between the electron and the physical nucleon. Both assumptions are expected to be valid in the conditions of the experiment described here, although the second one may well break down at energies not much greater[2].

For convenience a cross-section $\frac{d\sigma'}{d\Omega}$, loosely referred to as the 'point proton cross-section', may be defined by writing $F_1 = F_2 = 1$ in the formula; then experimental results can be expressed in terms of $F^2(q^2,\theta)$, where:

$$\frac{d\sigma}{d\Omega} = F^2(q^2,\theta)\frac{d\sigma'}{d\Omega} \qquad (2)$$

Clearly F can be expressed in terms of F_1 and F_2 as required.

Hofstadter *et al.*[3], using electrons with energies up to 650 MeV. from the Stanford linac, have studied the scattering at 75° ($q^2 \lesssim 11 f^{-2}$) and 135° ($q^2 \lesssim 17 f^{-2}$). Their results are well fitted by writing:

$$F = F_1 = F_2 = (1 + 0{\cdot}0533\, q^2)^{-2} \qquad (3)$$

A recent letter by Hand[4], who also used the Stanford linac, reports measurements at 135° for $q^2 \approx 26 f^{-2}$. These results are also consistent with equation (3).

This article reports an investigation of the scattering in which q^2 ranged up to $25 f^{-2}$ at 66° and at 112°. As will be seen, the results at the higher angle agree with Hand's. At the lower angle, on the other hand, a variation of F^2 with θ is revealed which can only mean that F_1 and F_2 are not equal.

Apparatus and Procedure

Figs. 1 and 2 show vertical and horizontal views of the general layout and of the counter telescope. The electron beam of the Cornell synchrotron spiralled inwards at the peak of the magnetic cycle,

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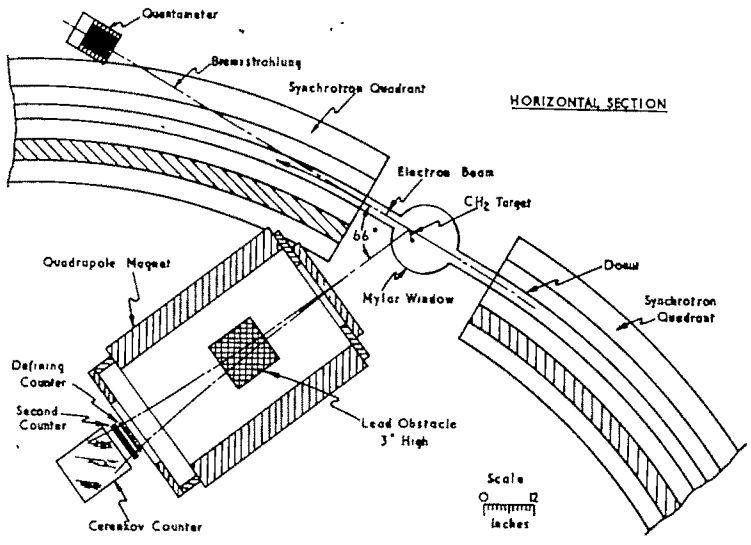

Fig. 1. Plan view of the apparatus described in the text

as a result of controlled decrease of the radiofrequency accelerating voltage. For periods of about 1 msec., repeated 30 times per sec., the electrons bombarded polyethylene or carbon targets in a scattering chamber located in one of the straight sections. The targets were in the form of rods about 1/16 in. square, disposed horizontally in the median plane of the synchrotron at an angle of 45° to the beam direction. The tips of the targets were 1·1 cm. inside the normal equilibrium orbit of the beam. Discoloration of the polyethylene showed that the targets were bombarded at distances up to 1/16 in. back from the tips.

A totally absorbing ion chamber, or quantameter[5], integrated absolutely the bremsstrahlung emitted from the target. Knowledge of the radiation-length of the target materials at the various electron energies gives directly the effective product of the target thickness and the incident electron charge, which is the quantity required for cross-section calculations. It was evident that on the average the electrons traversed the target about ten times before being finally lost from the synchrotron.

Photographs were taken of the bremsstrahlung spot immediately in front of the ion chamber. Usually these showed a clean spot about 1/4 in. in diameter, which checked that electrons were not hitting objects, other than the targets, in or near the scattering chamber. In the early stages of the experiment a second diffuse spot was sometimes caused by electrons hitting a beam-detecting device at the upstream entrance to the chamber; this improper mode of operation was associated with incorrect monitoring and low measured cross-sections. The trouble was eliminated by adjustment of the in-phase correction coils which steer the synchrotron beam at high energies.

Scattered electrons, or recoil protons, left the scattering chamber through a 0·005-in. 'Mylar' window and were then deflected magnetically by a single quadrupole lens. This produced vertical focusing of the particles passing over or under a central obstacle 3·7 in. high, made of lead and copper. The momentum window of the spectrometer was defined by this obstacle and by the plastic scintillator A, the maximum height of which was 1/8 in. In vertical section this scintillator had the shape of a truncated diamond, in order to obtain the best possible bias curve for the pulses.

The quadrupole lens was, of course, defocusing horizontally, and therefore scintillator A was made 8 in. wide. In a typical run the collected particles were emitted at semi-horizontal angles up to 0·97°, measured at the target with respect to the central ray; the total solid angle collected by the spectrometer was 4·41 millisteradians.

The momenta of the particles varied with the horizontal angle of emission, an effect which was only appreciable for recoil protons. To compensate for it, scintillator A was turned through a small angle (for example, 18° at 1,205 MeV.) round its vertical axis, counterclockwise as seen from above.

For a point target on the axis the theoretical curve of detection efficiency versus magnetic field gradient, for a fixed momentum particle, was trapezoidal in shape. It had an almost flat top and a typical full width of 3·1 per cent at half-efficiency. In practice the resolution curve was smeared by the finite height of the target and various multiple scattering processes, especially for recoil protons. However, the area under the peak should not be seriously changed by these effects, and so the cross-sections were computed by integrating peaks in the experimental counting-rate as a function of magnetic field gradient. Actually the voltage across a shunt in series with the exciting coils of the magnet was used as the independent variable, and the areas multiplied by an appropriate constant. At the highest momenta the field gradients were not quite proportional to the existing currents,

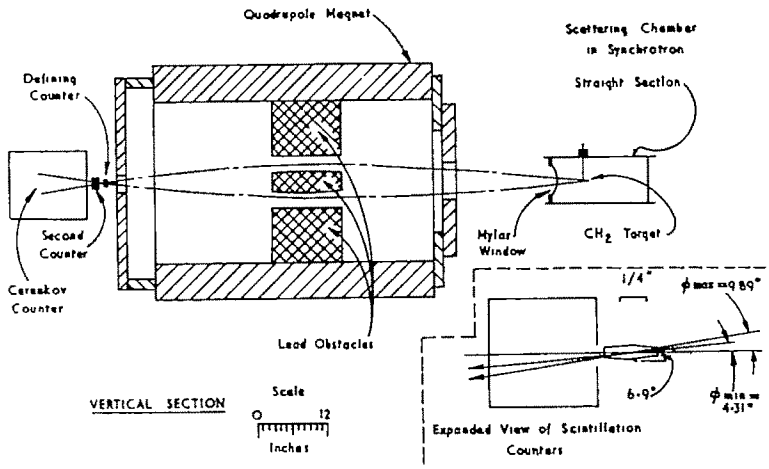

Fig. 2. Side view of the target, spectrometer, and counter telescope. The inset shows an enlarged view of the two scintillation counters

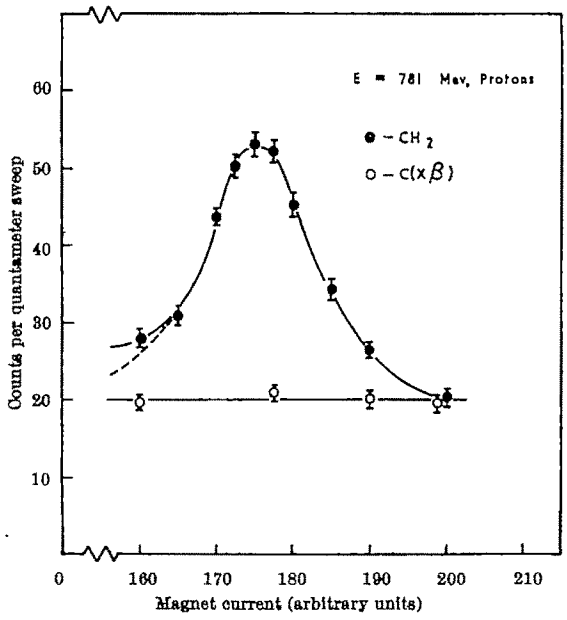

Fig. 3. The counting-rate as a function of magnet current; protons recoiling at 66° from collisions of 781-MeV. incident electrons

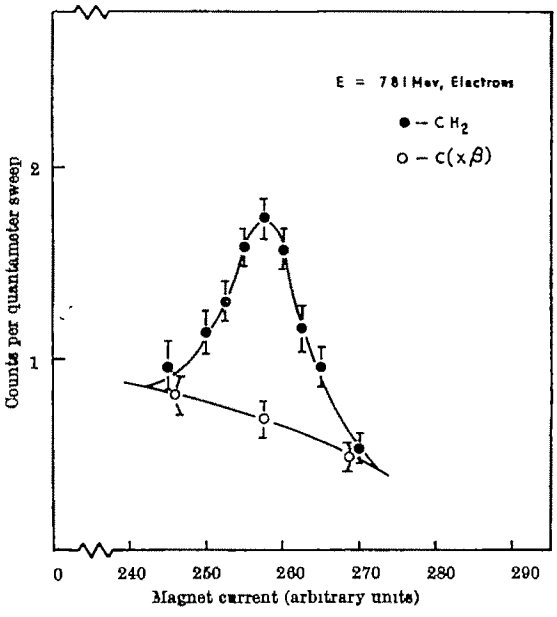

Fig. 4. The counting-rate as a function of magnet current; electrons scattered at 66° from collisions of 781-MeV. incident electrons

and a differential correction ($\gtrsim$ 9 per cent) was made for this.

The procedure just outlined was used for (*a*) the 66° scattering of 587, 684, 781, 879 and 1,034 MeV. electrons, (*b*) the 112° scattering of 320 and 761 MeV. electrons, and (*c*) the protons recoiling at 66° from the scattering of electrons with energies of 684, 781, 982, 1,034, 1,173 and 1,205 MeV.

The counting rate was measured only in the region of the peak for (*d*) the 66° scattering of 982, 1,085, 1,173, and 1,215 MeV. electrons, and (*e*) the 112° scattering of 909 MeV. electrons. The corresponding cross-sections were evaluated using the line shape established in the full sets of measurements.

The other two counters in the telescope were used to reduce backgrounds. Counter *C* was inoperative when the comparatively slow recoil protons were being detected, and the bias on the plastic scintillator counter *B* was raised so that relativistic particles were not detected. Coincidences between counters *A* and *B* were required, the effective pulse widths being about 0·5 μsec.

When electrons were being detected the bias on counter *B* was lowered, and counter *C* was brought into operation. This was a lead glass total absorption Čerenkov detector, which produced recognizably large pulses when the desired electrons arrived. Triple coincidences between counters *A*, *B* and *C* were required, the effective width of the mixed pulses being about 20 ns. for *A*, 200 ns. for *C*, and 0·7 μs. for *B*. Each triple coincidence event opened an electronic gate, allowing the output from counter *C* to reach a pulse-height analyser.

At all times the electronic equipment was gated by a 4 ms. pulse locked to the peak of the magnetic cycle of the synchrotron. This reduced corrections for cosmic ray events ($\lesssim$ 10 per cent, but usually negligible).

Results

Figs. 3 and 4 show respectively the recoil proton and the scattered electron peaks observed at 66° from 781-MeV. incident electrons. The ordinates are the coincidence counts observed per 'sweep' of the quantameter (1 sweep = $4 \cdot 97 \times 10^{12}$ MeV.), and the abscissæ are the voltages in the spectrometer shunt.

The counting-rate as a function of the magnet current after subtraction of the rate from carbon

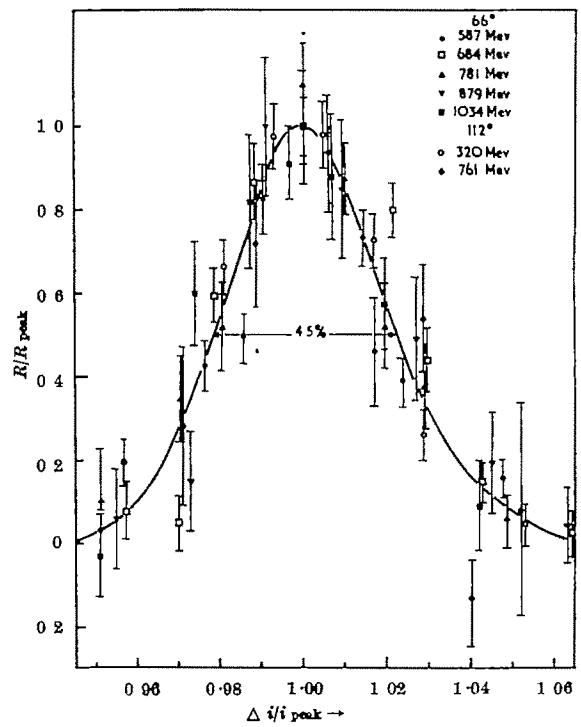

Fig. 5. Line shape of the peaks caused by elastically scattered electrons

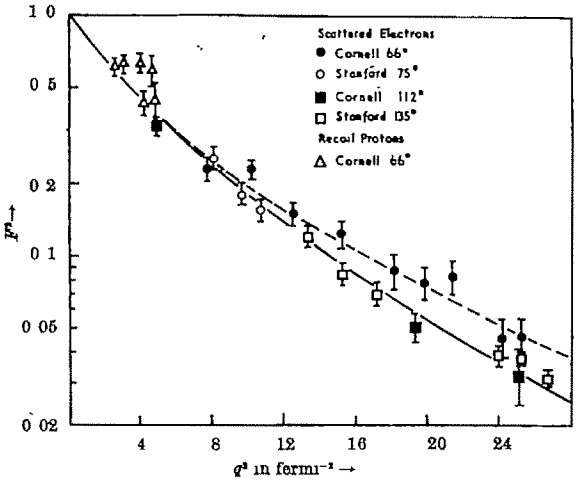

Fig. 6. Experimental results, including Stanford results at high q^2. The full line is given by the formula $F^2 = (1+0\ 0533\ q^2)^{-4}$, while the dashed line is fitted to the 66° experimental points at high q^2

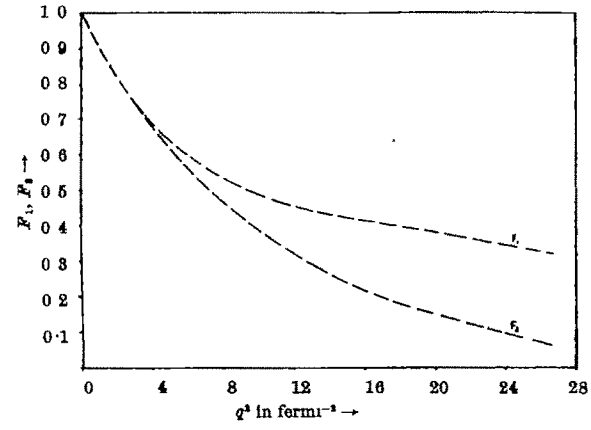

Fig. 7. The individual form factors required to reproduce the full line of Fig. 6 at 135°, and the dashed line of Fig. 6 at 66°

The carbon target results have been multiplied by a normalizing factor $\beta = 0{\cdot}89$, which equalizes the effects of the carbon nuclei in the two target materials. Rather clean elastic peaks are revealed in both figures, although there is a small inelastic tail in the proton distribution. Fig. 5 shows the line shapes observed in all the complete sets of electron measurements, before correction for saturation.

It was found that the height of a peak decreased slowly if a given polyethylene target was bombarded for a long time. Presumably this was due to ejection of the hydrogen from the target, an effect probably correlated with a brownish discoloration which also appeared. The polyethylene targets were changed every few hours and a suitable correction for ageing was established and applied ($\lesssim$ 3 per cent).

Finally, the usual radiation correction ($\lesssim$ 13 per cent) was applied to allow for the emission of bremsstrahlung in the electron-proton scattering process.

The results, expressed as a plot of F^2 against q^2, are shown in Fig. 6. For comparison some of the results of Hofstadter *et al.* are also shown, together with those of Hand.

Discussion

The results of the present experiment clearly agree well with the Stanford data wherever they overlap, that is for $q^2 \lesssim 11\ f^{-2}$ when $\theta < 90°$, and for $q^2 \lesssim 26\ f^{-2}$ when $\theta > 90°$. Often the form factors at low q^2 are expanded in the static approximation:

$$F_{1,2} = 1 - \frac{1}{6}\, a_{1,2}^2\, q^2 + \ \ldots \qquad (4)$$

where $a_{1,2}$ are the root mean square radii of the charge and the anomalous magnetic moment of the proton. Thus no change is indicated in the conclusion of Hofstadter *et al.* that these radii are about 0 8 f. It should be noted, however, that equation (4) is subject to relativistic and dynamic corrections of the order of q^2/M^2, so that the exact physical significance of this line of interpretation is not very clear.

At high values of q^2 the points for $\theta < 90°$ (circles and dashed line in Fig. 6) flatten out[6] and lie consistently higher than the points for $\theta > 90°$ (squares and full line in Fig. 6). This behaviour indicates that F_1 and F_2 are not equal, and in fact an average of the points near $q^2 = 20$ gives $\frac{F_2}{F_1} = 0{\cdot}37\ ^{+\,0{\cdot}17}_{-\,0{\cdot}14}$. Fig. 7 shows the individual values of F_1 and F_2 which would give the dashed and full lines of Fig. 6 at angles of 66° and 135° respectively. The two form factors must behave in this general fashion, although at present their values have clearly not been determined with precision. (This conclusion was reported by one of us (R. R. W.) to the Tenth Annual Rochester Conference on High Energy Physics (August 25–September 1, 1960). A subsequent paper by Prof. R. Hofstadter included a similar deduction on the basis of recent work at Stanford.)

The flattening out of F_1 at $q^2 \approx 12\ f^{-2}$ must be associated with the inner structure of the proton, at radii of the order of $0{\cdot}3\ f$. The charge density in this region may be expected to include contributions from virtual states containing nucleon–antinucleon pairs, kaons and multiple pions. It is likely to be some time before these various effects are disentangled with any certainty.

The most promising line of theoretical attack is based on the dispersion theory[7,8] of the isotopic scalar and vector parts of the nucleon form factors. Unfortunately there are no general theorems relating the neutron and proton form factors, so that data on electron–neutron scattering at high q^2, for both large and small angles, are needed before further progress can be made.

We are indebted to Dr. P. C. Stein and Mr. D. Edwards for help in taking readings, and to Mr. A. Contogouris for helpful discussions on theoretical matters. Mr. P. D. O'Neill gave valuable help with numerical computations. The co-operation of the synchrotron crew is gratefully acknowledged.

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SOME MOLECULAR DETAILS OF THE SECONDARY STRUCTURE OF RIBONUCLEIC ACID

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THE Watson-Crick structure for deoxyribonucleic acid[1] and the Pauling-Corey structure for the α-helix in proteins[2] represent unique chain conformations that permit maximum hydrogen bonding and impose rigidity on the otherwise flexible chains. The several highly specific functions of ribonucleic acid suggest that it also must have a unique spatial arrangement that only a periodic chain conformation, that is, a secondary structure, can provide.

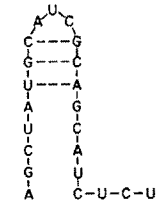
Nearly two years ago, it was shown that a number of physical chemical observations on ribonucleic acid were consistent with its having a partial (40–60 per cent) helical structure in dilute neutral saline at low temperature[3,4], and these conclusions have since received further support[5–8]. At that time it was proposed that each chain consists of a number of imperfect hairpin-like helices similar in character to those of deoxyribonucleic acid, united by flexible, unstructured regions. However, the proposal lacked definition on two important points: it was not clear how half the bases in ribonucleic acid could fit into helical regions; and in connexion with this, it was not known how large a helical region had to be in order to satisfy the observed thermal stability. The object of this communication is to show how recent experimental studies on synthetic polynucleotide analogues remove these difficulties and permit a more specific delineation of the secondary structure of ribonucleic acid.

Nature of the Base Pairs: It is now possible to propose with some confidence that the helical regions of ribonucleic acid are similar to those in deoxyribonucleic acid, that is, they contain the adenine-uracil and guanine-cytosine hydrogen-bonded base pairs. Of the many base pairs which have been examined in helical polynucleotide structures, these have been found to interact most strongly[3,9,10]. Furthermore, they appear to be the only pairs which are mutually conformable in a regular helical framework. Consequently, the structure common to the adenine-uracil and guanine-cytosine pairs can be expected to be favoured, and since in this framework all other base pairs are either sterically intolerable or are separated by too large a distance to form hydrogen bonds, their existence is regarded as unlikely. Consistent with this view, a linear correlation has now been demonstrated between the thermal stability of a variety of ribonucleic acids and their guanine-cytosine contents (Fresco, J. R., and Givelber, H., unpublished observations).

Accommodation of Successive Base Pairs: The consequence of adopting a deoxyribonucleic acid-like structure for the helical regions of ribonucleic acid is that severe sequence requirements would appear to be necessary in order to realize the 40–60 per cent level observed in ribosomal[3,4], tobacco mosaic virus[3,4], and transfer ribonucleic acid[11]. For example, a *random* sequence of the four bases can readily be shown to allow only about 20 per cent helical development even if two adjacent base pairs are accepted as 'helical regions' (see Fig. 1*a*). However, when it was found that a synthetic copolymer containing a random arrangement of adenylic, guanylic, cytidylic and uridylic nucleotides displays about the same helical content as ribonucleic acid[3,4], the notion that sequence restrictions make possible the high helical content had to be rejected.

An attractive solution to this dilemma has come from a recent study of helix formation between homopolymers and copolymers of adenylic and uridylic acids which revealed an additional degree of freedom in polynucleotide conformations[12]. In this work it became evident that when chains of poly-uridylic acid were mixed with chains of a copolymer of adenylic acid and uridylic acids (with adenylic acid the dominant component), the optimal base-pairing occurred when the number of uridylic acid residues in poly-uridylic acid equalled the number of adenylic acid residues in the poly-adenylic-uridylic acid chain. From this it was concluded that all the uridylic acid residues in the copolymer were looping out from the helical structure, so that only adenylic acid residues remained opposite the uridylic acid residues of the poly-uridylic acid chain. Comparable results were obtained when the interacting species were poly-uridylic-adenylic acid and poly-adenylic acid. The helix-with-loops thus formed is weaker than the equivalent helix without loops, because the presence of

For a particular random sequence polynucleotide of 22 residues the maximum helical region has 8 paired bases. The average is 2



When loops are permitted, the maximum helical region has 7 paired bases. The average is 6

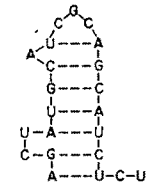


Fig. 1. Effect of loop formation on the efficiency of base-pair interaction

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loops brings about a concentration of negative charges and therefore increases electrostatic repulsive forces, and because the accommodation of the loops probably introduces some strain in the adjacent helical regions. Consequently, loops conspire with the shortness of the helical regions to lower the T_m value (where T_m is the temperature at the mid-point of the helix-coil transition) which is a measure of helix stability. In the case of poly-uridylic-adenylic acid and poly-uridylic acid, helical complexes were stable at 25° C. only if they contained less than about one-third of their residues in looped form. In these complexes all the loops occur only in the poly-uridylic-adenylic acid chain.

In ribonucleic acid the helical regions are shorter and the loops probably exist in both strands of these regions. These factors would tend to lower the fraction of residues that could be permitted in a helical region. However, the presence of the much stronger guanine-cytosine bonds[10] would probably more than compensate for this effect. For example, a helix having equal numbers of adenine-uracil pairs ($T_m = 61°$) (refs. 3, 4) and guanine-cytosine pairs ($T_m = 110°$) (ref. 10) bonds would have a T_m 20–25 deg. higher than an equivalent helix with only adenine-uracil bonds. Since ribonucleic acid can be expected to have many helical regions with at least this degree of content of guanine-cytosine bonds, it appears safe to conclude that these regions will be stable at 25° C. even if they contain as much as one-third of their residues looped outside the helix. Thus, loops permit a greatly increased incorporation of adenine-uracil and guanine-cytosine pairs into helical regions.

The Minimum Helix Size : Before exploiting the degree of freedom that loops provide in ribonucleic acid, one other restraint must be noted. Even without loops, the T_m of a given helical structure will decrease with decreasing length and will at some value pass below some temperature of interest, say 25° C. Current experiments (Fresco, J. R., Blake, R., and Doty, P., unpublished observations; also ref. 13) in which T_m has been determined for various helical complexes of long-chain poly-uridylic acid, and uniform oligonucleotides of adenylic acid show that T_m becomes equal to about 25° for the tetraadenylic acid. Again, this may be lowered still more if the long-chain poly-uridylic acid is replaced by a short oligo-uridylic acid. But, as before, the existence of guanine-cytosine bonds in ribonucleic acid will probably more than compensate for such weakening effects. Hence, we can estimate that the minimum size of helical regions stable at 25° C is about four nucleotide pairs, and that six nucleotide pairs, for example, would probably accommodate at least three looped-out residues at 25°. This, then, defines helical regions of minimum stability. Since the major part of the melting curve for all samples of ribonucleic acid occurs between 20° and 90°, it would be expected that the majority of helical regions in ribonucleic acid are longer or have a smaller percentage of loops.

Summary of the Features involved in the Secondary Structure of Ribonucleic Acid : The three points discussed above can be combined with the relevant observations of the earlier work to provide a summary of the behavioural characteristics of ribonucleic acid which should govern the elaboration of its secondary structure. The experimental support for these points is now fairly substantial, although further work can be expected to lead to minor revisions.

(1) Ribonucleic acid is a single-stranded molecule[14–17] the secondary structure of which arises from intramolecular interactions.

(2) The most stable of several possible secondary structures is the two-stranded helix of the deoxyribonucleic acid type in which adenine-uracil and guanine-cytosine pairs are hydrogen-bonded. The guanine-cytosine pair, being stronger, is preferred.

(3) At 25° and moderate ionic strength, the minimum length of helix without loops is about four nucleotide pairs.

(4) Under the above conditions, if the helical region contains an approximately equal quantity of adenine-uracil and guanine-cytosine bonds, six nucleotide pairs can accommodate at least three looped residues (one fifth of the total involved). Longer regions can have up to one-third of their residues looped out from the helical structure without destroying their stability.

(5) Ribonucleic acid takes up its most stable conformation as a result of a lateral mobility which permits exploration of most competitive conformations[12,18,19]. The chain adjustment made possible by the looping of residues in helical regions is a vital part of this process.

(6) The most stable helical regions arise from interactions between adjacent sections of the polynucleotide backbone. Entropy considerations suggest that interactions between distant sections are unlikely, since they would lead to very highly restrictive conformations. Thus, the helical regions take the form of hairpin turns which require a minimum of three unbonded nucleotides to connect the antiparallel hydrogen-bonded chain sections. The spatial parameters of the helix are probably close to those determined for poly-(adenylic + uridylic acids)[20].

Illustrations of Secondary Structure : Our proposal is that this set of conditions is sufficient to indicate the essential nature of the deployment of nucleotides in the characteristic conformation of ribonucleic acid. The kind of structure that develops from these conditions can be illustrated in two ways. In one we can take a short sequence of nucleotides chosen at random from an equimolar mixture and work out all conformations compatible with the above conditions. In another we can take a much longer sequence and show typical conformations which satisfy these conditions but may not represent the optimal conformation.

The first approach is summarized in Fig. 1. Here a particular random sequence of 22 nucleotides has been examined. Without the possibility of loops, the longest helical region has only three adjacent base pairs and is therefore below the stability condition specified. When loops are permitted, however, 7 adjacent base pairs can be formed, resulting in 63 per cent of the bases being in the helical region. Indeed, the average of all conformations is 6 pairs, or 54 per cent, of the nucleotides in helical regions, all above the minimum size permitted.

In the second example, we have taken a random sequence of 90 nucleotides, thus using a size comparable with that occurring in transfer ribonucleic acid. If one attempts to obtain maximum length of the helix, results such as that in Fig. 2 are obtained. Here 60 per cent of the bases are paired, but in the central section the concentration of loops is so high that this section would not remain helical according to the above conditions. Consequently, only about 40 per cent of the bases could be paired. Alternatively, one can explore many other conformations and these lead

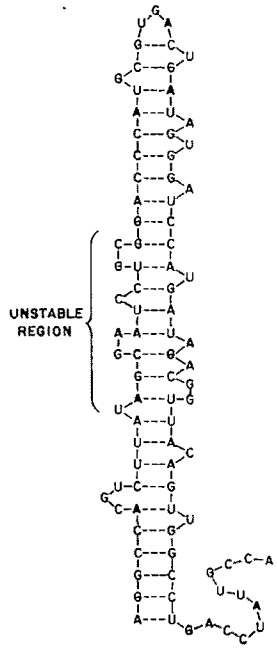

Fig 2. A less probable arrangement for a hypothetical ribonucleic acid chain

to results such as that shown in Fig. 3. Here there are three helical regions all exceeding the conditions of minimum stability, and 58 per cent of the bases are paired. In all cases examined, these helical regions were less than twelve nucleotide pairs in length and had only very short unbonded sections between them. Indeed, we have found that such short helical regions generally lead to the most stable conformations, since they make possible the greatest amount of chain adjustment and thereby satisfy the tendency towards maximum hydrogen bonding[13,18,19]. Thus the conformation in Fig. 3 is typical of a closely related group that is permitted by the above set of conditions and it is representative of the more specific definition of secondary structure in ribonucleic acid that we propose.

It should be emphasized that in the present treatment we have had to assume a random sequence of nucleotides in ribonucleic acid, because of the absence of definite information on this point. It is much more likely, however, that the actual sequences in individual ribonucleic acid molecules deviate from randomness, and in such ways that the amount and the stability of the helical regions are either greater

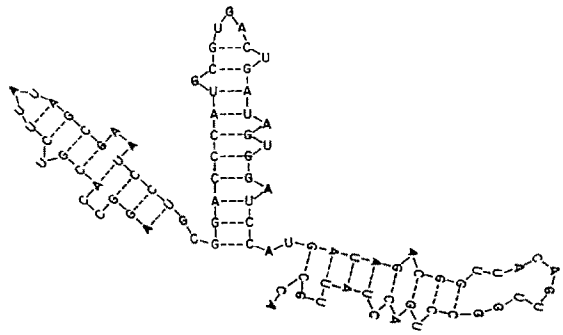

Fig. 3. A more probable arrangement for a hypothetical ribonucleic acid chain

or less than those obtained with our assumption. Thus, while the helical content and stability that we have estimated do approximate to those found in a number of ribonucleic acid samples, nevertheless the accuracy of our estimates is limited by the assumption of random sequence.

Discussion: Having arrived at this view of the secondary structure of ribonucleic acid, one must ask if it is compatible with what is known about that substance, and if there is any direct test of the structural proposal. In the first category there are three relevant data: those purporting to estimate the helical content, those dealing with size and shape and their dependence upon ionic strength, and those derived from X-ray diffraction.

Since in our model the fraction of bases in helical regions does lie in the vicinity of 60 per cent, agreement with the earlier estimates of helical content has been achieved. In addition, the range of temperature in which the helical regions melt is that expected from a polynucleotide having a series of helices that deviate in varying degrees from long, perfect helices involving the adenine-uracil and guanine-cytosine pairs.

Hydrodynamically, ribonucleic acid molecules behave as randomly coiled chains[4,5,15–17]; but this behaviour, as reflected in the dependence on molecular weight of the sedimentation-rate and the intrinsic viscosity, would also be expected from the model discussed here, since the mass distribution averaged over all orientations would probably approximate to a Gaussian distribution, as does a random coil. A more discriminating observation is that ribonucleic acid does now show a *strong* polyelectrolyte effect at *moderate* ionic strength[17], that is, it does not expand sharply with decreasing salt concentration. In fact, any expansion that does occur is accompanied by a simultaneous loss of some helical structure[6,8]. Thus, there do not appear to be many nucleotides in flexible chain regions except those that are liberated from previously disrupted helical regions. The model proposed here would behave similarly, since the random regions between the helices are very short, and most of the remaining nucleotides that are not hydrogen-bonded are in loops that can display only slight conformational response to changing ionic strength.

The last kind of observation to be considered is that of X-ray diffraction. The early diffraction studies[21] did not contribute much to our knowledge of the secondary structure of ribonucleic acid, although the reflexions were such as not to conflict with a helical structure. Current investigations by Zubay, Wilkins and Brown (ref. 22 and Brown, G., personal communication) have yielded much more definitive diffraction patterns for both ribosomal and transfer ribonucleic acid, and in each case they obtain considerable evidence for the deoxyribonucleic acid type helical regions which were proposed earlier[3,4]. These recent observations neither support nor contradict the looping feature of our model; but it is probably in this method, with the use of specially prepared polynucleotide helices, that a direct test of this feature can be made.

It may be useful at this point to make some general remarks about possible relations between the secondary structure of ribonucleic acid proposed here and the structural requirements for the functioning of ribonucleic acid. In the absence of specific information, two kinds of activity must be visualized for

ribonucleic acid. In the particular case of transfer ribonucleic acid, the specificity of amino-acid uptake may be due in part to the stabilized topology of a portion of the ribonucleic acid molecule in the vicinity of the acceptor end. This model provides adequate possibilities in this direction.

In ribosomes, ribonucleic acid must maintain stable connexions with the protein component so that a swollen matrix is preserved. While little appears to be known about the details of this organization, two recent observations suggest that our model is relevant to ribonucleic acid within the ribosomes. One is that the hydrogen-bond content of ribonucleic acid within the microsomes is similar to that estimated for the isolated ribonucleic acid[17,22]. The other is that the X-ray diffraction pattern of ribosomes bears a close similarity to that of the isolated ribonucleic acid, once the protein diffraction is subtracted[23]. Consequently, we can visualize that the unpaired bases in the loops or in open-chain regions provide potential sites for structural connexions with amino-acid residues of the ribosomal protein. Of course, the more significant role of ribonucleic acid in the ribosome would appear to be that of recognition of an incoming transfer ribonucleic acid–amino acid molecule, its momentary deposition at a particular locus, and its later ejection. The stability of many of the helical regions in ribosomal ribonucleic acid at cell temperature is marginal, and thermal fluctuations might well lead to the momentary opening of a significant proportion of the regions envisaged in our proposal. In that event the complementary region of the transfer ribonucleic acid molecule could readily be accepted by base-pair interactions, resulting in a short helical region. Subsequent disruption of this helical region at the time of a later thermal fluctuation, perhaps resulting from the formation of peptide bonds, might provide a means of return to the former state with the liberation of the temporarily bound ribonucleic acid molecule. Such possibilities are clearly inherent in the helical structure described here.

In concluding, we would like to emphasize that the secondary structure of ribonucleic acid that we have detailed is dictated to each molecule by its own nucleotide sequence; and that the unpaired bases in these molecules constitute a tertiary structure, in that they are in most cases held in fixed relation to each other either on the same helical region or on different ones. This provides for new possibilities in coding and information transfer that are not inherent in a structureless single strand or in a perfect base-paired helix.

This work has been supported by grants from the United States Public Health Service, *C*–2170, and from the American Heart Association.

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REPORT OF THE TELEVISION ADVISORY COMMITTEE, 1960

THE Television Advisory Committee, set up in October 1952 under the chairmanship of Admiral Sir Charles Daniel, had as terms of reference: "To advise the Postmaster General on the development of television and sound broadcasting at frequencies above 30 megacycles per second and related matters, including competitive television services and television for public showing in cinemas and elsewhere". The Committee has now issued its third report* (the earlier reports were issued in 1953 and 1954 respectively) and is concerned entirely with possible ways of allocating wave-bands to alternative programmes, and with possible new scanning-line standards to link up Britain with the rest of Europe. Colour television also is briefly referred to, but nothing new is said, though a later report on this specific subject will be issued by the Committee "as soon as they are in a position to do so".

The questions discussed in the present report are wholly technical, but even within this limited sphere it is a rather disappointing document. The various technical questions cannot fully be answered, as this Committee of course realized, without relating them to broader matters—a national programme policy, types of material and picture quality really needed, the degree of programme exchange with Europe (or, shortly, with the whole globe), the relative needs and urgencies of other services' demands on æther space, financial questions and many others. Thus it is good to find that the Postmaster General has at last announced the appointment of the long awaited committee to inquire into the future of broadcasting and television in the country; this new committee, under Sir Harry Pilkington, has the broadest terms of reference, covering all aspects of policy. It has been asked by the Postmaster General to consider this present technical report of the Television Advisory Committee; perhaps the new committee will take its technical inquiries a little further too.

Never again, in all probability, shall we in Britain have the opportunity to re-think the whole fundamentals on which our television service rests.

* General Post Office. Report of the Television Advisory Committee, 1960. Pp. 20. (London: H.M. Stationery Office, 1960.) 1s. net.

Thus we are forced to reconsider now, for several reasons; Surely we should seize our opportunity and act boldly, with the kind of enterprise and initiative which British industry showed in the 1930's when it took the world lead in television development? At that time we had reached our first point of departure and broke away from earlier television history, with its mechanical standards, to develop a whole new electronics industry. We have surely reached a similar point to-day. For we have the colour-television question forced on us, we have integration with Europe (and we should not restrict this to Europe, but adopt a global view now, with the techniques likely to emerge during the next twenty-five years, being the period under consideration by the Committee), and we have the æther congestion problem; we have a host of new techniques as yet unused.

Something has to be done at this point. Cannot we again break away from tradition and think boldly? We go on transmitting nearly identical frames 50 times a second, to be viewed on traditional (though improved) cathode-ray tubes; Is there no alternative? We go on speaking of wave-bands and other Fourier-like concepts, rather than of probabilities and information-rates. Cannot we devise a new kind of camera with much lower noise figures, and then take advantage of coding schemes? Is it inconceivable to develop receivers with cheap 'memories'? Endless such questions can be raised; it is all very well for a mere academic like myself to raise them, but the overriding question is: Has British industrial inventiveness vanished in this field where once it was so prominent?

The main conclusions of the present report of the Television Advisory Committee may be illustrated by the following table, which defines the four 'bands' which are at present available:

Band	Range (Mc./s)	
I	41–68	At present used by five B.B.C. channels.
III	174–216	Half this range used by four I.T.A. channels
IV	470–582	Not at present used, but propagation and other field-trials carried out.
V	606–960	

Nearly half band V has been appropriated already for tropospheric scatter links, leaving only the range 606–800 Mc./s. for possible use for television.

Apart from France, Eire and Britain, 625 lines are standard in Europe, both east and west. It seems wise for us to adopt the same, for our broadcasts will become increasingly integrated with those of Europe (though this is too restricted in my view). The conclusion offered is that, if 625 lines be adopted, the number of alternative programmes offered to the public cannot be increased, unless we spill over into the experimental bands IV and V. Dreams of a third programme begin to fade.

However, the Technical Sub-Committee advises that *if* television be confined to bands I and III, we *could* have a third programme working on 625 lines if we limit our channel spacing to 7 Mc./s. This point seems to me to be crucial. For the European standard bands are not 7 but 8 Mc./s., which we are told is needed for full picture quality on 625 lines. How can we get 8 Mc./s. into a 7 Mc./s. pot, and so put three programmes where two stand at present? By compression.

This word 'compression' is not mentioned at all in the present report. Throughout, it is accepted without question that picture quality depends solely upon band-width; it does not. We may not expect the Committee to recommend specific systems of recoding for band-width compression; far too little is understood yet, but it is a thousand pities it has not recommended urgent studies of the subject. Television by present techniques is about as wasteful of band-width as can be; we still have not learnt the lessons of statistical communication theory.

Calculation of signal information redundancy is one thing; invention of techniques for utilizing the results is quite another. Many writers have referred to television signals as being ten-to-one, hundreds-to-one, redundant, but this is going much too far at present. But to compress band-widths in fractional ratios of 7/8 or even, say, 2/3 raises no fundamental difficulties; and there need be no complexity of apparatus in the receiver, for coder and decoder need not be 'mirror-images'.

British industry is doing little about this, to the best of my knowledge. It needs development of new types of low-noise camera and multiplier, of storage systems, of new kinds of time-base particularly. Moreover, the implications of such work extend into many fields other than television. Again, it is conceivably possible to develop systems which would be compatible with existing receivers (by substitution of parts only, such as time-bases).

Whatever changes are proposed, compatibility must be considered, as this report rightly stresses, because some £600 million is tied up in existing receivers in Britain alone. The capital invested in the whole industry is gigantic. This report emphasizes the view so commonly expressed, that 'higher picture quality' necessarily means greater 'detail' (that is, adhesion to realism). If only we could educate the public to accept certain visual conventions and forms, how much we might save by coding techniques! It is a curious divergence, that while modern art does just this, in its abstracting out of reality, our mass-cultures such as television forever seek greater realism like the Victorian painters. This process is to-day very expensive.

COLIN CHERRY

OBITUARY

Prof. W. H. Lang, F.R.S.

BY the death of William Henry Lang on August 29 botanists have lost one of the most distinguished plant morphologists of this century. Born in 1874, Lang was educated in Glasgow and entered the University in 1889, where he studied science and medicine, graduating M.B., C.M., with high commendation in 1895. He had in the previous year while a medical student graduated B.Sc. with honours in botany and zoology. In 1900 he graduated D.Sc. and in 1932 the University conferred on him an honorary LL.D. In 1895 he was awarded a Robert Donaldson scholarship which enabled him to work on apogamy in ferns at the Jodrell Laboratory at Kew where D. H. Scott was then keeper. After returning to Glasgow he was appointed lecturer in Queen Margaret College in the University and continued research on ferns and on cycadean sporangia. His work on ferns was undoubtedly stimulated by his association with

Prof. F. O. Bower and his fellow lecturer and great friend Gwynne-Vaughan. He also worked on Hepaticae and published in 1901 a paper on apospory in *Anthoceros*: this was followed by other papers on *Cyathodium*, *Notothylas*. He continued research on Pteridophyta and made important contributions to our knowledge of the gametophytes of the Ophioglossaceae. In 1909 he produced an exceptionally interesting paper on a theory of alternation of generations in Archegoniatae, based on ontogeny, which led to an organized discussion on "Alternation" at the Linnean Society.

His appointment in the same year as first occupant of the Barker chair of cryptogamic botany in the University of Manchester provided him with much greater opportunity for research. Prof. F. E. Weiss, who occupied the chair of botany, was a most sympathetic and helpful colleague, and Lang had practically no administrative work. He gave lectures, only to the honours students, on cryptogams. In 1910 he went on an expedition with A. G. Tansley to Ceylon and Malaya to study tropical Cryptogams. On returning he continued work on the morphology of the Ophioglossaceae and between 1910 and 1914 published four papers in the *Annals of Botany*. In 1914 and 1915 there appeared in the *Memoirs of the Manchester Literary and Philosophical Society* his "Studies in the Morphology of *Isoëtes*", probably one of the most difficult subjects on which he had worked. The complex anatomy of the plant and its curious method of growth presented particularly difficult problems. Lang's descriptions are for the most part clear and unambiguous, but it requires close concentration on the part of the reader to follow his comparisons between the stelar morphology of *Isoetes* and that of other Pteridophyta. It was perhaps his most notable work up to that date.

The discovery by Dr. W. Mackie, of Elgin, of petrified plants in an astonishingly good state of preservation in chert of Middle or Lower Devonian Age in Aberdeenshire had far-reaching results. The investigation of the Rhynie fossils was carried out by Kidston and Lang. They commenced publication of their results in 1917 in the *Transactions of the Royal Society of Edinburgh* and completed it in 1921, when they gave an account of their discovery at the meeting of the British Association in Edinburgh. These memoirs on the Rhynie plants are models of accuracy in description and restraint in phylogenetical speculation. Lang was aware of the importance and significance of these discoveries and their bearing on problems of evolution and comparative anatomy, but wisely left it to others to indulge in speculation on the course of evolution of vascular plants. Later discoveries by him and others of complex Silurian and Lower Devonian plants fully justify the restraint shown by Kidston and Lang, whose names will always be associated with this, the most important contribution of the century to our knowledge of early plant life.

Those who were privileged to know and work in the same laboratory will remember him as a most exceptionally gifted man with many and varied interests not only in science but also in literature and the Fine Arts. He was extremely friendly and helpful, and his junior colleagues have reason to remember him with great respect and affection.

JOHN WALTON

NEWS and VIEWS

Physiology at Birmingham: Prof. H. P. Gilding

PROF. HENRY PERCY GILDING, who is retiring from the chair of physiology in the University of Birmingham, graduated at Oxford in 1923 and in the same year entered on a distinguished undergraduate and postgraduate career at St. Bartholomew's Hospital Medical College where, while the Department of Physiology was without a professor, he had charge of the teaching of physiology and the administration of the Harvey Laboratories. In 1928 he was a Fellow of the Rockefeller Institute, New York, where he carried out research with Dr. Peyton Rous. He returned to London to join the Physiology Department at University College and in 1932 was appointed reader. At University College he continued his researches on the circulation of the blood and on lymph and his interest in the applications of physiology was shown by his tenure of a research post with the Medical Research Council and the Thomas Young lectureship in clinical physiology at St. George's Hospital Medical School. When he was appointed to the chair of physiology in Birmingham in 1933, Gilding made great use of the opportunities given to him for planning and organization in the building of the new Medical School. He is well known for his interest in medical education, and when teaching in the new School was established, he initiated the scheme of integrated teaching of physiology and anatomy by co-operation between the two Departments which has attracted so much attention. When the Goodenough Committee was considering developments in medical education he played an active part in obtaining increased facilities for honours courses in physiology for medical students. A great demand for his services as an external examiner is not only a consequence of this interest but also a tribute to his personal qualities. He has for many years given useful service to the Physiological Society as a member and chairman of its Committee, as its treasurer and as its representative on the Council of International Abstracts of Biological Sciences. He served as a member of the Council of the British Association and was recorder and later president of its Section I (Physiology). Gilding saw much active service in the First World War which interrupted his undergraduate career and he was for a time a prisoner of war.

Prof. Ian E. Bush

DR. IAN E. BUSH has been appointed to succeed Prof. Gilding. He went from Bryanston School to Pembroke College, Cambridge, and was awarded first class honours in Natural Sciences Tripos Part 2 (Physiology) in 1949. The grant of a Medical Research Council scholarship in 1949 enabled him to work in the Physiology Laboratory, Cambridge, until 1950, when he moved to the National Institute for Medical Research, where he stayed until 1952. The degree of Ph.D. (Cantab.) was conferred in 1952. A Commonwealth Fund Fellowship provided the opportunity for him to travel to the United States, where he

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worked in the Biological Chemistry Department, University of Utah, and later at the Huntington Memorial Laboratory, Massachusetts General Hospital. In 1953 he became a medical student and part-time research assistant to the Medical Unit at St. Mary's Hospital, London. In 1956 he moved to Oxford with Sir George Pickering on the latter's appointment to the regius chair of medicine. He qualified M.B., B.Chir. (Cantab.) in 1957. He was placed in charge of a group for research into humoral physiology and pathology under Sir George Pickering. This work has attracted the support of the Medical Research Council and the Rockefeller Foundation. He has published numerous papers on steroid metabolism and is particularly well known for his able use of chromatography in the analysis of steroids in general.

Science Adviser to the U.S. Secretary of State

DR. WALTER G. WHITMAN, formerly chairman of the Department of Chemical Engineering of Massachusetts Institute of Technology, has been appointed science adviser to the U.S. Department of State, in succession to Wallace R. Brode, who has resigned. Dr. Brode, who has a long record of government service with various scientific agencies, has been serving as science adviser to the Secretary of State since January 1958. A science adviser and a number of science attachés at posts abroad were first appointed in 1951. During his tenure as science adviser, Dr. Brode revitalized the entire science attaché scheme. Ten embassies abroad have been staffed with science attachés, many of whom cover a number of countries on a regional basis. These attachés facilitate scientific exchanges with the United States, and interpret American science to scientists, science writers, editors, and others who influence foreign attitudes toward the United States, and its scientific and technological achievements. Further, as a function of prime importance to the Department of State, they help other members of the embassy staffs to give proper consideration to the scientific and technical factors involved in the decisions they must make.

Dr. Whitman, the new science adviser, served with the National Advisory Commission for Aeronautics during 1940–45, was director of the Lexington Project of the Atomic Energy Commission in 1948, and also served as secretary-general for the United Nations Conference on the Peaceful Uses of Atomic Energy in 1955. He was chairman of the Research and Development Board of the Department of Defense during 1951–53 and was a member of the National Advisory Commission for Aeronautics during the same two years. He is on terminal leave from the Massachusetts Institute of Technology.

British Steel Castings Research Association: Appointments

THE British Steel Castings Research Association, Sheffield, has announced the following new appointments. Mr. C. M. Stoch to be assistant director of research. Mr. Stoch, who joined the Association in 1951, has been in charge of the Plant Engineering and Industrial Health Section since 1953, and for the past two years has also been acting head of the Steelmaking Section. He was born in Poland, and, after having graduated in 1937 in metallurgy at the University of Krakow, he worked in the steelmaking department of the Baildon Steelworks, Katowice. He was called to the Forces in 1939 and took part in the fighting in Poland, rejoined the Polish Forces in France in 1940 and afterwards in Great Britain. Mr. Stoch has recently been investigating the development and improvement of dust control devices on grinding machines and fettling benches. Mr. K. Knaggs, deputy head of the Association's Steelmaking Section for the past two years, has been appointed head of this Section.

Joint British Committee for Electron Microscopy

A JOINT British Committee for Electron Microscopy has been set up with the following three objects in mind: first, to co-ordinate meetings in the whole field of electron microscopy, including the design, use and application of the instruments, and of cognate subjects arranged by its constituent bodies; secondly, to encourage the holding of joint meetings by its constituent bodies; thirdly, to act in the collective interest of the constituent bodies by maintaining liaison with the International Federation of Electron Microscope Societies and with National Societies covering this field, and also by maintaining liaison with oversea societies concerned with electron microscopy. Dr. V. E. Cosslett, University of Cambridge, has been elected the first chairman of the Committee. The foundation members are as follows: the Anatomical Society of Great Britain and Ireland; the Physics Group of the Textile Institute; the Biochemical Society; the Royal Microscopical Society; the Chemical Society; the Institute of Physics and the Physical Society; the Society for Experimental Biology; the Iron and Steel Institute; the Society for General Microbiology; the Linnean Society; the Pathological Society of Great Britain and Ireland; the Institute of Metals. Other societies interested in electron microscopy are welcome to adhere to this Committee. Further information can be obtained from the General Secretary, Royal Microscopical Society, Tavistock House South, Tavistock Square, London, W.C.1.

Funds for Basic Research in the United States: 1959–60

ESTIMATES by the National Science Foundation in "Reviews of Data on Research and Development", No. 22, put total funds for basic research in the United States in 1959–60 at 1,000 million dollars, compared with 430 million dollars in 1953–54 and 830 million dollars in 1957–58. Throughout this period funds for basic research were about 8 per cent of the total funds available for research and development. In 1957–58 expenditure on basic research by colleges and universities was 392 million dollars, an increase of 88 per cent on 1953–54, corresponding expenditure by the Federal Government being 111 million dollars (an increase of 136 per cent) and by industry 272 million dollars (80 per cent increase). The Federal Government, however, supplied 423 million dollars of the total funds for basic research and industry 249 million dollars, although these figures represent only 7 per cent of the total research and development funds from each of these sources. Of Federal funds for basic research in 1957–58, the universities and colleges received 57 per cent (compared with 61 per cent in 1953–54), industry 10 per cent (10 per cent in 1953–54), other non-profit institutions 7 per cent (5 per cent in 1953–54) and Federal Government institutions 26 per cent (24 per cent in 1953–54). Of the total 835 million dollars, 282 million dollars went to the biological and 553 million dollars to the physi-

cal sciences, of which 195 million and 197 million dollars, respectively, were in the universities and colleges; for industry the corresponding figures were 27 million and 245 million dollars, respectively; for other non-profit institutions, 27 million and 33 million dollars; and for Federal Government institutions, 33 million and 78 million dollars. For 1953–54, the corresponding figures are: colleges and universities, 92 million and 116 million dollars; industry, 9 million and 142 million dollars; other non-profit institutions, 14 million and 12 million dollars; and for Federal Government institutions, 17 million and 30 million dollars.

The Indian Potato Journal

The Indian Potato Journal, issued by the Indian Council of Agricultural Research (1; April 1959. Ed., P. L. Jaiswal. New Delhi. Rs. 6.00 per annum) as a half-yearly periodical, will be devoted exclusively to the improved cultivation of this crop. The journal contains original scientific papers, general articles and reviews of relevant research. Thus, in Vol. 1, No. 2, there are contributions on such topics as the effect of nitrogen fertilizers on the yield and chemical composition of potatoes; the crossability of diploid *Solanum* species; growth and tuber formation; control of sprouting by growth regulators; Kashmir as a potential seed potato area.

Geodesy and Artificial Satellites

In a recent issue of *Smithsonian Contributions to Astrophysics* (3, No. 9. Pp. iv+95–161. (Washington, D.C.: Government Printing Office, 1960.) 65 cents), entitled "Geodetic Uses of Artificial Satellites", G. Veis gives a detailed mathematical exposition of methods for extracting geodetic information from observations of artificial satellites. Most of the geodetic results so far obtained from satellites have stemmed from their orbital perturbations, this paper lays the foundation for the satellites' other role, when they act as aerial triangulation points and can be utilized directly, without the intervention of dynamical theory. A second recent publication on this topic is "Use of Near-Earth Satellite Orbits for Geodetic Information", by P. D. Thomas (Technical Bulletin No. 11 of U.S. Coast and Geodetic Survey. Pp. ii+36. (Washington, D.C.: Government Printing Office, 1960.) 45 cents). This is a lively and rather informal review of results up to the end of 1959 on the Earth's flattening, which satellites have shown to be 1/298·2 rather than 1/297, as previously believed. The paper also discusses the methods of observing satellites and some related topics.

Fluctuations in the Level of the Caspian Sea

The level of the Caspian Sea (*Nature*, 179, 1112; 1957), after many years of fall, in 1957 began to rise in spite of a marked decrease in the inflow of the river water. According to B. G. Richter (*Priroda*, 2, 45; 1960), this rise can be explained by the nature of the tectonic movements occurring in this region, and which tend to alter the volume of the hollow in which the Caspian Sea is situated. A map showing areas of elevation and areas of sinking explains the relative rapid rise of the land in the region of Baku and in parts of the eastern shore of the Caspian Sea, especially the rapid drying up of the salt-producing bay of Kara-Boghaz-Gol (*Nature*, 179, 409; 1957), which is discussed by V. D. Polyakov (*Priroda*, 3, 93; 1960).

Protease Inhibitor in Human Blood

Serum trypsin and chymotrypsin inhibitors have been determined with reasonable accuracy by a modified ultra-violet absorption method. The serum examined was diluted thirty times with normal saline. N. Aizawa reports in the April issue of the *Yokohama Medical Bulletin* that both inhibitors were found to be stable below 3° C. for about fifty days, and that 20 per cent of trypsin inhibitory activity was maintained even after heating at 60° C. for 30 min. On the other hand, inhibitory activity against chymotrypsin completely disappeared under the same conditions. It seems difficult to conclude that both inhibitory activities are exerted by a single inhibitor. Further experiments showed that the trypsin inhibitory principle was found to pass gradually through a 'Cellophane' membrane; it is probable that the inhibitory factor is a relatively lower molecular substance than hitherto supposed. From the fact that trypsin inhibitory activity was recovered by neutralization, even after the incubation of the serum for 24 hr. at less than *p*H 5·0, the *p*H inactivation may be a reversible change.

The Stone Age in Jersey: Saint Brelade's Cave

Saint Brelade's Cave in Jersey, British Channel Islands, has long been known as an important prehistoric site of the Stone Age. Following some preliminary digging it was partially excavated by the late Dr. R. R. Marett in 1913, but the First World War stopped the work, and though it was continued later, the bottom layers were never reached. An important Mousterian industry was, however, unearthed. Recently, Father Christian Burdo has re-examined the site, and excavated the lower layers where he has found an Acheulean assemblage. Dr. Zeuner dates the cave infilling to a period from the end of the Riss glaciation to the start of the Würm. The Société Jersiaise has published an excellent account of the finds which can be obtained from the Museum, 9 Pier Road, Jersey (Excavation of a Pre-Mousterian Horizon, 1950–1958. Pp. 77+8 plates. (Jersey, Ch. Is.: Société Jersiaise. 7*s*.)). Several of the implements are illustrated, and a list of the fauna and flora found given. There are also some excellent full-page photographs of the site itself.

James Picker Foundation: Radiological Research Awards

On behalf of the James Picker Foundation, the National Academy of Sciences–National Research Council is accepting applications for fellowships and grants in the field of radiology and nuclear medicine for the year 1961–62. The awards are made in four categories: *Advanced Fellowships in Academic Radiology*, offered for the first time during the past year, the purpose of which is to prepare the candidate who has completed his or her clinical training in radiology to meet in full the intellectual demands of an academic position in radiology; *Postdoctoral Fellowships in Radiological Research* are open to recent graduates who desire experience and training in scientific investigation, and while these awards are for a period of one year, requests for renewal will be considered; *Grants for Scholars* are a transitional form of support, designed to bridge the gap between the completion of research fellowship training and the period when the young scientist has thoroughly demonstrated his competence as an independent

investigator, and while the initial grants are limited to one year, renewal for two additional years may be recommended; *Grants-in-Aid of Research* are designed to encourage investigations offering promise of improvement in radiological methods of diagnosis or treatment of disease and are awarded to institutions, rather than to individuals. Applications in these four categories will be reviewed by the Committee on Radiology of the Academy–Research Council's Division of Medical Sciences. Final determination of awards is made by the Foundation on recommendation of the Division. These awards are not restricted to citizens of, or laboratories within, the United States. Application forms and further details can be obtained from the Division of Medical Sciences (Room 305, *AAUW*), National Academy of Sciences–National Research Council, 2101 Constitution Avenue, N.W., Washington 25, D.C. Applications must be submitted by December 1, 1960.

The Royal Institution of Naval Architects

THE Council of the Royal Institution of Naval Architects has made the following awards: *Royal Commissioners for the Exhibition of* 1851 *Postgraduate Scholarship in Naval Architecture* (1960), £600 per annum for two years, to Mr. B. S. Bowden, of King's College, Newcastle upon Tyne; *The Royal Institution of Naval Architects Scholarship in Naval Architecture* (1960), to Mr. M. A. Cubitt, of Messrs. Vosper, Ltd., Portsmouth (£400 per annum for three years at King's College, Newcastle upon Tyne); *Vickers-Armstrongs Scholarship in Naval Architecture* (1960), to Mr. Brian T. Procter, of Trinity Academy, Edinburgh (£400 per annum for four years at the University of Glasgow).

Naval Radiological Defense Laboratory

THE Naval Radiological Defense Laboratory in San Francisco has created a new position with the title of 'scientist-in-residence'. The scientist appointed will be expected to work on a matter of his own choosing within broad categories of the Laboratory's field of interest, which are the basic thermal and ionizing radiations from all types of nuclear reactions, their chemical, physical and biological effects, both topical and environmental, and ways of predicting, preventing or minimizing them. Candidates should have demonstrated superior ability for creative research. It is a full-time appointment, normally for one year. Two places are available this year; later there may be six. Applications should be addressed to Scientist-in-Residence Committee, U.S. Naval Radiological Defense Laboratory, San Francisco 24, California.

Natural Resources in Scotland

THE Scottish Council's Committee on Natural Resources is holding a symposium on "Natural Resources in Scotland" at the Royal Society of Edinburgh, 24 George Street, Edinburgh, during October 31–November 2. The three days will be devoted as follows: first day, "Basic Resource Facts"; second day, "Utilization of Resources"; third day, "Resource Administration and Development". The chairmen on each of the three days will be: the Rt. Hon. Lord Bilsland (president, Scottish Council, and Development and Industry), Sir Cecil M. Weir (chairman, London Executive Committee, Scottish Council, and Development and Industry), Sir Edward Appleton (principal, University of Edinburgh). Further information can be obtained from the Organizing Secretary, The Scottish Council (Development and Industry), 1 Castle Street, Edinburgh, 2.

William Thomas Brande

MR. E. E. IRONMONGER, Westminster College, North Hinksey, Oxford, writes: "I am collecting information concerning the life and work of William Thomas Brande (1788–1866), who was professor of chemistry at the Royal Institution during 1813–52 and secretary to the Royal Society during 1816–26. I should be glad to hear of any letters, manuscript material, etc., of which readers of *Nature* may have information".

Announcements

MR. A. V. S. DE REUCK, formerly assistant editor of *Nature*, has been appointed deputy director of the Ciba Foundation for the Promotion of International Co-operation in Medical and Chemical Research, London. Miss M. P. Cameron has returned to the Ciba Foundation as scientific assistant and librarian after five years in the United States.

THE first award of the Ellis Medal of the Institution of Works Managers goes to Mr. W. Huddleston, of the Springfields Atomic Factory, Salwick, Lancs. The Ellis Medal commemorates the work of John Milton Ellis, who helped to establish the Institution's training course, and will be awarded annually to a student of the Institution, under the age of thirty, who, having qualified at the end of the two-year course in works management, satisfies the assessors that he has most fully appreciated the practical implications of the training he has received in the art and science of works management.

AT the inaugural meeting of the first British Congress on the History of Medicine and Pharmacy, held in London on September 29, Sir Geoffrey Keynes and Prof. Owsei Temkin were awarded the honorary fellowship of the Faculty of the History of Medicine of the Worshipful Society of Apothecaries of London. The fellowship, which is an exclusive award to be held by no more than twelve at any one time, irrespective of nationality, is bestowed for outstanding services to scholarship in the history of medicine and pharmacy. Sir Geoffrey Keynes, whose work on Harvey, Sir Thomas Browne, John Ray and Robert Hooke is fundamental, is the first recipient of the new honour. Prof. Temkin, who is director of the Institute of the History of Medicine in Johns Hopkins University, Baltimore, has made many erudite studies of classical and medieval medicine, his authoritative monograph on "The Falling Sickness" being the most widely known of his works.

THE Medical Research Council states that in future all requests for compounds in the Steroid Reference Collection should be addressed to Prof. W. Klyne, Chemistry Department, Westfield College, Hampstead, London, N.W.3, and not to the Postgraduate Medical School at Hammersmith.

ERRATUM. Dr. C. W. Beklemishev has written in connexion with his communication entitled "Southern Atmospheric Cyclones and the Whale Feeding Grounds in the Antarctic" in *Nature* of August 6, p. 530; his address should read: "Oceanological Institute, 8 Bahrushin Street, Moscow 127".

PHYSICS EDUCATION

"THE difference between agriculture and farming" (a percipient candidate recently observed in an Ordinary Level General Certificate of Education examination) "is that in farming you actually do it". The gulf separating the doers and the talkers is conspicuous in the field of education, but the teachers who attended the recent International Conference on Physics Education managed to illuminate several important problems with little help from the platitudes so often displayed on such occasions.

Eighty invited representatives from twenty-eight countries formed the membership of the conference, which met at Unesco House, Paris, during July 28–August 4, under the sponsorship of the United Nations Educational, Scientific and Cultural Organization, the Organization for European Economic Co-operation and the International Union of Pure and Applied Physics. Prof. Sanborn C. Brown of the Massachusetts Institute of Technology was in the chair, and Mr. Norman Clarke of the Institute of Physics was secretary of the conference.

The main topics on which discussion centred were: (*a*) the need for instruction in physics from an early age (seven years was proposed without dissent); (*b*) the inadequacy of present-day methods of teaching physics in European and North American schools; (*c*) the difficulties found in trying to introduce Western educational ideas into Oriental countries; and (*d*) the need for radical innovations, exemplified by the concurrent exhibition of new teaching aids and the fully documented account of the Physical Science Study Committee's work in the United States.

The proceedings opened with a vigorous iconoclasm, presented by a working party appointed to examine the teaching of physics in schools. It found that contemporary physics courses in most European countries involve no scientific knowledge that has been discovered during the past few decades. Generally they offer a number of so-called facts and laws, combined with simple but pointless experiments to form "a somewhat desiccated and often strongly mathematical course based upon a few elementary physical principles". The presentation of physics in schools was condemned for failing to exploit the natural curiosity of children about the world in which they live, or to recognize their present-day familiarity with outstanding examples of applied science.

Strong criticism was expressed of physics courses intended primarily for the instruction of future specialists and of the truncated fragments which are all that can be acquired by pupils who leave school at sixteen. It was agreed that physics should be taught to all pupils and that the needs of those who do not intend to specialize must predominate. Neglect of this requirement was blamed for the drift towards a world of two cultures with a false antithesis between sciences and humanities. Lack of time was not regarded as a justification for early specialization. On the contrary, it was insisted that future specialists would be all the better for an early course of a broader kind and that a couple of years after the age of sixteen should provide ample time for additional instruction to meet university entrance requirements.

Discussing the content of an ideal physics course, the conference affirmed the basic position of mechanics, but recommended that it should be taught as a science, with a constant appeal to Nature, and not allowed to degenerate into a branch of applied mathematics. The child's introduction to physics should be through a consideration of atoms, molecules and electrons, rather than by the customary study of mechanics and hydrostatics. Practical work, it was suggested, should become more realistic, though the changes needed cannot be defined without further investigation. The proportion of time spent on practical work done by the pupils (about half all the time devoted to physics) in many English schools was judged to be excessive, particularly since much of it involved merely the measurement of standard quantities by methods possibly of historical interest, but of no use to the practising physicist.

Having diagnosed the malady and prescribed the treatment, the conference acknowledged the shortage of teachers qualified to administer it. Low salaries were reported as a major discouragement in some countries, though improved scales did not always have any obvious effect on recruitment. Working conditions, opportunities for advancement, contact with other scientists and—perhaps most of all—social prestige were named as factors influencing the choice of a career among those who might be attracted to teaching.

European and American ideas on the teaching of physics in schools and universities have been adopted with varying degrees of success in other parts of the world. After the proclamation of the Turkish republic nearly forty years ago, many drastic reforms were accomplished in the desire to break away from the old philosophy and to embrace Western ideas. In this movement the encouragement of scientific studies was important both in aiding the country's industrial development and in promoting the attitude of mind favourable to the absorption of Western culture. Educational methods drawn from British and American experience are combined in the system now used successfully for the teaching of physics at school- and university-level in Turkey.

Japanese delegates told a different story. When their country first embraced Western civilization, nearly a century ago, physics was made a compulsory subject in high schools and retained this status until 1948. By then an educational mission from the United States had reported unfavourably on the exaggerated respect for authority inculcated by the prevailing system of teaching which, in physics, involved cramming from a text-book with little experimental work. Under the new dispensation, the study of physics in high schools was made optional and was promptly abandoned by two-thirds of the senior pupils. For several years the school curriculum included only one science subject, in which the university entrance examination was also taken. Many pupils offered biology—which they thought to be easily learned—even though intending to study physics or engineering at the university. Some universities, in defiance of the Ministry of Education, started their own entrance examinations in physics to ensure that students were adequately prepared.

Public opinion supporting this stand, the high school curriculum was modified in 1956 to include two science subjects, and the enrolment in physics has now increased from 33 per cent to 75 per cent. Nevertheless the present arrangements for teaching physics in Japanese schools were reported by Haruo Ootuka (Tokyo) to be "almost completely unsuccessful".

The Western traditions which form the basis of these experiments are themselves under close scrutiny in the United States, where the Physical Science Study Committee has spent 5,000,000 dollars since 1956 on the preparation of a radically new curriculum for high school physics. The Committee's syllabus, intended for a one-year course to pupils aged 15–17 years, discards much that has been familiar to teachers and students during the past half-century, offering instead a penetrating analysis of selected topics contributing to a logical picture of the universe. The student who follows the course will know little about hydrostatics, the tangent galvanometer or the compound pendulum—but he will have measured the thickness of a tissue by counting interference fringes, he will have studied the Franck–Hertz experiment on atomic energy-levels, and he will have a working knowledge of vector kinematics.

Text-books and laboratory guides are supplemented by a large collection of films, some still in preparation, and by a series of paper-backed books. Apparatus for experiment and demonstration is being manufactured at modest cost by an American scientific instrument firm.

More than 30,000 students have taken the course in its preliminary versions. A considerable expansion of the programme is expected when the literature and other teaching aids become available on a large scale towards the end of 1960.

Many ideas brought forward in the discussions were underlined in the exhibition of apparatus, arranged by G. R. Noakes (Uppingham). The United States, Britain and France provided most of the material on view, but interesting contributions came from a few other European countries. Manufacturers showed real ingenuity in devising simple apparatus for studying and illustrating the principles of contemporary physics.

Speaking in Brussels on April 27, Lord Hailsham asked: "Can we feel sure that, in evaluating the methods of science teaching now in use, and the possible way in which they might be improved, we are ourselves approaching the matter scientifically? Can we be sure that we are practising what we preach?" The International Conference on Physics Education has helped to answer this question. Further gatherings, perhaps with more limited objectives, would make a modest but distinctive contribution to the cause of education. J. M. A. LENIHAN

SEVENTH CONGRESS OF THE INTERNATIONAL SOIL SCIENCE SOCIETY

THE seventh Congress of the International Soil Science Society was held at Madison, University of Wisconsin, under the presidentship of Prof. Richard Bradfield of Cornell University, during August 15–23, with the motto "Promote Peace and Health throughout the World by alleviating Hunger through Soil Science". In the seventh Congress, sixteen hundred delegates, representing more than fifty countries, assembled and discussed nearly four hundred original contributions on different aspects of soil science and soil improvement in seven commissions or divisions. Moreover, there were seven general lectures and one symposium on tropical soil resources under the Food and Agriculture Organization. In the opening session on August 15, the members of the Congress were welcomed by the Governor of Wisconsin and the president of the University, and addresses were delivered by the director-general of the Food and Agriculture Organization, Mr. B. R. Sen, Prof. Bradfield and Dr. C. E. Kellog, the vice-president of the Congress.

Three tours were organized in which the activities and achievements of the universities and Government Departments of the United States in agriculture and soil conservation were demonstrated. Numerous soil profiles in many parts of the country were intensively studied and photographed. Lysimeter tests were exhibited at the soil and water conservation research station at Coshocton, Ohio.

The chief topics for study and discussion at the Congress were: soil classification, cartography and maps of soils, soil physics, moisture retention, irrigation, fertility, structure, morphology, soil chemistry, analysis, diagnosis, organic matter, humus, composts, soil fauna and soil formation, micro-organisms, interaction of organic and inorganic matter in soils, clay minerals, genesis, the use of isotopes, liming, fertilization by nitrogen, phosphate, potash, trace elements, management of forest soil, saline soils, alkaline soils, etc.

Dr. F. E. Bear, a leader of soil science in the United States, in his report on "Soil in Relation to Nutritional Needs in Foods", stated that man can effect organic and mineral nutrient balance in his diet by taking a variety of plant products from many soils and meat, eggs and milk, but unfortunately such a selection is not always possible. Dr. G. D. Scarseth reported that the soils of humid tropics are highly leached and are poor, and when cleared for farming have to be adequately fertilized. According to Dr. K. H. Schutte and S. Amdurer, trace-element deficiency is widespread in South Africa. Dr. W. H. Allaway claimed that there is little evidence of harmful results from chemical fertilizers as envisaged by the late Dr. A. Carrel in his book "Man the Unknown".

In an important paper on the "Relation of Radioactive Contamination of Crops to Soil Fertility", Drs. R. F. Reitemeir and R. G. Menzel stated that the hazard associated with accumulation in the soil of the shorter-lived fission products, for example, iodine-131 and barium-140, is slight, but longer-lived isotopes like strontium-89, strontium-90 and cæsium-137 are more dangerous. Addition of large amounts of organic matter to soil reduces the uptake of radio strontium and calcium. Prof. E. Turog

described the development of soil testing methods in the United States during the past fifty years.

A large number of important communications on soil nitrogen, nitrification, nitrogen fixation, soil humus, composts, loss of nitrogen from soils, residual fertility, etc., were taken up in several sections of the Congress, because it is well established that nitrogen is the key element in cereal and other food production. Field trials in temperate countries show that one pound of nitrogen applied produces 16–17 lb. of cereals or other tillage crops, while in tropical countries the production is ten times the nitrogen input. This increase seems to be determined by the humus content in the soil; the soil humus is greater in cool countries than in the tropics. It has been estimated that approximately 1,000 million tons of grains, including corn and 700 million tons of other food materials, are produced in the world at present. This food production requires 100 million tons of combined nitrogen. But the chemical nitrogen industry is providing 7 million tons, legumes 5 million tons, precipitation about 5 million tons and farmyard manure about 2 million tons in world agriculture. In the United States 1·5–2 million tons of chemical nitrogen, 2 million tons of legume nitrogen and perhaps 1 million tons of farmyard manure nitrogen are applied, although approximately 15 million tons of nitrogen are taken out annually from the 510 million acres of agricultural lands. Hence even to-day the majority of the nitrogen need of world crops is being met by the soil nitrogen, which must be augmented in permanent agriculture. One of the easiest methods of increasing the soil nitrogen is to plough in straw after removal of grains, cornstalks, dung, grasses, legumes, etc., mixed with 50–100 lb. phosphate (as Thomas (basic) slag) per acre, as advocated by Prof. N. R. Dhar in the Congress and elsewhere. In this manner 100 lb. of atmospheric nitrogen can be fixed per acre of land and this method is applicable to both tropical and temperate countries, which require an interval of 100–150 days for adequate nitrogen fixation and liberation of available nitrogen, phosphate and potash for crop-growth in these lands. In this connexion, it is of interest to record that the British Association for the Advancement of Science meeting held in 1949 and presided over by Sir John Russell concluded that only 3 per cent of world food production could be attributed to artificial nitrogen. Moreover, as the application of phosphates increases the yield of crop to the extent of 5–7 times the amount of phosphorus incorporated in the soil, a very large number of papers on phosphorus availability, placement, etc., were considered at the congress.

In reaching Madison, Wisconsin, via Tour 1 and leaving Madison via Tours 2 and 3, the delegates passed through the heart of the Corn Belt, located in the twelve North Central States, which occupy the upper portion of the Mississippi Valley. The United States produces more than half the world's maize and soy beans, and approximately one-sixth of the wheat. The bulk of these is produced in the prairie soils rich in nitrogen and humus, obtained by the natural incorporation of tall grasses in the land and by absorption of sunlight at the surface soil. It seems that no other large area in the world equals these parts of the United States as regards favourable conditions of soils (prairie, chernozem and grey-brown podzolic) and climate for the production of crops. The State of Iowa is the main producing area for maize and pork, Illinois for soy beans, Wisconsin for hay and canning crops and dairy products, which form one-seventh of the milk and half the cheese produced in the United States. The legume alfalfa (lucerne) is the main hay crop and is extensively grown.

The representatives of soil science, from many countries, including the U.S.S.R., Japan, China, India, South Africa, Ghana, Sudan, Congo and all European nations, assembled in Madison, and carried on deliberations in a cordial and friendly atmosphere for creating new knowledge, leading to the progress and welfare of the common man in the world and contributed to international friendship, co-operation and stabilizing world peace.

N. R. DHAR

SOIL SURVEY IN THE WEST INDIES

UNDER the general direction of Dr. T. A. Jones steady progress has been made with the soil survey work of the Regional Research Centre of the British Caribbean, which has its headquarters at the Imperial College of Tropical Agriculture in Trinidad. The first three monographs to appear, namely, "The Parish of St. Catherine, Jamaica", "The Rupununi Savannas of British Guiana", and "St. Vincent" were reviewed in *Nature*, 184, 27 (1959). A further seven have now been published, covering another four of the parishes of Jamaica (St. Andrew, Clarendon, St. James and St. Mary), two further groups of selected areas in British Guiana and the island of Grenada (with Carriacou)*. Two other parishes of Jamaica are reported as completed, leaving six to be done. Each memoir follows the same plan, and as each is intended to be used as a self-contained guide there is a large amount of repetition. Each is divided into three parts: (1) Factors affecting land use (climate, geology and lithology, relief and drainage, the people and their agriculture, present position of services); (2) the soils and their capabilities; (3) recommendations. Each monograph has a soil map in a pocket and for Jamaica the scale of 1 : 50,000 has been adopted; for Grenada the rather strange scale of 1 : 18,750 has been used. The use of a series of tints and symbols in red over a black outline has enabled much detailed information to be shown on the maps with, doubtless, a minimum of expense.

Although called a "Soil and Land-Use Survey" the existing land use has not in fact been surveyed: throughout, the aim is the severely practical one of relating potential use to soils. It is interesting to note that this has led to the re-use of the older approach to soil study—the grouping of the soils according to parent geological material—since it is found that this has the closest bearing on potential. Soil series are named and used, but take a subordinate place. In fact, Dr. Jones has given his reasons

* Regional Research Centre of the British Caribbean at the Imperial College of Tropical Agriculture, Trinidad, W.I. Soil and Land-Use Surveys. Monographs 4–10. 1959–60.

elsewhere (*J. Soil Sci.*, 10, 196; 1959) why the soil-profile should be abandoned as a basis of classification since soil is "essentially a part of the landscape".

It is almost inevitable, as well as desirable, that this sustained and intensive soil work in the tropics should give rise to serious heart-searching among soil scientists. At one extreme are those pedologists who contend that soils should be studied *quâ* soils, without any consideration for their economic use, and some who even consider only 'natural' soils should be mapped, and that those where pedogenic processes have been impeded by cultivation should be ignored. At the other end of the scale are those who urge that a soil map or a soil study has little value *per se*, unless related to the potential use of the land. At this end of the scale the extreme position is taken, as by Basil Furneaux, that there is little use in mapping at all and that the only useful approach is the *ad hoc* investigation of a soil in relation to its specific utilization. The West Indian work is nearing the latter approach, except that detailed mapping has been combined with full laboratory investigation. Each soil type which is mapped is given in tabular form a recommended cultivation practice. It is hoped the farmer will not be alarmed to find his land requires, for example, *PS/3 ND/VW*, which means contour ploughing in three strips, with two in cover but no drains though with vegetative barriers and stone walls. Next he is told what crops out of some 15 may be grown, and warned of special hazards, peculiarities and nutrient requirements.

Most of the West Indian islands have problems of severe population pressure on land resources, and here is a scientific approach to the solution. But how far will the recommendations be followed? How successful would they be? It is too much to hope that they will be applied experimentally over some considerable test areas? The proof of the pudding must be in the eating. L. DUDLEY STAMP

THE AUSTRALIAN ATOMIC ENERGY COMMISSION

STEADY progress is the keynote of the seventh annual report of the Australian Atomic Energy Commission. The report, which covers the financial year ended June 30, 1959, was presented to the Senate on March 10, 1960, by Senator W. H. Spooner, the Minister of State for National Development, who stated that earlier years had been years of innovation and trial as one new activity or another was begun in furtherance of the Commission's objectives, but, as the report shows, that phase had now been left behind*.

The report is divided into seven sections dealing respectively with the search for uranium; uranium mining; raw materials including beryllium and thorium; the research programme; prospects in Australia and overseas for nuclear power; international agencies and conferences; and general activities. The financial accounts and details of research contracts, postgraduate research studentships and undergraduate scholarships, in addition to a list of the Research Establishment buildings at Lucas Heights and of the members of the staff of the Commission, are given in six appendixes.

Air-borne surveys for uranium were on a smaller scale than in previous years, because of a shift in emphasis from uranium search to regional geological mapping, and a contraction of air-borne work in general. At Rum Jungle a detailed programme of geochemical testing was carried out to the west, north-west and south of the mine, and the area was systematically explored for additional ore. Five discoveries of radioactive minerals were reported to the Commission during the year, but none proved significant as possible sources of production.

The production figures given in the report for operations at Rum Jungle show that the uranium section of the plants proceeded satisfactorily, although the production of oxide was only about three-quarters of that during 1958 because of lower grade of head feed to the treatment plant. Two companies, the United Uranium N.L., and the South Alligator Uranium N.L., both operating in the South Alligator River area, concluded an arrangement with the United Kingdom Atomic Energy Authority for the sale of uranium oxide to the United Kingdom of a total value of approximately six million pounds. The United Uranium's contract, of approximately five million pounds, is for the delivery of oxide during May 1959 and December 1966, and the South Alligator Uranium's contract for the delivery of the remainder during August 1959 and early 1963.

The report comments on the fact that there is at present a world surplus in uranium and that the lull in demand foreseen for the decade 1960–70 sets problems for the Australian mining industry which is now in steady production and which has sufficient ore reserves to fulfil current contracts and to meet Australia's domestic requirements until about 1980. The Commission wishes to maintain an active mining industry in order that new reserves may be developed and to ensure that Australia's long-range needs may be met. It is therefore important that producers should secure overseas markets for their output during the late 'sixties, but in accordance with the Commonwealth Government's principles the exports must be strictly for peaceful purposes. The stockpiling of monazite was continued, but some relaxation on export was allowed. Export of beryllium ores and concentrates remained prohibited.

New buildings to provide additional permanent workshop and laboratory space at Lucas Heights were started during the year under review. These included a large metallurgy/engineering building, a special building for beryllium research, and another devoted to isotopes and technical physics. The reactor *Hifar* was taken up to full power, after two years of calibration and testing, and although the reactor is primarily a materials testing reactor, it has begun also production of radioisotopes for medical, scientific and industrial use. Australian industry is still hesitant in adopting radioisotope techniques, but some improvement was reported during the year. In the reactor physics section theoretical investigations were carried out with the aid of computers on the slowing down of neutrons in beryllium and graphite, and the variation with neutron energy of

* Commonwealth of Australia, 1959. (Sydney: Australian Atomic Energy Commission, 1960.)

absorption in thorium was studied in relation to conversion factor, that is, breeding uranium-233 fuel from thorium. The technical physics section provided additional safety instrumentation for *Hifar* and designed and constructed a wide variety of instruments for nucleonic and physical measurements. Generally, more emphasis was placed on the high-temperature gas-cooled reactor project than on the liquid metal cooled reactor system since it was shown that this system would require a longer period of development. Work on liquid metals was largely restricted to sodium technology required for *Hifar* irradiations. Optimum conditions for the vacuum hot-pressing of reduced beryllium powder and electrolytic powder were established, and laboratory-scale extrusion processes for beryllium metal were developed. Research on the impregnation of graphite with furfuryl alcohol to produce graphite of very low gas permeability was carried out, and a number of sample fuel elements of uranium and thorium dispersed in a diluent were prepared.

The number of staff at the Establishment rose from 295 to 484 during the year, but there was difficulty in recruiting research officers of the required ability and experimental officers. The Commission was represented at the inaugural meeting of the council of the Australian Institute of Nuclear Science and Engineering which was held on December 4, 1958, and at the Second International Conference on the Peaceful Uses of Atomic Energy in Geneva. The major publication during the year under review was "Australian Atomic Energy Symposium, 1958", the record of the proceedings of the symposium on the Peaceful Uses of Atomic Energy in Australia, held in Sydney during June 1958. Other publications included the booklet entitled "An Introduction to Nuclear Science", prepared at the request of the New South Wales Department of Education as a teaching aid in schools, and the quarterly journal *Atomic Energy*. A total of approximately £A.30,000 was provided for extra-mural research contracts to universities. Thirty-five separate research programmes were being undertaken in eight universities and two hospitals and except for a few which were held up by staffing difficulties they were making good progress. Several were nearing completion. No new undergraduate scholarships were awarded, but fifteen undergraduate students continued their training in addition to forty postgraduate research studentship holders.

PUBLIC OPINION POLLS IN JAPAN

PUBLIC opinion polls are an item of American culture which the Japanese have adopted since Hiroshima. "At the height of their popularity during 1946–50 polling agencies in Japan conducted surveys on everything from attitudes towards the Emperor, housing and daylight saving time, to telephone service, prostitution, school lunches and Typhoon 'Jane' ". Dr. Matsumoto, who is chief of the Department of Medical Sociology of the Atomic Bomb Casualty Commission, is very well aware of the limitations of this kind of democratized publicity, but he has had the interesting idea of investigating how far this widely ranging material displays a consistent pattern which is in contrast to the ethos of traditional Japanese society*. He considers four main fields of opinion: attitudes towards family and sex relationships, attitudes towards occupation and labour, attitudes towards village life, attitudes towards political leadership.

* Contemporary Japan: the Individual and the Group. By Yoshiharu Scott Matsumoto. Transactions of the American Philosophical Society. New Series, Vol. 50, Part 1. Pp. 75. (Philadelphia: American Philosophical Society, 1960.) 2 dollars.

After a brief description of the orthodox values of the traditional society, Dr. Matsumoto gives the results of a large number of opinion surveys dealing with such questions as: Should an individual choose his own marriage partner or should the parents decide? Do you feel that abortion should generally be permitted? Is there a social necessity for organized prostitution? Do you think the labour unions are protecting the interests of the workers? How do you feel about the abdication of the present Emperor? The book ends with an "Interpretation and Summary" which is sensible but not profound. It scarcely needed a study of this scale to discover that "Japan has been under strong pressure to conform to Western ideology in her post-war situation. On one hand individualistic orientations are heralded; on the other communistic values are proclaimed". There is a good deal of such writing, but so long as Dr. Matsumoto evades the pressure to conform to the clichés of American sociology he is quite fascinating. The bibliography of Japanese sociological studies at the end of the book should be very useful to specialists.

EDMUND LEACH

MASS DENSITY NEAR THE SUN

IT has been known for many years that there is a close relation between the gravitational force of our Galaxy near, and perpendicular to, its plane, the distribution of stellar velocities and the density distribution of matter. The classical investigation of this subject was made by J. H. Oort in 1932, and a number of other investigations have been made since that time

E. R. Hill has recently published (*Bull. Astron. Inst. Netherlands*, 15, No. 494, 1; 1960) a comprehensive discussion and a new analysis of the available data. His work is based on stars of type *K*; this type was chosen because *K*-type stars occur in relatively large numbers at high galactic latitudes and statistical data on their brightness and motions are much more complete than for other kinds of stars. The velocity distribution of the stars perpendicular to the galactic plane has been represented as the sum of three components, two of low velocity and one of high velocity The distribution of velocities parallel to the plane was studied as a function of height above the galactic plane. The distribution of giant *K*-stars was derived from the observed distribution of all stars of type *K* by using the observed

total proper-motion distributions of K stars to assess the proportions of giants at various apparent magnitudes.

All this information was then combined to yield the force of attraction of the Galaxy perpendicular to its plane, in the solar neighbourhood, as a function of distance from the plane. Finally, the total density of matter in the plane of the Galaxy near the Sun was calculated. The result is $9 \cdot 2 \times 10^{-24}$ gm./cm.^{3}, or 0 13 solar mass per cubic parsec. This is somewhat larger than obtained by Oort in 1932.

Hill's work suffers from the disadvantage that for distances of more than 500 parsecs from the galactic plane the force obtained conflicts with the requirements of Poisson's law.

In another paper, J. H. Oort (*Bull. Astron. Inst Netherlands*, 15, No. 494, 45; 1960) re-determines the force so that it is consistent both with the observational data assembled by Hill and with Poisson's law. He obtains 0·15 solar mass per cubic parsec for the density of matter in the solar neighbourhood, in excellent agreement with the result of Hill.

DWARF MISTLETOES

A COMPREHENSIVE account of morphological aspects of the parasitism of dwarf mistletoes (*Arceuthobium* spp., Loranthaceae) on North American conifer species has been given by J. Knight (*Univ. California Pub. Bot.*, 30, No. 5, 337; 1960). Some of the literature, terminology and main features of the development of these parasitic plants are critically reviewed and new observations submitted relating to *A. americana* and other species. At the time of penetration into the host the radicular apex loses its histological organization and becomes resolved into simple uniseriate filaments. Such filaments eventually become vascularized endophytic strands. It is possible that all radial sinkers and some aerial shoots may take their origin directly from uniseriate filaments.

All species of *Arceuthobium* may at maturity show a localized distribution pattern of the endophytic system and shoot emergence from the host. Such infections are in some cases associated with brooming phenomena of the tree. In addition, some species when infecting certain hosts induce a remarkable brooming response where the endophytic system keeps up with longitudinal host extension and where a great regularity of shoot emergence prevails. This is described as 'isophasic' parasitism.

There are recognizable differences in isophasic behaviour among species in which it occurs. These differences involve the position of mistletoe shoots in relation to host organs, dominance and precociousness of mistletoe shoots at the girdles, duration of reproductive activity, and so on. A mistletoe species causing an isophasic response on one host species may not do so on another; similarly, a tree when infected by one mistletoe may form an isophasic broom, whereas infection by a second species may result in an entirely different type of parasitism. The isophasic capacity does not therefore reside solely in either host or parasite, but is the result of mutual interaction. The endophytic system is most extensively developed in isophasic brooms. In those of *A. americana* on *Pinus contorta* and of *A. douglasii* on *Pseudotsuga menziesii*, the ultimate filaments are present in the apical meristems of the host branches and probably remain there throughout the yearly growth-cycle. In the latter broom, an actual emergence of endophytic filaments takes place just above the youngest bud scales. The author suggests that the endophyte may be present in the apical meristem of the host branches of all isophasic brooms, and that such presence in the host apex is a corollary of regularity in shoot emergence.

FACT AND FICTION ON THE BREEDING OF THE WANDERING ALBATROSS

By DR. R. CARRICK, K. KEITH and DR. A. M. GWYNN

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THE reputation of the wandering albatross (*Diomedea exulans*) as a parent has suffered on occasion at the hands of the ornithologist, professional and amateur alike. The starvation theory held that the young albatross was fed from hatching in March until about June, and then deserted throughout the Antarctic winter while it subsisted on reserves of stored fat. Some writers state or imply that there is no resumption of parental feeding before the fledgling takes wing about December; others cite observations of feeding, or of fresh food in the nestling's stomach, in spring. The relevant evidence and opinions of successive writers are:

1865. Hutton[1] stated that Harris at Kerguelen saw no adults between June and October, and no feeding from October onwards.

1866. Andersson[2] quoted the opinion of a sealer that young albatrosses live on their own fat after being abandoned by the parents.

1891. Chapman[3] stated that Fairchild observed albatrosses, nearly all young, on the islands below New Zealand in October, 1890, and concluded that the large full-grown chicks are abandoned and live on their own fat until they fly.

1905. Buller[4] quoted Buckland, who visited islands to the south of New Zealand, to the effect that the

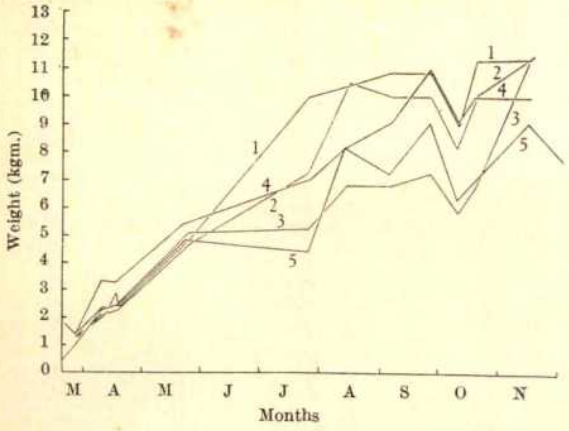

Fig. 1. Growth curves of five young wandering albatrosses at Macquarie Island during 1956

nestling becomes so fat that it exceeds the full-grown adult in weight, and is then deserted for at least four months until October.

1929. Matthews[5] spent the winter of 1925 at South Georgia and identified Nototheniid fish in the stomachs of young wandering albatrosses in early September; at that time the parents return about once a day and remain only a few minutes to feed the nestling. From observations in November and December 1925 and January 1926, Matthews concluded: "The adult albatross do not breed every year, as they do not finish feeding their young until after the new season's eggs are laid (by other birds) and incubation has started. Consequently there must be an interval of at least one season between the consecutive matings of any one bird".

1936. Murphy[6], who visited South Georgia during December 1912–February 1913, stated: "With the setting in of the antarctic autumn, the adult albatrosses completely abandon their nestling offspring, not for a matter of days or weeks but forever". (An extravagant misstatement in view of Matthews's evidence.) He found several young with empty stomachs shortly before they were due to fledge.

1951. Rankin[7] observed a breeding colony at Albatross Island, South Georgia, during December 1946–March 1947. On the assumption that the rate of increase in weight at the end of March would be maintained, nestling weight at the end of June was estimated at about 27–31 lb., and considered to be "far in excess of that of the adult"; the heaviest adult male weighed was 26¾ lb., and the average of fourteen adults was 23 lb. He concluded that "by finishing with their family cares in June or July, the parents have a clear four or five months before the beginning of the next breeding season, so it is possible for them to reproduce every year". His caption of Fig. 42 is: "Throughout the long Antarctic winter the young albatross is tended by its parents".

1951. Matthews[8] re-stated his previous evidence and conclusions, referred to "a year of devoted care" by the parents, and stated "at most they can breed only every other year".

1952. Richdale[9] fully reviewed winter feeding of young wandering and royal (*D. epomophora*) albatrosses, establishing beyond doubt that it occurs in the latter species, and quoting Turbott's observation of wandering albatross chicks being fed early in November 1950 at Antipodes Island.

1953. Paulian[10] observed and photographed feeding at Kerguelen during August and September.

1954. Fisher and Lockley[11] discussed the starvation period of nestling Procellariiformes, and agreed with Richdale[9] that *D. exulans* has little, if any.

1958. Jameson[12] stated: "*Facts* about the all-important period from May to November—the Antarctic winter and spring—are lacking". "... but I believe, with Matthews, Murphy and Rankin, that the young are abandoned for several months" (not at all fair to Matthews). Jameson does not refer to Paulian[10].

1960. Tickell[13] studied the wandering albatross at Bird Island, South Georgia, during October 1958–March 1959. In November–December "nestlings being handled frequently regurgitated large fresh meals and the sight of the adults feeding young was fairly common". Despite the evidence[5,8,9,10,13] for feeding of chicks every month from August onwards, Tickell computed a hypothetical weight which the nestling would have to attain by July in order to fledge at the December weight without further feeding. This is based on the physiologically dubious assumption that the unfed downy chick during winter might lose weight at the same rate as the large feathered chick in summer. He concluded that "the evidence now available clearly indicates that the young are fed throughout the fledgling period".

By 1953, if not by 1929, the starvation hypothesis had become untenable, on five counts. Matthews[5], Turbott (in Richdale[9]) and Paulian[10] had published evidence of feeding during August–December. Richdale's[9] detailed and accurate study of the royal albatross, and the well-known life-history of the king penguin (*Aptenodytes patagonica*), had shown that the other two sub-Antarctic sea-birds, the young of which develop throughout winter, do not neglect them. The energy requirements of a non-hibernating and growing bird, in this cold environment, must be very considerable indeed, and necessitate regular replenishment. Hormonal control of the annual cycle in birds precludes suspension of parental feeding behaviour for a lengthy period; a break with the proximate stimuli involved causes birds either to

Fig. 2. Adult male wandering albatross (C.S.I.R.O. band number 140–00149; colour-bands red-orange) feeding its own chick at nest No. 2, Macquarie Island, on July 26, 1956

revert to the onset of breeding or to proceed to the next phase, usually the moult. Ornithology offers no precedent for temporary cessation of parental care; so novel a suggestion requires undeniable proof.

Throughout 1956 Keith (biologist, Australian National Antarctic Research Expeditions) kept records of the development of wandering albatross nestlings at Macquarie Island. The five growth-curves (Fig. 1) show the increase in weight during winter; and Fig. 2 shows a young albatross being fed on July 26.

Tickell[13] also discussed whether adults feed their own or random chicks, a point on which there can be no doubt if the birds are marked. In view of the mounting evidence on this subject, of which only Sladen's[14] study of the Adelie penguin (*Pygoscelis adeliae*), the young of which form crèches, need be mentioned in addition to Richdale's[9] proof in the case of the royal albatross, it would be surprising indeed if the original parent-nestling bond were not maintained. Many observations of banded birds at Macquarie Island confirm that wandering albatross parents feed only their own young, but nests there are much more widely spaced than at Bird Island. Tickell's[13] final conclusion, ". . . it must be held that the wandering albatross, like the royal albatross, breeds only once every two years", also requires birds, the identity, and history during several years, of which are known. Matthews's[5,8] conclusion (quoted above) on similar evidence is more carefully correct. Since 1954, 48 adults and 37 young have been banded on Macquarie Island; frequency of breeding follows the pattern established by Richdale[9] in the royal albatross, namely that successful pairs breed in alternate years and early nest failures enable the next attempt to be made the following summer. Constancy of site and mate is the rule. The full results of the Macquarie Island studies are included in an Australian National Antarctic Research Expeditions report on the birds of this Island to be completed during 1961.

The wandering albatross is a noble bird which has long excited the imagination of poet, voyager and scientist, but canards ill become it. In 1929, after spending a full year at South Georgia and studying large wandering albatross colonies at the end of August, September, November to January, and March, Matthews[5] produced the evidence and correct conclusions on both winter feeding of the young and non-annual breeding of successful parents. Subsequent writers up to 1960, after at most a summer contact with the bird, have done his work less than justice. The time has come to consign much past writing on the wandering albatross to the limbo of ornithological mythology, and to replace speculation with the direct evidence, based on individual identification whenever possible, which modern ornithology demands.

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CHEMISTRY OF VISUAL ADAPTATION IN THE RAT

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Rhodopsin Concentration and Visual Sensitivity

THE loss of visual sensitivity after light adaptation, and the recovery of sensitivity during dark adaptation, are common phenomena. Hecht was the first to emphasize the idea that these processes represent the bleaching and synthesis of visual pigment. However, until very recently, experimental attempts to formulate the relationship between visual pigment concentration and visual sensitivity or threshold have not been fruitful, principally because in man, in whom visual thresholds are most commonly determined, pigment concentrations cannot easily be measured. In experimental animals, on the other hand, pigment concentrations can readily be measured, but special means must be employed to estimate visual thresholds.

Recently, in a study of vitamin A deficiency in rats[1], I used the electroretinogram to assay retinal function and sensitivity. I found that the electroretinogram threshold of the eye rose regularly and linearly with time on the deficient diet, similar to the rise of psychophysical thresholds in studies of human vitamin A deficiency[2]. When the measurements of electroretinogram threshold in the deficient rats were compared with the rhodopsin concentrations in the retinas of the same animals, it was found that the logarithm of the electroretinogram threshold rose linearly with fall in rhodopsin concentration.

I have now extended this analysis to light and dark adaptation. That one can use the electroretinogram to reflect the sensitivity of the eye has been demonstrated by several workers[3,4]. The most familiar way to do this is to evaluate the change of the electroretinogram during dark adaptation on the basis of stimulus response curves, so estimating the light intensities needed to elicit constant electroretinogram responses. I achieved essentially the same result by measuring, at various times during dark adaptation, the brightness of stimulus needed to evoke a just-perceptible electroretinogram. The electroretinogram threshold is perhaps preferable to measuring larger, super-threshold responses, which may be complicated by complex and changing waveforms.

$$N = \frac{Q}{\beta - \frac{A}{n}\sin^2 I} \qquad (6)$$

or, when I is small:

$$N \simeq \frac{Q}{\beta}\left[1 + \frac{A}{\beta n} I^2\right] \qquad (7)$$

Now, Q is practically independent of solar zenith angle at heights well above the peak for electron production, and this condition is fulfilled above 260 km. according to Ratcliffe *et al.* It follows that the variation of N with I is approximately parabolic, with a minimum at the dip equator. Croom, Robbins and Thomas[4] have published curves of N against I at various heights obtained from a reduction of ionograms. Their Fig. 1 clearly shows this feature.

The slope of the N/I curve, from equation 7, is given by:

$$\frac{\partial N}{\partial I} = \frac{2QA}{\beta^2 n} I \qquad (8)$$

Since $\beta^2 n$ decreases with height more rapidly than Q, the slopes of the N/I curves are expected to increase with height. This feature, also, is shown in Fig. 1 of Croom *et al.* Data from any pair of heights can be used to eliminate the constant A, which is not, at present, well established. At a dip angle of 25°, the curves of Croom *et al.* can then be used to evaluate the scale height for β if the scale heights for Q and n are taken to be roughly equal. For the pairs of curves at 300 and 320, as well as 320 and 340 km., consistent values of about 50 km. are obtained, in good agreement with the value given in Ratcliffe *et al.*

Since it is clear that N must always be positive, an examination of the denominator of equation 6 indicates that the theory presented here may be expected to break down at greater heights and larger values of dip angle. The fact that N/h profiles cease to be exponential away from the dip equator may be considered as one aspect of this theory, which suggests, indeed, that diffusion prevents them from retaining an exponential shape there. Equation 6 also indicates that, at greater heights, this breakdown must occur at smaller values of I. This is evidenced in Fig. 1 of Croom *et al.* by a shift towards the dip equator of the maxima of the N/I curves with increasing height.

It is concluded that quite simple considerations of vertical diffusion account for the major features of the 'geomagnetic anomaly' as presented by Croom *et al.*, and that this anomaly consists of excess ionization, due to diffusion, away from the equator, rather than a deficiency of ionization at the equator.

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GEOPHYSICS

Stress-induced Magnetic Anisotropy of Rocks

ROCKS containing 1 or 2 per cent of magnetic minerals are so slightly ferromagnetic that reliable measurements of magnetostriction by the direct observation of changes in dimensions would, at best, be extremely difficult. However, an understanding of the magnetostriction of rocks is very desirable on account of the disagreement which has arisen concerning its possible role in palæomagnetism[1-4]. The purpose of this communication is to report an experiment which shows that the saturation magnetostrictions of rocks are easily measured in terms of stress-induced anisotropy, and that, in the few rocks examined, they have values which would be expected from their known magnetic mineral contents.

Five specimens have been used: two samples of Tasmanian dolerite, two of basalt from Kiama, New South Wales, and one of monchiquite, also from Kiama. In all these rocks the natural (unstressed) anisotropies are very small, and, regardless of any slight alignment of grain elongations, the crystallographic axes of the magnetic grains have been shown to be randomly oriented (by the method described by Stacey[5]). In this case the theoretical treatment of magneto-elastic energy, E_s, is simple[6]. When a specimen is subjected to an axial stress (measured as positive for a compression) at an angle θ to a strong field, in which it is magnetically saturated, E_s is given by:

$$E_s = \frac{3}{2}\lambda_s \sigma \cos^2\theta \qquad (1)$$

where λ_s is the saturation magnetostriction. The torque T_s exerted on the specimen by the field exceeds the torque T_0 due to its natural anisotropy by an amount:

$$T_s(\theta) - T_0(\theta) = -\frac{dE_s}{d\theta} = \frac{3}{2}\lambda_s \sigma \sin 2\theta \qquad (2)$$

Torque curves $T_s(\theta)$ and $T_0(\theta)$ have been measured for the five specimens.

Each specimen was cut and ground to the shape of a cylinder, 21 mm. in diameter by 15 mm. long, with an axial hole 9·5 mm. in diameter. It was compressed between copper washers, 3 mm. thick, and thin lead washers by tightening a copper nut and bolt which were inserted through the axial hole. The load applied was the same in all cases and was controlled by tightening the copper bolt until it was felt to yield. The load was measured by pairs of electrical resistance strain gauges which were stuck on to two of the specimens, making rock load cells. These cells were calibrated in a mechanical load-testing machine, and the stress applied to the specimens by means of the copper bolt was measured as 520 kgm./cm.^{2} ± 10 per cent ($5{\cdot}2 \times 10^8$ dynes/cm.^{2}).

The specimen plus copper bolt was sufficiently small to be suspended on a simple torque-meter, described previously[7]. First the torque $T_0(\theta)$ exerted on the unstressed specimen (plus copper bolt) by a 10·6 kilo-oersted field was measured as a function of the angle θ between the axis of the bolt and the field direction. The torque curve $T_s(\theta)$ in the stressed state was then measured in the same way, and afterwards the $T_0(\theta)$ curve was repeated to show

The relative breaking stresses measured by me with different liquids agree well with those obtained by Culf[3], who measured the extension of cone cracks in glass under different liquids. They can best be explained by a mechanism involving a lowering of the interfacial free energy γ, which according to Griffith's formula $\sigma \simeq \sqrt{\frac{E \cdot \gamma}{c}}$ leads to a reduction of the tensile stress σ necessary to propagate a crack of length c in a solid having Young's modulus E. Available data on free energies of immersion[4] indicate that $\gamma_{SO}-\gamma_{SL}$ is largest for water, intermediate for polar organic compounds, and lowest for nonpolar compounds, where γ_{SO} is the free energy of the solid surface in a vacuum and γ_{SL} is the free energy of the solid-liquid interface. The relative order of magnitude of the free energies of immersion agrees well with the order of breaking strengths obtained with different liquids (Table 1). If the strength impairment of glass were exclusively a chemical solution process, the effect of oleylamine, in which quartz is virtually insoluble, on the breaking strength could not be explained. Charles[5] has pointed out the close correspondence between the concepts of failure by stress corrosion and by lowering of surface energy, which are both compatible with the Griffith criterion. By measuring crack propagation in polar systems that are non-solvents for the solids under consideration, the mechanisms can be separated.

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RADIOPHYSICS

Effects of Vertical Diffusion of Electrons near the Magnetic Equator

If electrodynamic movements are neglected, the continuity equation for the electron density N at a fixed height h in region F of the ionosphere may be written:

$$\frac{\partial N}{\partial t} = Q - \beta N + D \qquad (1)$$

where Q is the rate of production of electrons, βN is the effective rate of loss due to recombination processes and D is the contribution due to diffusion. If diffusion is considered to be predominantly vertical, the expression of Ferraro[1] reduces to the following form:

$$D = \frac{b}{n} \sin^2 I \left[\frac{\partial^2 N}{\partial h^2} + \frac{3}{2H}\frac{\partial N}{\partial h} + \frac{N}{2H^2}\right] \qquad (2)$$

where b is a constant, I is the dip angle of the Earth's magnetic field, n is the density of neutral particles, and H is the scale height, here assumed constant. It is also assumed that H is the same for the neutral atmosphere as for the ions: if this is not true, the conclusions reached here will remain essentially unchanged, but the values of the constants will be modified.

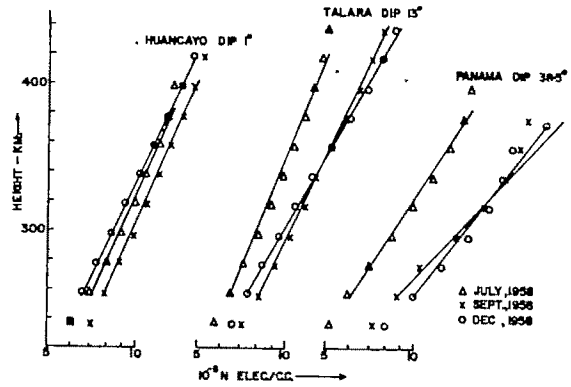

Fig. 1. Mean noon N/h profiles

The effects of diffusion on a parabolic layer have been investigated by a number of authors; among them Martyn[2] and Ratcliffe, Schmerling, Setty and Thomas[3]. Their conclusions cannot be presented in any simple form, since both the magnitude and sign of the diffusion term depend drastically on the ratio of the parabolic thickness to the scale height.

In the vicinity of the magnetic equator, it is found that the electron density/height profiles are closely exponential in shape below the $F2$ peak during the day. This is illustrated in Fig. 1, where monthly-mean noon profiles are shown for the three stations Huancayo (Peru), Talara (Peru) and Panama (Canal Zone) for summer, equinox and winter months in 1958. A logarithmic scale has been used for N, and it is seen that the profiles are closely exponential at Huancayo (dip 1°) and Talara (dip 13°) for a range of height of 260–400 km. Even at Panama (dip 38·5°), the deviations from this shape are small in the range 260–360 km. It must be noted that, at Panama, there is some distortion in the mean profiles due to large day-to-day variations of height; profiles for individual days are frequently even closer to exponential form below 360 km.

Representing the profiles by:

$$N = N_0 \exp kh \qquad (3)$$

where N_0 and k are constants, we obtain:

$$D = \frac{b}{n} N \sin^2 I \left[k^2 + \frac{3}{2}\frac{k}{H} + \frac{1}{2H^2}\right] \qquad (4)$$

It is immediately seen that D is always positive and proportional to N. The effect of diffusion is, therefore, always to increase the electron density (below the electron peak). Equation 1 may then be written:

$$\frac{\partial N}{\partial t} = Q - N\left[\beta - \frac{A}{n}\sin^2 I\right] \qquad (5)$$

where A is a constant, simply related to b, k and H.

A few simple deductions follow immediately from equation 5. Assuming quasi-equilibrium near noon for heights below 360 km.:

Table 1. OVER-VOLTAGE (FIXED) ON THE SECOND COUNTER, 220 V. Distance between two counters, 5 cm.; inclination between axes of counters, 45°; counter slopes, 0·03 and 0·02 per cent per V.; plateau lengths, 220 and 380 V.

Over-voltage on the source counter (V.)	Coincidences per 10 min. without filter	Coincidences per 10 min. with filter
20	8	Nil
60	18	2
100	408	56
140	486	54
180	548	59

Table 2. OVER-VOLTAGE (FIXED) ON THE SOURCE COUNTER, 180 V.

Over-voltage on the second counter (V.)	Coincidences per 10 min. without filter	Coincidences per 10 min. with filter
20	13	Nil
60	459	5
100	567	8
140	540	45
180	532	51
220	541	62

set the voltage on the source counter was fixed and that on the second counter was changed within its plateau, keeping the channel directed towards its cathode at a fixed angle.

Observations were taken with different distances between the counters. Typical results are given in Tables 1 and 2.

The increase in the number of coincidences in Table 1 with the over-voltage on the source counter is due to greater yield of ultra-violet photons from it with rise in its operating voltage. The increase in the coincidences with the over-voltage on the second counter with filter in Table 2 is, we believe, due to its greater photoelectric efficiency with the rise in the electric field on its counter cathode. The change in the photoelectric efficiency with the electric field on the counter cathode may be due to the 'return' to the cathode of photo-electrons released from it by photons; a phenomenon which has scarcely been studied so far in self-quenching Geiger-Müller counters.

A comparison of the results in Table 2 with filter and without it indicates that the coincidences without filter are mainly due to the photoelectric effect of photons of the source counter falling on the cathode of the second and that photons other than those of wave-length 2537 Å. must be present to account for their greater number. We believe, however, that the hard component of the ultra-violet photons is also causing coincidences by ionization. That photo-ionization is also occurring has been checked by firing the photon beam axially across the second counter and noting the coincidences with and without filter. In the former case there was not a single coincidence in 10 min., whereas in the latter 100–200 coincidences were obtained in the same interval of time.

In other experiments we have shown that ultra-violet photons of long wave-length can travel across a tube 10 cm. long, filled with alcohol at a pressure of 1–3 cm. mercury or even higher. These photons were detected at the end of their journey by a self-quenching Geiger-Müller counter due to their photo-electric effect on its cathode. The ultra-violet radiation was produced by a mercury arc with a quartz window on a side tube. These results are in agreement with our work with counters.

Our results may be of interest also in connexion with the preparation of self-quenching Geiger–Müller counters with a filling of permanent gases[4].

We are grateful for the supply in 1959 under the Colombo Plan of electronic equipment, some of which was used in this work.

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Impairment of Strength of Quartz Glass through Wetting by Liquids

IN a recent communication[1], Radd and Oertle attributed the impairment of the tensile strength of glass fibre fabrics to a chemical solution process. Recently I have measured the tensile strength of quartz-glass rods immersed in various liquids. The rods, which were supplied by the Amersil Quartz Division of Engelhardt Industries, Inc., were selected for a uniform diameter of 1 mm. and cut to a length of 10 cm. They were annealed to remove residual strains. Three-point bending, using a calibrated spring, was used to apply a maximum stress at the centre, where the rods were scratched before they were broken. Scratches of identical depth were made on the underside of each rod by cutting with a diamond cutting tool that was applied with a constant force. All experiments were performed in a moisture-free atmosphere on previously dried rods. The mean loads at fracture, together with the 95 per cent confidence interval for the liquids water, oleylamine, and *n*-hexadecane, are shown in Table 1. Great care was taken to free the *n*-hexadecane of all polar impurities and the oleylamine of water. The last column shows the probability of the null hypothesis $M_1 - M_2 = 0$ being correct for the means of the two pairs water–oleylamine and oleylamine–*n*-hexadecane, respectively[2].

Table 1

Environment	Mean fracture load (gm.)	Probability of null hypothesis $M_1 - M_2 = 0$
Distilled water	13·3 ± 2·1	$0·001 < P < 0·005$
Oleylamine	18·8 ± 3·0	$0·01 < P < 0·025$
n-Hexadecane	24·5 ± 3·8	

In another experiment I measured the time that elapsed before delayed fracture set in when seven quartz-glass rods were immersed in *n*-hexadecane and seven were immersed in oleylamine, all of which were then subjected to the same load, which corresponded to 95 per cent of the mean rapid fracture load measured with oleylamine. The breaking times until fracture are listed in Table 2.

The breaking stress–time relationship apparently results from the gradual penetration into the crack of substances that are adsorbed on the crack wall and lower the interfacial free energy.

Table 2

Environment	Time until fracture (sec.)
n-Hexadecane	1,326; 2,886; 16,560; 480; 2,127, 11,775; 990
Oleylamine	15, 0; 55; 10, 5; 0; 2

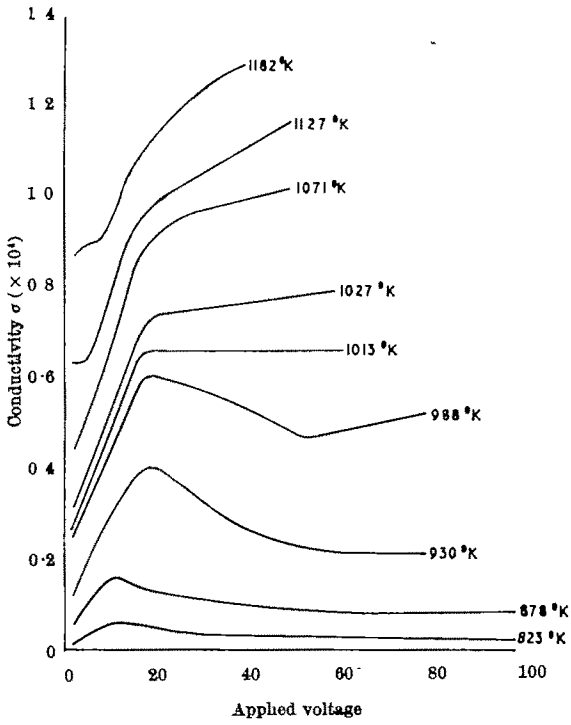

Fig. 1. Electrical conductivity (d.c.) of strontium oxide as a function of applied voltage over the temperature-range 823–1182° K.

above 1013° K. over the whole range of applied voltage. This is interesting in itself.

Some confirmation of this interpretation comes from the results with alternating currents (5 kc./s.); there was no fall in conductivity with field and no plateau at 1013° K. Contact with oxygen at 10^{-3} mm. mercury pressure of the well-activated strontium oxide surface scarcely affected the a.c. conductivity, which still showed the same features of temperature and field; this was much enhanced on contact with hydrogen. The results so far show that oxidation and reduction treatments produce a desirable quality—a conditioning towards a homogeneous oxide.

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Soft Ultra-violet Photons in Self-quenching Geiger–Müller Counters

Though it is now certain that, in a self-quenching Geiger–Muller counter filled with a conventional argon–alcohol mixture, both photo-ionization[1] and photo-emission[2] cause the spread of the discharge along its anode, the production of ultra-violet photons which are responsible for these two processes and their relative importance in determining the counter characteristics have not yet been fully understood. Further, no reliable data are available for the energy spectrum of these photons, which may be emitted by any of the following mechanisms: (1) de-excitation of excited argon atoms formed in Townsend avalanches giving rise to wave-lengths in the energy-range 11·5–15·7 eV.; (2) charge-exchange between argon ions and alcohol molecules, producing monochromatic photons of energy $(I_1 - I_2)$ eV. corresponding to a wave-length of about 2800 Å., I_1 and I_2 being the ionization potentials of argon and alcohol respectively; (3) recombination of argon ions with electrons in the vicinity of the anode to the excited levels of argon atoms.

Soft ultra-violet photons which may liberate secondary electrons from the cathode will arise from (2) and (3). There will be no soft ultra-violet photons, other than those of wave-length 2800 Å., if process (3) did not occur within the time-interval of a major pulse, namely, about a microsecond.

Some workers[3] believe that soft photons do not play any important part in the spread of the discharge. We have shown that this is not so. The present work has led us to the following conclusions: (i) soft ultra-violet photons energetic enough to liberate photo electrons from the counter cathode are produced in the counter due to recombination of argon ions; (ii) ultra-violet photons have a much smaller absorption coefficient in alcohol than is usually assumed; (iii) the photoelectric efficiency of a self-quenching counter is dependent on its over-voltage, a point of considerable interest in the operation of these tubes.

Two brass counters, each 5·5 cm. in active length and 4·3 cm. in diameter, with tungsten anodes 0·2 mm. thick are housed in a specially constructed steel chamber 12 in. in diameter and 9 in. deep. They are supported in position within the chamber with two Wilson seals passing through its steel bottom plate. A second steel plate with a central window 9 cm. in diameter and covered with a polystyrene disk closes the top of the chamber. The two steel plates are screwed together with steel rods and the chamber is made air-tight with 'O' rings pressed between its wall and the two end-plates, while the polystyrene disk is fixed with 'Araldite'. A third Wilson seal also passing through the bottom steel plate carries within the chamber a framework which holds a narrow-band ultra-violet interference filter which was inserted in between the two counters when desired. The filter, type *U* 417, supplied by Messrs. Barr and Stroud, Ltd., of Glasgow, has peak transmission at 2537 Å. and has a band-width (half-peak to half-peak) of 160 Å.

One counter acts as a source of photons and is irradiated by a collimated gamma-ray beam to give a counting rate of about 2,000 c./m. while the other counts 300–400 c./m. The end facing the second counter is closed by an insulating cap carrying a narrow channel 2 cm. long at its centre. The two counters had their anodes on a common axis when facing each other and were adjusted by means of the Wilson seals. The chamber was filled with an argon–alcohol mixture containing 10 per cent alcohol at a total pressure of 10 cm. of mercury.

The pulses from the counters were fed into a coincidence unit, type 1036 *B*, with a resolving time of 1 μsec. and the coincidence pulses were recorded in the scaler, type 200 *A*. The counter voltages were supplied from stabilized power units.

Coincidences were observed with the channel of the source counter directed towards different parts of the second counter with and without the ultra-violet filter between them.

In one set of experiments the over-voltage of the source counter was changed, keeping that on the second counter fixed in its plateau range. In another

of the film to rotate abruptly into the equivalent antiparallel directions, thus forming more or less oppositely directed domains bounded by walls of something less than 180°. At the higher values of $H_\perp$, rotation within these domains occurs. The local deviations of the direction of anisotropy account for the rotational hysteresis. This idea is supported by the experimentally observed fact that those films which have less hysteresis for $h_\perp > 1$ obey equation 3 to larger values of $H_\perp$ ($h_\perp < 1$).

Fig. 1*b* suggests the use of equation 3 to determine H_K. To within the accuracy with which y_0 represents ΔR_0, equation (3) can be written as $y/y_0 = (xD_x/H_K)^2$, where D_x is the horizontal scale factor in oe./cm. Photographic enlargements of the oscilloscope traces are projected on to graph paper from which x, y, and y_0 are measured. The slope of the linear portion of a plot of y against x^2 is used to calculate H_K. Fig. 2 shows such plots for the traces of Figs. 1 *b*, *c* and *d*. That for Fig. 1*d* corresponds to one lobe of the hysteresis curve. The initial slopes yield values of H_K in agreement with the extrapolated linear portions of the magnetic hysteresis curves in Fig. 1*a*. Table 1 lists the values of H_K obtained by the two methods for four films. These values are in agreement to within the accuracy of the magnetic method. It is perhaps significant that H_K as measured by either method is dependent on the amplitude of the sinusoidal magnetizing field.

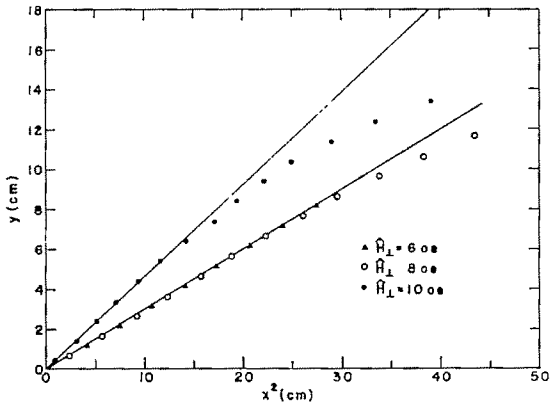

Fig. 2

For film studies there are some advantages in the magnetoresistive method. The proportionality of the signal to the square of the cosine of the angle between current and magnetization and the independence of the signal on rate of magnetization make it possible to distinguish experimentally between domain rotation and 180°-wall motion. Furthermore, the independence of rate makes observation of the magnetization process at low magnetizing frequencies particularly easy. Compare the signal-levels obtained from the two methods at 500 c./s. and 20 c./s. (Fig. 1). The direct current in this case was 30 m.amp.; however, it is limited only by the maximum safe current density. For this particular film, currents as high as 300 m.amp. have been applied with no apparent ill effects. The large ratio of surface to volume of a film is favourable for the dissipation of Joule heating. Finally, the simplicity of the magnetoresistive method makes it particularly useful for remote measurements; for example, in a cryostat, or *in vacuo*.

The samples were prepared in this laboratory by R. E. Wimberly, J. W. Chambers and L. J. Boudreaux.

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Electrical Conductivity of Strontium Oxide

THE part which strontium oxide plays in the functioning of the oxide cathode is not well understood; a suitable model of the combined barium and strontium oxides on the band theory is still not satisfactory. Further, lack of sufficient observations in the soft X-ray region over the operating temperature-range prevents a fuller knowledge of how the valence band densities are related in the solid solution of the oxides. It is, of course, possible to go some way towards understanding the oxide cathode if the main and relevant properties of each component can be studied.

With this in view, we have concentrated attention on the electrical properties of strontium oxide and find, using a double platinum 'probes' technique, that the electrical conductivity (d.c.) varies with the applied voltage over the temperature-range (823–1182° K.) in the manner shown in Fig. 1. The voltage between the probes has been plotted rather than the field, since the latter is bound to be 'patchy' owing to the presence of a non-uniform porous dielectric.

It is remarkable that, in contrast to the behaviour of barium oxide, the electrical conductivity varies with the field; there appear to be two transitions involved—one due to the field, the other due to temperature. A 'knee' is seen to develop at an applied voltage of about 20 V., and the conductivity is sensitive to the effects of the field only below this, or above 1013° K. Why, at this particular temperature and field, strontium oxide behaves according to classical theory (with the usual assumptions) is not clear; the fall in conductivity with field at the lower temperatures is curious, and might be attributed to electrostatic effects, accompanying changes in current density, between irregular crystallites which affect and alter the contact resistance between them.

The change of slope from negative to positive at the knee voltage around 1013° K. indicates a predominating effect due purely to thermionic emission; indeed, this could explain the rise of conductivity with field wherever it is observed on the curves. A rough estimate of the effect shows that the Langmuir–Child space charge law has a maximum index of about 1·3, and could be fitted to each set of results

LETTERS TO THE EDITORS

PHYSICS

Magnetoresistive Measurements on Domain Rotation in Nickel - Iron Alloy Films

For low saturating magnetic fields, the magnetoresistive effect in a polycrystalline ferromagnet is described by the relation[1]:

$$\Delta R = \Delta R_0 \cos^2\varphi \qquad (1)$$

where ΔR_0 is the positive resistance change measured when the electric current i is oriented first normal then parallel to the saturation magnetization M_s; and φ is the angle between the current and the induction. This relation has been verified for evaporated nickel films by Rappeneau[2].

A film which has uniaxial anisotropy energy E is described by the relation $E = K \sin^2 \theta$, where θ is the angle between M_s and the direction of minimum anisotropy energy, called the K-axis. If such a film is magnetized by a field $H_\perp$ in the film plane normal to the K-axis, the equilibrium angle θ for any field less than, or equal to, $H_K = 2K/M_s$ is given by:

$$\sin \theta = h_\perp, \quad h_\perp = H_\perp/H_K \qquad (2)$$

provided that the magnetization rotates uniformly in the plane of the film[3,4]. If the current is normal to the K-axis, substitution of $\sin^2 \theta$ for $\cos^2 \varphi$ in equation (1) yields:

$$\Delta R/\Delta R_0 = h_\perp^2 \qquad (3)$$

If the current is parallel to the K-axis, the result is $\Delta R/\Delta R_0 = 1 - h_\perp^2$. Thus, a plot of $\Delta R/\Delta R_0$ against $h_\perp$ should be a parabola over that range of $h_\perp$ for which equation (2) is valid in a given film.

Fig. 1*a* shows the magnetic hysteresis curves for a field-evaporated 80–20 nickel–iron film, 2000 Å. thick, magnetized by a sinusoidal field of 500 c./s. of amplitude $\hat{H}_\perp$ normal to the K-axis. The closed loop at low field demonstrates the applicability of equation (2), see refs. 3, 4. The value of field at which this curve is extrapolated to saturation is usually taken as a measure of H_K. Figs. 1 *b*, *c* and *d* are the magnetoresistive hysteresis curves taken for those values of $\hat{H}_\perp$ in Fig. 1*a*. The measuring circuit used to obtain the latter is described by Hellenthal[5]; namely, a sinusoidal magnetizing field (20 c./s.) produces, as a result of the magnetoresistive effect, an alternating voltage across a film through which a constant direct current (30 m.amp.) is passing. The voltage is amplified and displayed on the vertical plates of an oscilloscope. The magnitude y of the vertical display is proportional to ΔR, while the horizontal display x is proportional to $H_\perp$. The voltage to produce x comes from the voltage drop across a resistance in series with the magnetizing coils. In the present experiment, the films are rectangular (5 mm. × 20 mm.) and deposited on soft glass.

For these experimental conditions the magnetoresistive curve for $\hat{H}_\perp$ sufficiently small should be a parabola described by equation (3). Fig. 1*b* shows that such is indeed the case. Figs. 1 *c* and *d* show

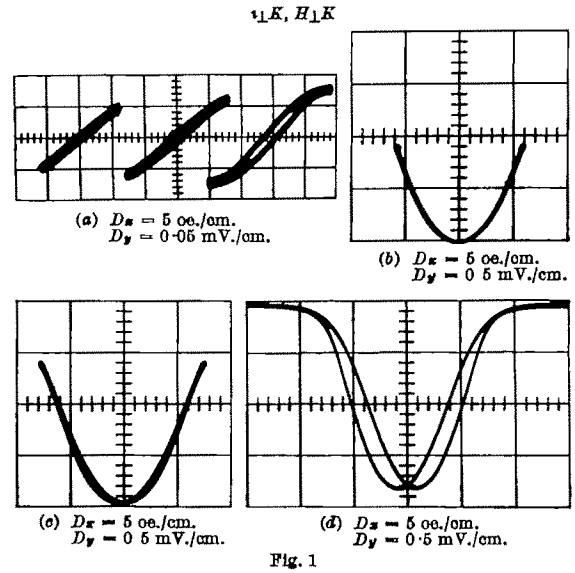

Fig. 1

that as $\hat{H}_\perp$ is increased the parabola opens up, and hysteresis occurs. Fig. 1*d*, for $h_\perp > 1$, is especially significant. The maximum change of d.c. resistance ΔR_0 for this film was found to be 0·060 ohm by potentiometric measurements in a static magnetic field. This value agrees with that calculated from the maximum change y_0 in Fig. 1*d* to within the accuracy of both measurements (±5 per cent). This result has been verified for all the films which have been studied (Table 1), and it indicates that the process of magnetization when $H_\perp$ is applied is predominantly one of domain rotation accompanied by rotational hysteresis.

Table 1

Sample	1	2	3	4
Thickness (cm.) × 10^4	2 00	2·00	0 62	0 62
$\Delta R_0/R$	0 0058	0 0058	0·0185	0·0170
ΔR_0 (ohm) d.c. measurement	0 060	0 052	0 246	0 215
ΔR_0 (ohm) corresponding to y_0	0·060	0 052	0·24	0·18
H_K (oe.) magnetic	9 0 (6) 8 5 (8) 6 5 (10)	8 0 (6) 8·0 (8) 7 0 (10)	7 0 (5) — —	4·0 (3) — —
H_K (oe.) magnetoresistive	8·3 (6) 8·8 (8) 6 6 (25)	7·3 (7) — 6 6 (25)	7·8 (5) — —	4 7 (2) — —

Numbers in parentheses are values of $\hat{H}_\perp$ at which H_K was determined

These observations, together with those of Bradley and Prutton[6,7], suggest the following description of the transverse magnetization process in nickel–iron alloy films having uniaxial anisotropy. When the film has been previously saturated along the K-axis and $H_\perp$ is sufficiently small, the process is one of uniform reversible rotation of the magnetization within the plane of the film. However, with increasing $H_\perp$, the local deviations of the direction of anisotropy within the film as proposed by Harte[8], together with the demagnetizing field of the film relative to the average K-axis, make it favourable for some regions

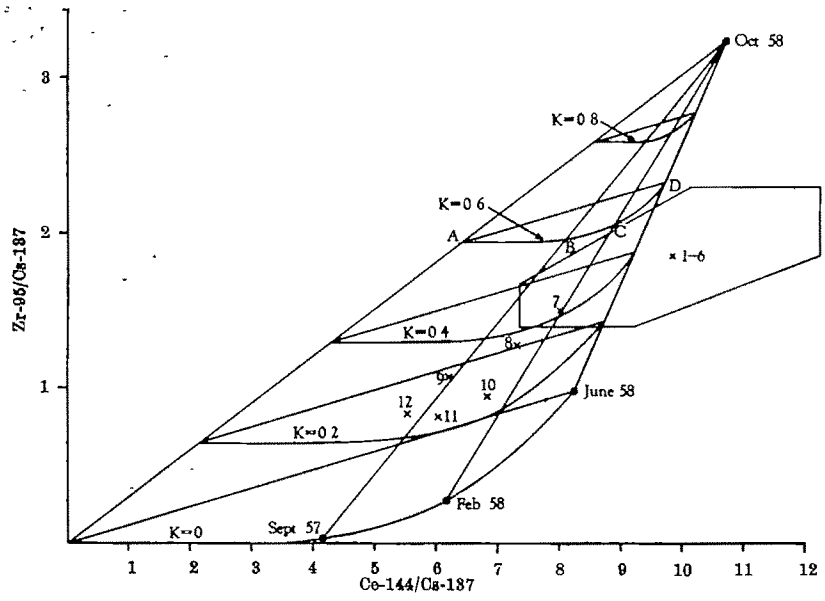

Fig. 6. *X*, observed values. The numbers 1–12 indicate sampling months, 1959

ponents, both of which have approximately the same shape. These results are consistent with the observations reported by Ambrosen[5] on activity in precipitation and by Peirson *et al.*[6] on tropospheric activity, that about 50 per cent of the long-lived activity, sampled in the first six months of 1959, emanated from October 1958.

By a similar analysis of the results during May–July 1958 (Fig. 7) it is found that at most 30 per cent of the cæsium-137 emanates from February 1958, and a large part of the remainder comes from 1957. During the autumn of 1958, the cæsium-137 level is fairly constant and high compared with the same period in 1959. A possible reason for this is the February 1958 tests, if it is assumed that these tests gave a contribution of the same type as the October 1958 tests with a maximum about six months after the tests.

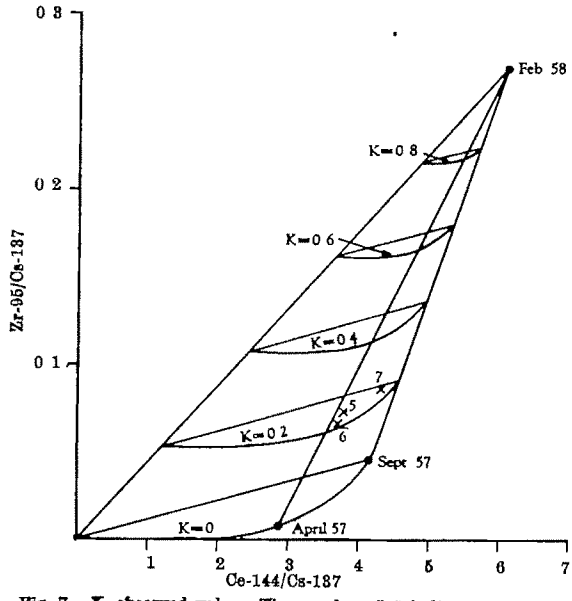

Fig. 7. *X*, observed values. The numbers 5–7 indicate sampling months, 1958

The additional information that can be obtained from the antimony-125 values is rather limited because of the large variation in yield with fission mode for this mass-chain (cf. Table 2). The antimony-125/cæsium-137 ratio is given in Fig. 5. It is seen that the values for the period April–September 1958 are fairly constant, and have a mean value of 0·37, whereas the period April–July 1959 has a mean value of 0·52. If it is assumed that the antimony-125 yields are the same for the different injections, this increase corresponds to a decrease in age of about one year; that is, that the mean age of the debris at the time of sampling was the same. The rather large variations for September 1957–March 1958 and October 1958–January 1959 might be due to experimental errors in the determination of antimony-125, as the samples from these periods were very weak.

The main feature of the observations reported in this article and elsewhere[7] is a pronounced seasonal variation of the cæsium-137 content in ground-level air during 1958 and 1959. This, however, does not necessarily imply a seasonal variation in the transport properties of the upper atmosphere, as the major injections of debris in high northern latitudes took place in the autumns of 1957 and 1958, and the variations thus may be explained by assuming a mean residence time in the stratosphere of about six months for such debris, independent of the time of injection. Only when the contributions from the preceding autumn have been subtracted from the total content is it possible to get a fairly unequivocal indication of a 'true' seasonal variation. As is found, a pronounced variation of this type seems to exist during 1959 and there are indications of it during 1958. These observations are thus in concordance with the model of stratospheric fall-out presented by Stewart[8] and Machta[9].

However, it has not been verified that this type of variation applies to injections at high latitudes. As is pointed out by Martell[10], there are indications that the mechanism of stratospheric fall-out from such injections differs in such a way that the residence time is considerably shorter (~ 6 months) than for injections at low latitudes, and not very dependent on the time of the year. The results presented here do not contradict this theory. On the contrary, some features seem to support it, for example, the relatively high cæsium-137 values during the autumn of 1958 which may be due to the February 1958 tests.

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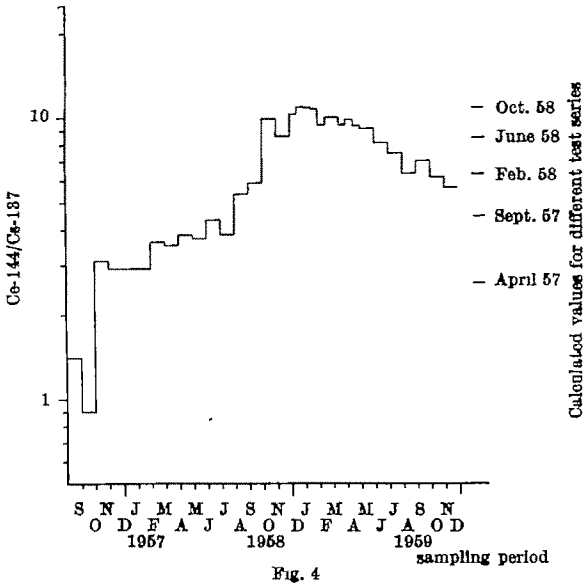

Fig. 4

ratios is given for mixtures where one component originates from October 1958 and the remainder is from June 1958 or earlier. The ratios refer to October 18, 1959. The K-values are the fraction of cæsium-137 originating from October 1958. A binary mixture is given by a straight line in the diagram between the points representing the pure components. A point on this line defines a K-value. If this value is kept constant and the origin of the older component is varied from very old (that is, zirconium-95/cæsium-137 and cerium 144/cæsium-137 ≈ 0) to June 1958, an arc is obtained (for example, $ABCD$). All mixtures of two or more components with a given K-value will be represented by points in the area obtained by connecting the ends of this arc by a straight line.

By inserting observed values in Fig. 6, some indication of the mixing-ratios and the age of the older components can be obtained.

For an evaluation of the uncertainty in this estimation, it is necessary to consider both the errors in the experimental and the theoretical values. The former are partly statistical and partly systematic, due to difficulties in the interpretation of the γ-spectra. The latter are systematic and are a result of uncertainties in yield values and half-lives, as well as fractionation. From a practical point of view, it is advantageous to attribute all these errors to the experimental points and regard the theoretical values as fixed. An indication of the magnitude of the statistical errors is given by the measurements from the period January–June 1959, during which no systematic variation in the observed ratios could be seen. From an analysis of these values, it is found that the standard deviations are 6 per cent for the ratios zirconium-95/cæsium-137 and cerium-144/cæsium-137, and 3 per cent for the zirconium-95/cerium-144. The systematic errors from uncertainties in yield values and half-lives can be roughly estimated to 15–20 per cent. As an estimate of the total maximal errors, the following values have been chosen: zirconium-95/cerium-144, 20 per cent; cerium-144/cæsium-137, 25 per cent; and zirconium-95/cæsium-137, 25 per cent.

In Fig. 6 an experimental point corresponding to the mean values for the sampling period January–June 1959 has been inserted. Adding the errors as assumed above, a hexagonal area as indicated in the figure is obtained. As this area is rather large, no very accurate conclusions about mixing ratios can be made. However, it can be seen that between 20 and 55 per cent of the cæsium-137 originates from October 1958, and that a large part of the older component emanates from September 1957 or later. The experimental points for the second half of 1959 indicate an increased mixing ratio of older components with time, and the mean age of these older components also seems to increase with time. This trend can be considered significant, as the greater part of the assumed errors is systematic and to a large extent common for all points.

From the possible mixing ratios for samples from 1959, estimated as above, it is concluded that between 50 and 100 per cent of the zirconium-95 in these samples can be attributed to the October 1958 tests. The activity of zirconium-95 plotted in Fig. 2 thus gives, as regards 1959, a fairly good picture of the time-variation of the activity of this origin (corrected for radioactive decay). The maximum occurs about 6 months after the tests, and has a half-width of 5–6 months. The peak value corresponds to $(1–2) \times 10^7$ fissions per kgm. air. One year after the tests the level is only a few per cent of the maximum value.

Only 55 per cent of the cæsium-137 peak in the spring 1959, given in Fig. 1, can originate from October 1958, as concluded from Fig. 6. If this contribution is subtracted from the total cæsium-137 activity, a pronounced peak still remains. It thus seems that the peak in 1959 consists of two com-

Table 3. HIGH-YIELD EXPLOSIONS ON THE NORTHERN HEMISPHERE 1957–58

Test period	Country	Explosion date used in the calculations
April 3–16, 1957	U.S.S.R.	April 10, 1957
Aug. 22–Oct. 6, 1957	U.S.S.R.	Sept. 15, 1957
Feb. 23–27, 1958	U.S.S.R.	Feb 25, 1958
June 28, 1958	U.S.A.	June 28, 1958
Sept 30–Oct. 24, 1958	U.S.S.R.	Oct. 18, 1958

The American tests in August 1958 are not included as they were performed at very high altitude. Nor have the British tests at Christmas Island been included.

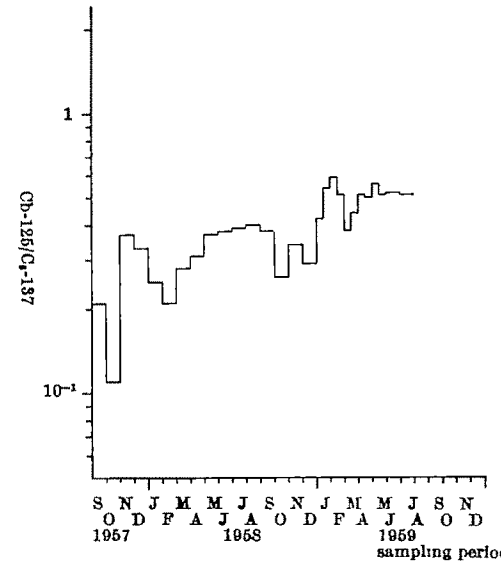

Fig. 5

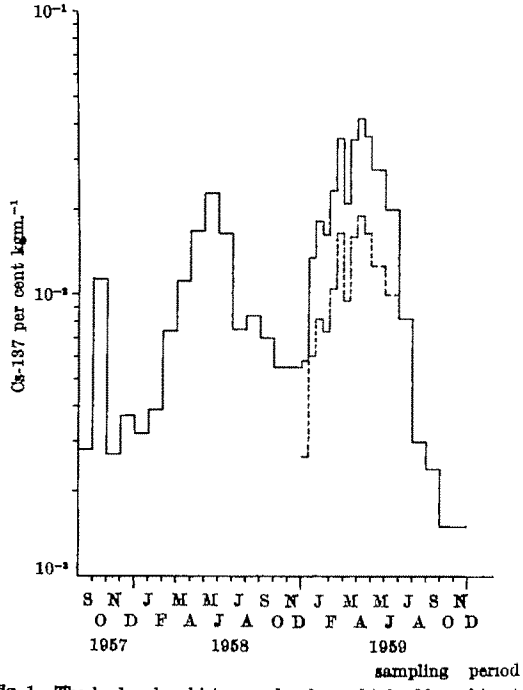

Fig. 1. The broken-line histogram has been obtained by subtracting the maximum contribution from the October 1958 tests

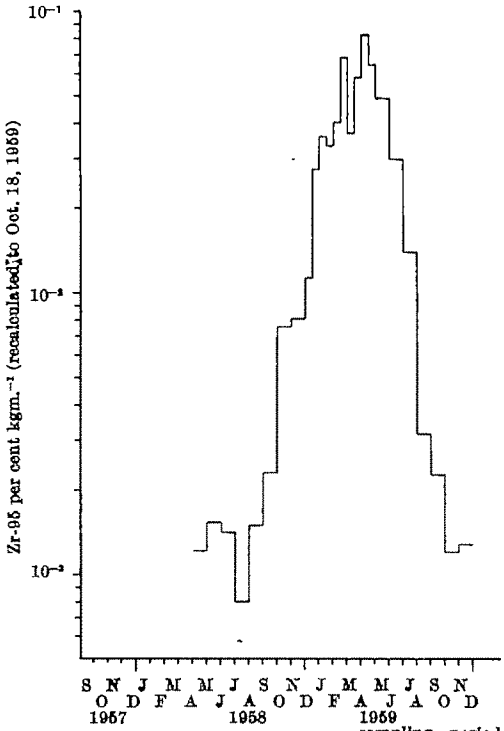

Fig. 2

cæsium-137 and cerium-144/cæsium-137 ratios with calculated values. The calculation of these ratios implies large uncertainties as the type of fission (fissionable material, neutron energy-spectrum) can only be roughly estimated, and furthermore, the yield-values are quite uncertain in many cases. In Table 2 yield values for the possible fission modes are given[3]. Mean values of the yields for fast and

Table 2. YIELD VALUES (PER CENT)

Mass chain	Type of fission U-235 fast	U-238 fast	Pu-239 fast	U-235 14 MeV.	U-238 14 MeV.
95	6 74	5 64	5 16	5 24	5·21
125	0 122	0 052	0 254	1 33	1·09
137	6 16	6 13	6 07	5 14	5 62
144	4 75	4 55	3 62	3 24	3 23

14-MeV. fission of uranium-238 have been used for the calculations.

A source of error is also introduced by fractionation phenomena[4]. For example, it has been found experimentally that the mass-chain 95 is enriched in larger particles, which can be explained from the chemical properties of the fission products during the period of particle formation. To estimate the influence of this on the ratios studied it is necessary to have some knowledge of the particle spectrum. Such work is under way at this laboratory. Although the quantitative evaluation of the particle spectra is not yet concluded, it is possible to say that the contribution of larger particles with appreciable fractionation to the total activity is small for debris older than about three months. For this reason we assume in the following that, except for debris with components younger than a few months, the error due to fractionation is small compared with errors in the measurements and theoretical calculations.

In Figs. 3 and 4 the calculated ratios for the publicly known high-yield explosions on the northern hemisphere since 1957 have been indicated (cf. Table 3). It is observed that the experimental zirconium-95/cæsium-137 ratio for the first six months of 1959 is nearly constant, and about 0·6 times the theoretical ratio for debris from October 1958, thus indicating an admixture of older debris.

In Fig. 6 the theoretical relationship between the zirconium-95/cæsium-137 and cerium-144/cæsium-137

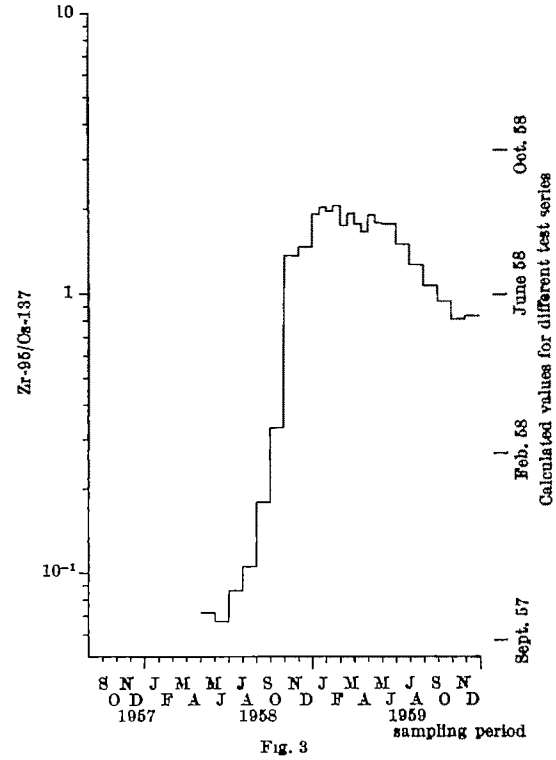

Fig. 3

CONCENTRATION OF SOME FISSION PRODUCT NUCLIDES IN GROUND-LEVEL AIR

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IN ground-level air the fission product activity originating from nuclear weapon tests varies considerably with time, both in intensity and composition. In order to map these variations, especially regarding the long-lived components, γ-spectrometric measurements have been made on monthly samples of ground-level air taken near Stockholm, Sweden. An attempt has been made to correlate the activity variations with known nuclear weapon tests.

The sampling apparatus consisted of a commercial centrifugal blower (Stephan-Werke, Hameln/Weser, West Germany), to which a filter holder (area 18 × 18 cm.^{2}) was attached on the inlet side. The filter medium was glass-fibre paper with a thickness of 55–60 gm./m.^{2}. The filtering capacity was about 4 kgm. air per min.

The samplers were run continuously, and the filters changed every 24 hr. Thus, each sample contained the particulate activity from about 5,000 kgm. air.

The samples were allowed to stand for 3 days in order to let the short-lived radium and thorium daughter products decay. After that, one quarter of the sample was measured for total γ-activity with a scintillation counter. (The remainder was used for autoradiographic and other investigations.) When the measured samples were strong enough (> 2 mc.), individual nuclides were determined by γ-spectrometry. These measurements of daily samples are reported elsewhere[1,2]. The samples were then pooled to give monthly, or sometimes half-monthly, samples. The γ-spectra of these pooled samples (each corresponding to (1–4 × 10^4 kgm. air) were measured with a spectrometer consisting of a 10 cm. × 10 cm. sodium iodide(Tl)-crystal connected to a 70-channel kick-sorter.

The results given in this article cover the period September 1957–December 1959 for a sampling station near Stockholm (59·2° N., 18·1° E.). The measurements were mainly performed at the end of 1959 and beginning of 1960, and the concentrations of zirconium-95, antimony-125, cæsium-137 and cerium-144 were determined. The results are given in Table 1, where all activities have been recalculated to October 18, 1959. For the period May 1958–September 1958 the zirconium-95 values were obtained from measurements made in June 1959. For older pooled samples zirconium-95 values are lacking. Contributions to the γ-spectra were also observed from ruthenium-(103 + 106). The relative amounts of ruthenium-103 and -106 could not be determined as their main γ-lines are quite close in energy. An indication of manganese-54 was also observed in most of the samples. In samples from the second half of 1959, which were measured a few months after sampling, beryllium-7 (54 *d*) was also detected. In these samples it has not yet been possible to determine the antimony-125 content, because the γ-line of this nuclide is masked by the one from beryllium-7.

In Fig. 1 the time-variation of the concentration of cæsium-137 is plotted. The main features are two broad peaks with half-widths of 4–6 months and maxima in June 1958 and May 1959, respectively. A temporary increase is observed in October 1957. From earlier measurements on daily samples, it has been found that about 75 per cent of the cæsium-137 activity during this month was collected in one sample (October 13–14). In this sample, considerable amounts of iodine-131, presumably originating from the Windscale accident, were found, and probably most of the cæsium-137 has the same source. In Figs. 2, 3, 4 and 5 the values for zirconium-95 and the zirconium-95/cæsium-137, cerium-144/cæsium-137 and antimony-125/cæsium-137 ratios are plotted. The rather sharp increase of the concentration of zirconium-95 at the end of 1958, combined with the increase in the zirconium-95/cæsium-137 ratio, is a proof of the appearance of activity of considerably more recent origin. From more detailed age-determinations (for example, from the barium-140/(zirconium + niobium)-95 ratio) made on debris sampled during the end of 1958 and beginning of 1959, it was concluded that this debris originated mainly from October 1958. According to Press data, Russian high-yield tests were performed during October 12–22, 1958.

In the following an attempt is made to calculate the possible dates of origin and mixing ratios of the debris by comparing the measured zirconium-95/

Table 1

Period of sampling		Measuring date	Zr-95 (pc./kgm. ×10^3)	Sb-125 (pc./kgm. ×10^3)	Cs-137 (pc./kgm. ×10^3)	Ce-144 (pc./kgm. ×10^3)
Sept. 57		3.3.60		0 6	2 8	4·0
Oct.		2.3		1·2	11 4	9 8
Nov.		29.2		1·0	2·7	8 5
Dec.		25.2		1·2	3·7	10 8
Jan. 58		16.2		(0 8)	3·2	9·3
Feb.		17.2		(0 8)	3 9	11·2
March		15.2		2 1	7·4	26 9
April		15 2		3·4	11·1	39 2
May		4.2	1 2	6·3	16·9	64 3
June		5.2	1 5	8·6	22 9	84·3
July		4.2	1 4	6 5	16 5	70·4
Aug.		5.2	0·8	3 0	7 5	29 0
Sept		6.2.60	1 5	3·2	8·4	44·8
Oct.		10.11.59	2·3	1 8	7 0	41·1
Nov.		11.11	7·6	1 9	5·5	54·1
Dec.		11.11	8·1	1 6	5 5	47·3
Jan. 59	1	28.10	11·3	2 5	5 9	60·0
	2	28.10	27·5	7·4	13·6	147
Feb. 59	1	29.10	35·9	10 7	18·2	195
	2	2.11	33·3	8·3	16·4	174
Mar. 59	1	2.11	40·7	8·9	23·2	215
	2	3.11	68·9	15·6	35·7	353
April 59	1	4.11	37·1	10·7	21·0	208
	2	4.11	58·7	17 6	35·4	330
May 59	1	6.11	83·8	24 8	44·2	428
	2	6.11	65·0	18 5	36 5	336
June		7.11	49·2	14·4	27 8	251
July		7.11	29 9	10 1	20·0	159
Aug.		9.11	10 4	< 4 1	8·2	59 8
Sept.		10.11	3·2		3 0	18·4
Oct.		27.11	2 3		2 4	16·5
Nov.		11.12.59	1·2		1·5	8 8
Dec.		13.1.60	1·3		1 5	8·4

The concentration of the measured nuclides have been recalculated to October 18, 1959, using the following half-lives. zirconium-95, 65 days; antimony-125, 2 years; cæsium-137, 30 years; cerium-144, 285 days. As no absolute calibration has been made for antimony-125 the absolute values of this nuclide may be in error by ± 30 per cent.

Table 1

Brain Stem Reticular		*Thalamic Reticular*
Neurophysiological Characteristics	*Behavioural Characteristics*	*Neurophysiological Characteristics*
Tonic reaction	Adaptation Long term . . . . . Short term	Phasic reaction
Long latency period	Threshold High . . . . . Low	Short latency period
Response to stimulus long	Sustenance Long . . . . . Short	Response rarely outlasts stimulus
Rapid habituation	Habituation Flexible . . . . . Rigid	Resistant to habituation
Slow recovery from habituation state	Extinction Slow . . . . . Quick	Quick recovery from habituation state
Controls sensory input	Blocking Input . . Suppress or augment cortical activity	Suppressive and facilitory action
Intensity generalization	Ability to cope . . . . with intensity changes in stimulation . . . . High external reality testing	Quality or fine discrimination, continual response to varied stimulus

especially concentration with emotional tone[10]. Simultaneous activity of diffuse-specific projection systems can lead to changes in cortical activity, which is dependent on timing of electrical impulses on the thalamic reticular system[4,10]. Thus it is suggested that sub-cortical blockage of input by stress stimuli delivered at given certain rates would either abolish, increase, or decrease cortical activity (similarly to an artificial stimuli).

Consider now the problem of why performance of the stressed in some cases is organized and in other disorganized (essentially the problem of cognitive motivation). First, studies seem to indicate that the cognitive control mechanism lies in the suppression of reticular activity by the cortex via cortico-thalamic tracts. Integrating the work of Kluver and Bucy, and Forbes and Morrison[11], it would seem that the temporal lobe and amygdaloid complex intact could modulate emotions by affecting brain activity through the secondary sensory discharge. With lesions we obtain uninhibited emotional discharge. The cortex controls the activating mechanism of the brain stem reticular system, thereby influencing its own level of arousal. A second mechanism lies in the activity of the brain stem reticular system, which would have to be prepotent with respect to the thalamic reticular system in order to provide a 'cognitive crutch' for the tolerators of stress, while control by the thalamic reticular system of the alpha rhythm[1], by cutting attention, could provide a 'cocoonizing' response to stress. In the latter case we would have a passive response where reality is ignored temporarily, and in the former case an active apprehension, and a longer lasting if not impervious face to stress. While the thalamic reticular system may provide a subsidiary stress control mechanism, it is proposed that the major function is to lead to disorganized responses as supported by Landis's study[12], as well as the isomorphic relations suggested below.

Finally, the question of how stress or emotion can limit disorganization to certain sense modalities (auditory or visual) or disorganize the whole organism is considered. It is known that the thalamic reticular system can localize its activity to one hemisphere, or even one lobe[10], and I have already proposed that the thalamic reticular system is responsible for disorganizing effects. Another secondary mechanism could lie in the key finding[13] that there is an ordering of the various sensory modes with respect to their effectiveness in inducing cortical activity.

Such rationales for suggesting that the brain stem reticular system and the thalamic reticular system control organized and disorganized behaviour respectively may be considered too tenuous in the face of what we know of brain-behaviour relationships. Undoubtedly such a picture is tentative, and the following isomorphic relationships (between known neurophysiological reactions and known or deduced psychological data) over-simplified. However, there is also support in that these systems control other variables which are related to the dichotomous effects, namely, that of disorganization–organization[2].

Additional effects of stress variability due to change and rate of change of stimulation, and the non-linear relationship between increased stress and increased disorganization are discussed with respect to experimentation[2]. Further considered is the influence of individual (especially satiation-level) and cultural factors on disorganization–organization, neurochemical composition of the reticular formation and learning, old-age as a 'natural' sensory deprived group, and the utilization of brain injured and 'quitters' as catalysts for research in concept formation[2].

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DISORGANIZATION–ORGANIZATION AND THE RETICULAR FORMATION

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WHEN a phenomenon seems to defy elucidation, scientists are often forced to 'look before and after' in the hope that the longer route will prove, in the end, to be the shortest. It is perhaps, therefore, that in seeking an answer to the question: 'What is emotion?' that many workers have studied the subsequent effects of an emotional state. While earlier Darwin and Cannon suggested that emotion gave rise to highly organized response sequences (supported in recent times by Leeper, Duffy, and Webb), others, such as Young, have interpreted emotions as leading to disrupting and disorganizing responses. No satisfactory envisagement of the subject of emotions has been arrived at, and Lindsley[1] has suggested that one reason could be that recent neurological findings have rendered certain prominent theories inadequate.

A critical discussion of theoretical compromises and a major experiment relevant to the Leeper-Young controversy has been presented[2]. It was shown that these compromises by Bindra[3] and Hebb[3], as well as the experimental conclusions of Thompson and Higgins[3], were untenable on biological, scientific and logical grounds, and in certain cases actually argue for the disorganization point of view.

Therefore a simple alternative solution is suggested, which proposes that any emotion (or stress) may in effect be disorganizing or organizing, depending on whether there is interference from an internal modulating system, namely, cognitive motivation, which can influence and organize brain activity independent of sensory input in the reticular formation[2,4]; and that emotions are a single sub-class of behaviour to be differentiated from the subsequent effects which may, or may not, be similar to the non-demonstrated effect. The effect of organization would follow from the organism being in such a state of equilibrium with its environment that it may be said to possess the property of adaptability (that is, make for adaption but not necessarily eventuating in it). To ensure that such stability will follow, there is a selection of variables such as not to lead to a critical state (that is, all essential variables lie within their physiological limits). This selection may be automatic as in homeostatic mechanisms (Ashby's principle of ultra-stability), or it may be by the utilization of rational decisions or non-automatic choice as in cognitive motivation. That is, cognitive motivation may be measured by the ratio of maximum use of cognitive control for long-term psychological and physiological survival to a minimum of short-term solutions, overriding all other conflicting needs. By short-term is meant what is temporarily expedient but would not necessarily eventuate, and possibly conflict with survival in the long run; and by psychological survival is simply denoted behavioural equilibrium through a reduction of conflicting responses.

Support for the alternative hypothesis lies not only in experiments which fail to show that stress (or sensory deprivation) necessarily leads to disorganized responses[5], contrary to the McGill experiments on sensory deprivation, but also in the studies using different species and different emotional, intellectual, social, and audio-visual stresses[6]; demonstrating that stress effects on performance should not be studied independently of the cognitive characteristics of the individual, that stress tolerators do their own reality testing, show organized flexible behaviour with no cognitive disruption, while 'quitters' are unable to maintain rational thought and rely heavily on external reality testing. Such a hypothesis explains both the disorganized and the organized, unlike current theories of sensory deprivation which rely heavily on the deprivation characteristics of the stimulating environment to explain only the disorganized. Studies in other areas[7] also demonstrate the consistently dichotomous response of the disorganized-organized individuals in varied situations, as well as in respect to neurophysiological variables (that is, disorganized—'quitters', low-satiation threshold, extroverted, poor control primary processes, rigidity, poor cognitive organization, high reality testing, brain injury, thalamic reticular system; organized—'tolerators', high-satiation threshold, introverted, strong control primary processes, flexibility, strong cognitive organization, low reality testing, normals, brain stem reticular system). It is noted[2] that the satiation phenomenon is centrally involved in these studies and is related to metabolic efficiency (Wertheimer) and the reticular formation[2], while metabolic activity has been related to stress (Pace).

The usefulness of postulating a neurophysiological model for behaviour has been emphasized by Bertalanffy, Hebb, Krech, and Le Gros Clark, and such an attempt is made with dichotomous effects and the intervening internal modulating system. Adrian and Mathews[8] state that anæsthetics may produce 'unconsciousness' by suppressing sensory activity so that behaviour is rigid. It is suggested here[2] that stress essentially replicates the action of pharmaceuticals, thus making stress act as a 'behavioural anæsthetic', and blocking input. Four types of blockage have been discussed in detail[2]. One, differential depressant action, augmenting responses in the non-specific sensory system, by inhibition of the sub-cortical system[9]; second, if sensory input is 'allowed' to be received it is not necessarily elaborated for awareness, depending on inhibition-activation balance sub-cortically[9]; third, cortical stimulation blocks conduction in reticular formation[4], providing a neurophysiological basis for behaviour involving aberrations under emotional stress; fourth, if the alpha rhythm corresponds to the electrical correlate of external sensory input, then the alpha rhythm is readily blocked by concentration of attention,

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resulted in the manner shown in Fig. 2*A*. Frequently cracks perpendicular to the surface developed, following which each block of soil acted as a separate unit: during expansion a plane of no movement was found up-slope of the centre of the block, and during contraction a corresponding plane down-slope of the centre, resulting in a net down-slope movement of each block (Fig. 2*B*). Difficulty was encountered in preventing movement from occurring mainly at the junction of the soil with the base of the trough, but in some cases differential down-slope movement of the upper layer of soil relative to the lower took place.

Creep due to wetting and drying was further reproduced under semi-natural conditions. An undisturbed block of soil 100 × 20 × 20 cm., with overlying turf, was placed in a glass-sided trough, which was tilted to 25° and exposed to natural weather conditions in Sheffield. Movements were recorded monthly for 2 years. Expansion and contraction of the soil corresponded closely with periods of rainfall and drought. The soil acted as a single block, with movement taking place mainly, but not entirely, along the base, at a rate of 5·0 mm./yr. In a second trough filled to 30 cm. depth with disturbed and re-packed soil, the rate of movement decreased regularly from the surface downwards.

These results suggested an indirect means of measuring soil-creep. At three sites on a slope, on the 26° steepest part and at 18° and 7° on the concavity, variations in moisture content of the soil at three depths were obtained by monthly sampling during 2 years. By means of shrinkage tests, the percentage expansion and contraction of the soil for unit change in moisture content at each of these nine points was obtained. Combining these results and interpolating between the sampled depths gave

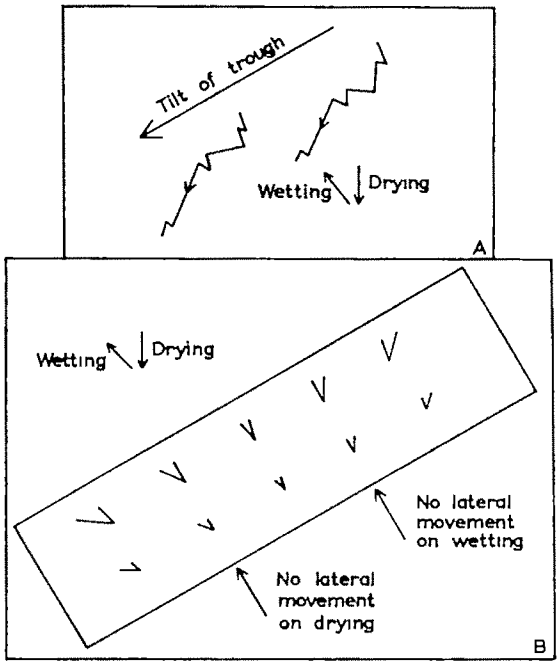

Fig. 2. Movements in a tilted block of soil subjected to alternate wetting and drying. *A*, trace of movements during five periods of drying separated by four of wetting; *B*, diagrammatic representation of movement in a single cohesive block of soil during one cycle of drying and wetting

Table 1

Slope angle	Depth (cm.)	Linear shrinkage for 1 per cent moisture loss* (per cent)	Moisture change + and − (per cent/yr.)	Change in linear dimensions (per cent/yr.)	Down-slope movement (cm./yr.)	Volumetric down-slope movement (cm.³/cm./yr.)
26°	0–5	0·08	37	3	0·86	1·07
	5–10	0·06	20	1	0·41	
	20–30	0·02	11	0·2	0·08	
18°	0–5	0·06	34	2	0·58	0·83
	5–10	0·06	15	1	0·33	
	20–30	0·03	9	0·3	0·08	
7°	0–5	0·10	46	5	0·61	0·79
	5–10	0·14	24	3	0·36	
	20–30	0·04	13	0·5	0·05	

* Prior to residual shrinkage, and corrected for gravel content of soil.

annual expansion and contraction of the soil on the slope. It was assumed that down-slope movement = sin (slope angle) × expansion and contraction perpendicular to the ground-surface. The results are summarized in Table 1. They show a movement of 0·5–1·0 mm./yr. close to the ground-surface, and 0·05–0·1 mm./yr. below 20 cm. depth. The volume of soil movement is 0·8–1·0 cm.³/cm./yr. The most striking feature is that movement on the 7°-concavity was only slightly less than that of the 26°-slope; this is attributable to the greater fineness of the soil and larger variation in moisture content on the concavity, and probably also to the presence there of expanding-lattice clay minerals.

The rate of the movement of the soil by slope-wash was measured on sites close to those used for soil-creep. Tins were placed in the soil with projecting lips on their up-slope sides (length 30 cm.) inserted just below the boundary of the A_0 horizon and the upper surface of the mineral soil (Fig. 1*D*). Soil was collected from the tins at 6–18 month intervals during 3 years. The mean of 49 results was 5·1 gm./yr. of soil, equivalent to a down-slope movement of 0·08 cm.³/cm./yr.

The relative ineffectiveness of slope wash is explicable from the presence of an organic cover, the A_{00} horizon of grass roots or leaf litter and the A_0 humus horizon. Besides their direct protective effect, these have a large capacity for absorbing moisture during storms, afterwards releasing it slowly to the soil beneath. Samples of the humus horizon taken during storms showed it to be capable of holding moisture contents of 75–90 per cent by weight, while retaining a firm structure.

These interim results indicate that on the slopes investigated the rate of down-slope soil movement by soil-creep is of the order of ten times as rapid as that by slope-wash.

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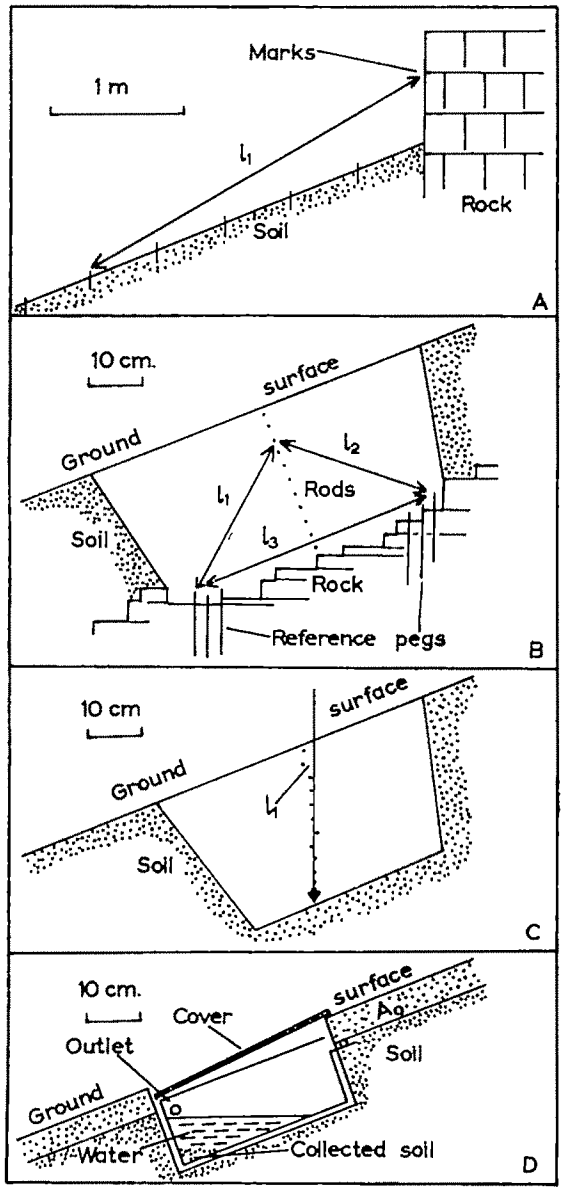

Fig. 1. Techniques for field measurement of the rate of soil-creep and slope wash. l_1, l_2, l_3 are measured lengths

accelerated soil erosion. This article describes techniques evolved for measurement of the rate of soil-creep under natural conditions, and reports interim results; experiments reproducing this process are described, and the relative effectiveness of soil-creep and slope-wash compared.

In the initial attempt at measuring soil-creep, metal pegs were inserted into the ground surface at short distances downslope of a bedrock outcrop (Fig. 1*A*). Three marks were engraved on the rock, and distances from each of these to the pegs measured at intervals of time. Down-slope movements are directly obtained by this method, but their interpretation is uncertain; if the surface soil moves more rapidly than that beneath, it will tilt the pegs, exaggerating movements of their upper ends. Measurements during $3\frac{1}{2}$ years indicate that, on grassed slopes of 30°, down-slope movement close to the ground-surface is of the order of 1 mm. They also show clearly that on slopes steeper than 35°, with a scarred or incomplete turf cover or with terracettes, rate of movement increases rapidly with increase in angle. All results refer to valley slopes in the basin of the Upper Derwent, Southern Pennines, underlain by sandstones with interbedded shales, belonging to the Millstone Grit Series.

To obtain movements of soil in depth, it is necessary to bury markers and afterwards re-excavate, since a vertical soil-face left exposed to the air creates artificial conditions of moisture, temperature and biological activity. Two methods of making such measurements have been employed. In the first (Fig. 1*B*) a pit was dug through the soil to the rock beneath, and six pegs driven firmly into the rock; when filling the pit, these were protected by covers. A line of metal rods (diameter 2 mm., length 10 cm.) was inserted into one side of the pit, the ends of the rods being flush with the undisturbed soil. Measurements from pegs to rods fixed the positions of the latter in two dimensions. In the second method (Fig. 1*C*), a vertical line of fine rods, 1-mm. diameter, was inserted flush with the pit side, and their position measured with respect to a plumb-line suspended close to their ends; on re-measurement, the deepest rods, close to bed-rock, were assumed to have remained stationary. This method is of comparatively high accuracy, but gives only the horizontal component of movement. Nine pits were established, and measured on re-excavation at intervals of 6–12 months over 2 years. Disturbances of rods during burial and excavation were distinguishable as random movements, contrasted with systematic movement of adjacent rods due to soil movement. Results indicate that, on grassed and wooded slopes of 20°–30°, down-slope movement of the upper 10 cm. of soil (excluding the organic horizons) is of the order of 0·25 mm./yr. The unit for measuring volumetric down-slope movement of soil is the volume of soil moved annually across a plane perpendicular to the ground-surface and parallel with the contour of the slope, for unit horizontal distance along the plane, expressed in cm.^{3}/cm./yr. The interim results show a movement of the order of 0·6 cm.^{3}/cm./yr. They also show that movements in the organic A_0 horizon, both under grass and woodland, were very much greater than in the immediately subjacent mineral soil, amounting to 0·5–2·0 mm./yr. It is hoped to obtain more precise results by re-measuring after the pits have been left undisturbed for 3–5 years.

A list of the causes of soil-creep has been given by Sharpe[10]. The majority of these are essentially causes of disturbance in the relative positions of soil particles; down-slope movement is produced by the constant factor of gravity acting on re-adjustments to these positions. Quantitatively, one of the greatest causes of disturbance is the swelling and shrinkage of colloidal components of the soil on wetting and drying. Experiments to reproduce soil-creep by this means have been carried out. Blocks of soil were placed in glass-sided troughs, and pins inserted into the sides of the soil to record movements; the troughs were placed at an angle of 30°, and the soil surface wetted and dried artificially. On wetting, expansion took place perpendicular to the surface; on drying, gravity tends to cause contraction in a vertical direction, but due to cohesion the observed contraction was in a direction intermediate between vertical and perpendicular to the surface. Net down-slope movement

larvæ were washed in water several times and transferred in threes to test-tubes containing a mixture of 1 per cent potassium cyanide with 1 per cent potassium ferricyanide in proportion of 1 to 1·5. The hæm content was then determined by the modified Czeczuga method[1].

The results are given on Fig. 1. Each point on the graph was plotted from the average of three measurements. The curve shows that the concentrations of polyvinyl alcohol from 0·001 to 0·1 per cent have a stimulating effect on hæm content. The greatest increase is seen when the solution contained a concentration of 0·005 per cent polyvinyl alcohol. At higher concentrations of polyvinyl alcohol the amount of hæm decreases.

From this experiment and those on increased chlorophyll synthesis, it can be presumed that the same mechanism is operating in both cases. Probably polyvinyl alcohol effects the biosynthesis of the porphyrine parts or makes easier the synthesis of metalloporphyrine.

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Increase in Level of Chlorophyll in *Pisum sativum* L.

IN experiments on the effect of polyvinyl alcohol on the development of *Pisum sativum* L., it was found that plants growing in water cultures to which the substance had been added grow more rapidly than control plants[1]. Polyvinyl alcohol has a similar effect on the growth of the plant mass. We wished to determine whether this substance has the same effect on the growth of *Pisum sativum* in soil to which it had been added as in the aqueous cultures.

For our experiments pea seeds of the variety 'May' were used. Seventy seeds were planted in boxes each containing hot-bed soil. The boxes were then placed in a room where the average daily temperature varied from 22° C. to 4° C. All the boxes were placed on window sills in the same light.

Four boxes with *Pisum sativum* sowings (group 1) were watered with an aqueous solution of polyvinyl alcohol at a concentration of 0·0001 per cent and four boxes (control, group 2) with water. Seventeen days after the plants had germinated, the shoots above ground were measured (from two boxes in each group). Those parts of the shoots which appeared above ground were then cut off in order to determine the amount of fresh plant bulk. Chlorophyll was extracted by the T. Godniewa method and its level determined by means of a Lang photocolorimeter. The plants in the next four boxes were measured and cut on the twenty-second day of the experiment in exactly the same manner. The level of chlorophyll was calculated in mgm. per 1 gm. of fresh shoot mass above ground.

As a standard, a solution of 8 per cent chlorophyll solution appropriately diluted (R. Marck, Darmstadt) was used. The results are given in Table 1.

Table 1. COMPARISON OF THE RESULTS OF THE EXPERIMENT
Plants growing in soil to which an aqueous solution of polyalcohol vinyl had been added

Box No.	Date of shoot cutting	Average length of plants	Fresh plant mass in gm.	Amount of chlorophyll in mgm. per gm. of fresh plant mass
1	July 10	27 5 cm.	13,500	2 25
2	,, 10	26 0 ,,	14,100	3 55
3	,, 14	42·0 ,,	24,200	3·66
4	,, 14	44 0 ,,	26,500	3·39
		Control plants		
5	July 10	22·0 cm.	9,650	1 56
6	,, 10	25 5 ,,	13,400	2 23
7	,, 14	34 0 ,,	9,800	3 32
8	,, 14	39 0 ,,	18,500	2 08

The observations presented in our first report[1] on the intensity of coloration in the parts above ground, which is, in our opinion, directly connected with an increase in chlorophyll content, have been confirmed in this experiment.

In series I, the difference in chlorophyll content between plants growing in polyvinyl alcohol and the controls is considerable—1·01 mgm./1 gm. of fresh mass; in series II this difference is 0·85 mgm./1 gm. of fresh mass. The average for series I and II is 0·93 mgm./1 gm. of fresh shoot mass above ground.

This experiment demonstrates that not only in water solutions but also in soil the growth of plants treated with polyvinyl alcohol is more rapid than the growth of control plants.

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SOIL MOVEMENT BY DENUDATIONAL PROCESSES ON SLOPES

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TWO aspects of geomorphology which have recently received increased attention are the rate at which changes in landforms take place, and the study of erosional and denudational processes. Estimates of the rate of landform evolution have been made from indirect geological evidence[1–3], or by relating measured river loads[4–6] or rates of sedimentation[7–9] to the catchment areas from which they are derived. These results combine the material removed in bank and bed erosion with that supplied to the rivers by denudational processes. Direct measurements of the rapidity of denudational processes on hill slopes have related mainly to slope-wash, undertaken in connexion with investigations of

Table 1 CHLOROPHYLL-LEVEL IN *Chlorella pyridinosa* WITH VARIOUS CONCENTRATIONS OF POLYVINYL ALCOHOL

Concentration of polyvinyl alcohol in culture	Determination I	II	III	Average of the 3 determinations	Average error*
1	0 035	0 028	0 025	0 029	0 00447
0 5	0 075	0 070	0·070	0 071	0 00242
0 1	0 288	0 300	0 316	0 301	0 01180
0 01	0 248	0 248	0 248	0 248	0 00000
0·001	0·172	0 224	0 216	0 204	0 02600
0 0001	0 148	0 176	0 176	0 167	0 01500
0 00001	0 160	0 140	0·140	0 147	0 01260
Control	0·136	0·115	0 100	0 115	0 01260

* The average error was calculated from the formula: $Ed^2/n(n-1)$ where Ed is total divergence from average, n is number of measurements.

of chlorophyll was determined by means of a colorimeter on a wave-length of 650 mμ. 10 ml. of the culture were taken at the same time in order to determine the number of cells. The specimens were fixed in formalin and tested 14 days later.

On calculating the average content in each of the specimens tested, it was found that the level of chlorophyll varied according to the concentration of polyvinyl alcohol used (see Table 1). Comparing the results with those for the controls, it is seen that chlorophyll content increases consistently with the increase in the concentration of polyvinyl alcohol. With 0·001 per cent concentration of polyvinyl alcohol, the amount of chlorophyll was doubled, and the optimal solution used in our experiments (0·1 per cent) practically tripled the amount of chlorophyll. In those cases where the concentrations of polyvinyl alcohol exceeded the optimal, inhibition in development of the algae and a marked decrease in chlorophyll-level was observed (see Fig. 1).

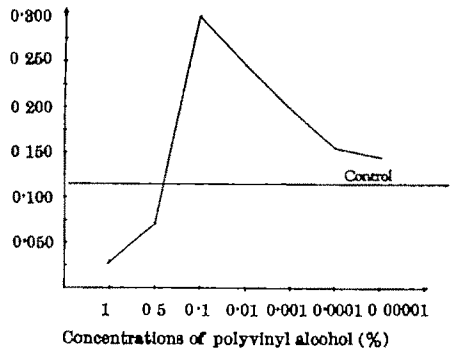

Fig. 1. Curve showing the chlorophyll-level in *Chlorella pyridinosa* cultures of various concentrations of polyvinyl alcohols

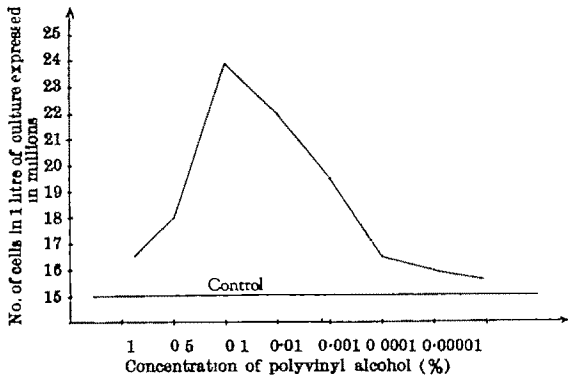

Fig. 2. Curve showing the dependence of the number of cells is dependent on the concentration of polyvinyl alcohol in the culture

The differences in the number of cells were not so marked as the variation in chlorophyll-level. At the optimal concentrations the number of cells as compared with that of the controls showed an increase of only about 60 per cent. These results are presented in Fig. 2.

Aqueous solutions of polyvinyl alcohol have a marked effect on the chlorophyll-level in algae of the *Chlorella* type. This polymer also affects cells, causing an increase in their number. The rise in the level of chlorophyll in *Chlorella* and the increase in the number of cells are not closely connected and are in the proportion of 3·3 : 1. The significant rise in chlorophyll-level in algae growing in aqueous solutions of polyvinyl alcohol may be due to increased intracellular synthesis.

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Hæm Content of Larvæ of *Tendipes* f.l. *plumosus* L.

EXPERIMENTS on the effect of polyvinyl alcohol on the chlorophyll content of algae and other plants showed that this polymer at a concentration of 0·0001 per cent doubles the level of chlorophyll. Since chlorophyll has essentially a similar structure to that of hæm, we decided to investigate whether polyvinyl alcohol has a similar effect so far as hæm is concerned.

The experiments were carried out on *Tendipes* f.l. *plumosus* from the ponds in Dojlidy, Białystok. The larvæ were transported to the laboratory and placed in glass aquaria of 500-ml. capacity. 100 c.c. of silt was put at the bottom of each vessel and 250 ml. of pond water, filtered through triply folded gauze, were poured over the silt. The larvæ were transferred to the aquaria, one larva in each vessel, after which an aqueous solution of polyvinyl alcohol was added so that the final concentrations were: 0·001, 0·005, 0·01, 0·05, and 0·1 per cent. One aquarium was left without polyvinyl alcohol as a control. Meanwhile, 50 larvæ from the same place and collected at the same time as the larvæ used for the experiment were dried at a temperature of 105° C. in a drier in order to calculate the average dry mass of one larva. The hæm content found during the experiment was expressed as the proportion to this average dry mass 14 days later. The

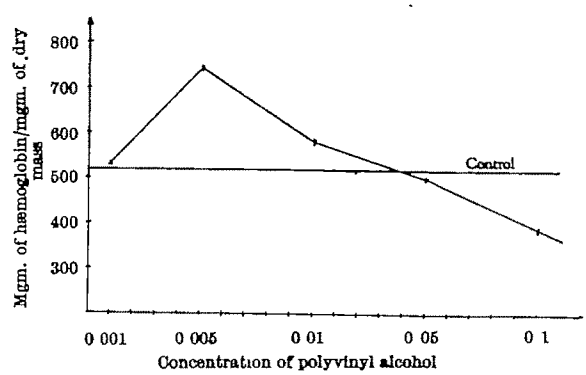

Fig 1. Graph showing level of hæmoglobin in *Tendipes* f.l. *plumosus* L. in various concentrations of polyvinyl alcohol

Vitamin A exists in the tissues in several geometric configurations, *cis-trans* isomers of one another[24]. The bleaching and synthesis of rhodopsin involves a cycle of stereo-isomerization: rhodopsin is synthesized from 11-*cis* (neo-*b*) retinene, and on bleaching releases all-*trans* retinene[25].

11-*cis* Vitamin A has not been identified in any tissue of the body, except in the eye[26]. There Krinsky has found that up to 65 per cent of the vitamin A in the pigment epithelium may be 11-*cis*[23]. It is of interest to inquire what isomer of vitamin A is found in the pigment epithelium after prolonged light adaptation. With this in view, the vitamin A was extracted from the pigment layers of six light-adapted animals as described above. The content of 11-*cis* vitamin A was determined by isomerizing with light in the presence of iodine, according to the method of Wald and Brown[27]. In two such experiments, no 11-*cis* vitamin A was detected.

There is considerable evidence, however, that in some animals the pigment epithelium does isomerize vitamin A[18,23,28], and it seems reasonable that vitamin A while in the pigment epithelium of the rat might undergo isomerization. Recently, Hubbard and Colman have shown that the amount of 11-*cis* vitamin A in the eye of the frog remains relatively low during the course of dark adaptation. Then, when the retina has ceased to remove it to form rhodopsin, the amount of 11-*cis* vitamin A in the eye increases 2–3 fold[18]. It seemed, therefore, that my failure to detect 11-*cis* vitamin A might be due to insufficient time for detectable quantities of 11-*cis* vitamin A to accumulate. I have tested this thesis in preliminary experiments by incubating the backs of light-adapted rat eyes in phosphate buffer for periods up to 4 hr., but have not as yet been successful in demonstrating the production of 11-*cis* vitamin A.

In summary, most of the vitamin A formed from retinene during light adaptation rapidly moves into the pigment epithelium. After 60 min. of light adaptation, 75–80 per cent of the total ocular vitamin A is found in the pigment epithelium, mainly as vitamin A ester. During dark adaptation, the vitamin A returns from the pigment epithelium to the retina as rhodopsin is regenerated. In the fully dark-adapted state, the pigment epithelium contains no detectable amount of vitamin A.

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I should like to thank Prof. George Wald for many helpful discussions and suggestions.

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EFFECT OF POLYVINYL ALCOHOL ON CHLOROPHYLL AND HÆM IN *CHLORELLA* AND *TENDIPES*

The Level of Chlorophyll in *Chlorella pyridinosa*

IN experiments on *Pisum sativum* L., it was found that polyvinyl alcohol when applied to soil increased the chlorophyll content of the green parts of the plants (ref. 1, and unpublished work by H.F.N. and L.R.). In order to determine what additional factors contribute to this increase we decided to study the alga *Chlorella pyridinosa* which had been bred directly in an aqueous solution of polyvinyl alcohol. Polyvinyl alcohol produced in Poland (known as 'Salvar', 'Polyviol', 'Alvyl', and by other names) was used for these experiments. It was intended to carry out the experiments in aqueous cultures with Pruess medium, on which a rapid growth of *Chlorella* has been observed[2]. However, preliminary experiments showed that one of the elements of that medium, casein, led to errors in measurement. In view of this, cultures from ponds in Białystok were set up in aquaria of 500-ml. capacity. In order to avoid contamination and to remove zooplankton organisms, the culture was filtered by means of a triply folded gauze, after which 400 ml. of the filtrate from the *Chlorella* culture were poured into each aquarium.

The polyvinyl alcohol was prepared as a 10 per cent aqueous solution and different quantities added to the different cultures to give various concentrations of polyvinyl alcohol in them. Concentrations which gave an increase in chlorophyll content were used; they were: 0·00001, 0·0001, 0·001, 0·01, 0·1, 0·5, and 1 per cent. Two aquaria with cultures but no polyvinyl alcohol were used as controls. The experiment lasted 14 days. As early as the tenth day of the experiment, a difference in the intensity of the green colour could be detected with the naked eye. On the fourteenth day of the experiment, 50-ml. specimens were taken from each aquarium and filtered through No. 5 gauzes. The filtered specimens were then dried for three days in a dark room at a temperature of +18° C. Chlorophyll was extracted with ethanol and the content

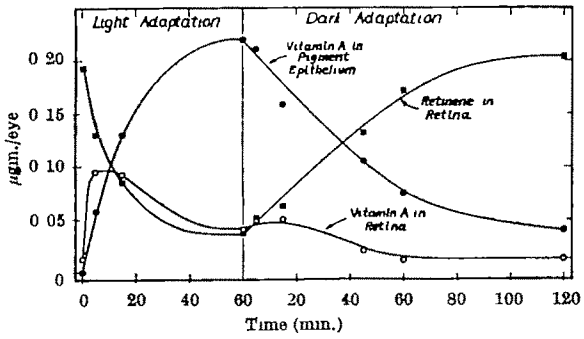

Fig. 4. Distribution of retinene and vitamin A in the eye during light- and dark-adaptation. During light adaptation, the retinene content of the eye falls, as the retinene, liberated on bleaching of rhodopsin, is reduced to vitamin A. Vitamin A in the retina rises for a time, and then declines, while the bulk of the vitamin A moves into the pigment layers. During dark adaptation, these processes are reversed. The retinene content of the eye increases, as rhodopsin is re-formed, and reciprocally the vitamin A in the pigment layers and retina declines. Dark adaptation is completed in about 100–120 min.

dark adaptation, the animals were placed in a small darkroom. At selected times during light- or dark-adaptation, the animals were anæsthetized with nembutal (15 mgm.), their eyes enucleated, and the retinas and pigment layers dissected apart, and placed separately in small mortars. (Throughout this article I shall refer to the back of the eye (pigment epithelium, choroid and sclera) as the pigment layers, even though there is no pigment in these tissues in the albino rat.) For each measurement, three animals (six eyes) were used.

The tissues were dried by grinding with a small amount of sodium sulphate, and the resulting powder transferred to a test-tube and extracted by vigorous stirring in 3 ml. of chloroform. After centrifugation, the clear chloroform extract (2·2–2·4 ml.) was drawn off, evaporated to dryness, and 0·3 ml. of fresh chloroform added. The amount of vitamin A and retinene in the extracts was determined by the Carr–Price reaction. For this, 0·25 ml. of the chloroform extract was mixed with 0·5 ml. of saturated antimony trichloride solution and the absorption spectrum from 700 to 500 mμ run immediately in the Cary recording spectrophotometer. Retinene absorbs maximally at 664 mμ, and vitamin A absorbs maximally at 620 mμ. When mixed, the amounts of vitamin A and retinene can be calculated by means of simultaneous equations[21].

Fig. 4 shows the results. It is convenient to express these in terms of the total potential vitamin A content of the eye; that is, vitamin A plus retinene, free and bound.

In completely dark-adapted animals, about 95 per cent of this potential vitamin A is bound as retinene in rhodopsin. About 5 per cent is stored as vitamin A in the retina. No vitamin A is found in the pigment layers.

On exposure to bright light, rhodopsin is bleached, liberating retinene. The retinene content of the retina, however, rapidly falls, as the released retinene is reduced to vitamin A. Reciprocally, the retinal vitamin A increases, and almost immediately vitamin A appears in the pigment layers.

With further time in the light the retinene content of the retina continues to fall, and after 30 min. reaches a level 10–15 per cent of the total potential vitamin A content of the eye. The retinal vitamin A, on the other hand, increases during the first 10 min. of light adaptation to a maximal level representing about 30 per cent of the total, and then gradually declines. After 45–60 min., it forms plateaux at a level of 10–12 per cent of the total.

The vitamin A in the pigment layers increases throughout the period of light adaptation. After 60 min., 75–80 per cent of the ocular vitamin A is found here. Retinene is never found in the pigment layers; the reduction of retinene to vitamin A takes place solely in the retina, and it is only vitamin A that migrates from the retina into the pigment layers.

It appears from Fig. 4 that there is more vitamin A present in the pigment epithelium after 1 hr. of light adaptation than there is total vitamin A (including retinene) in the eye to begin with. This is probably not the case; this artefact seems caused by my method of extraction, which removes vitamin A more efficiently than retinene. With equal amounts of vitamin A and retinene in a tissue, I extract only about 85 per cent as much retinene as vitamin A. This discrepancy could readily be corrected in the figure, but the raw data as they stand seem explicit enough.

During dark adaptation, these processes are reversed. The retina recaptures vitamin A by binding it as retinene in rhodopsin. The increase in retinene concentration during dark adaptation closely parallels the measured increase of rhodopsin concentration (compare Figs. 2 and 4).

With this increase of retinene, there is a reciprocal fall of vitamin A concentration in the pigment layers. The retinal vitamin A, on the other hand, stays relatively constant during the early stages of dark adaptation, and then gradually declines to its dark-adapted level of 4–5 per cent of the total vitamin A.

Dark adaptation is completed in about 100–120 min. I find at this time, however, a small amount of vitamin A in the pigment layers, which gradually disappears over the next few hours. During this time there is no increase of retinene or retinal vitamin A, so presumably this bit of vitamin A diffuses away into the blood stream. The origin and significance of this superfluous vitamin A is obscure.

Vitamin A in both the eye and body may exist in two forms: it circulates in the plasma as the free alcohol, but it is stored in the tissues primarily as the ester. It has been suggested that the vitamin A alcohol of the tissues is in equilibrium with that of the blood, and that through esterification a tissue can concentrate vitamin A independently of this equilibrium[22]. Krinsky has demonstrated the esterification of vitamin A in the eye tissues of cattle, and has found that much of the vitamin A, both in the retina and in the pigment epithelium, is esterified[23].

It is of interest to inquire as to the state of vitamin A in the pigment layers of the rat after 60 min. of light adaptation. For this, six animals were light adapted for 1 hr., their eyes enucleated, dissected, and the pigment layers extracted for vitamin A, as described above. The ester and alcohol fractions were separated on a column of alumina 'weakened' with 5 per cent water. Esterified vitamin A is eluted from such a column with 4 per cent acetone in petroleum ether, while free vitamin A is eluted with 20 per cent acetone in petroleum ether[24]. The fractions were assayed for vitamin A by the Carr–Price reaction. In two experiments, it was found that 92 per cent of the vitamin A in the pigment epithelium after 60 min. of light adaptation was esterified. Krinsky found that in cattle 87 per cent of the vitamin A in the pigment epithelium was esterified[23].

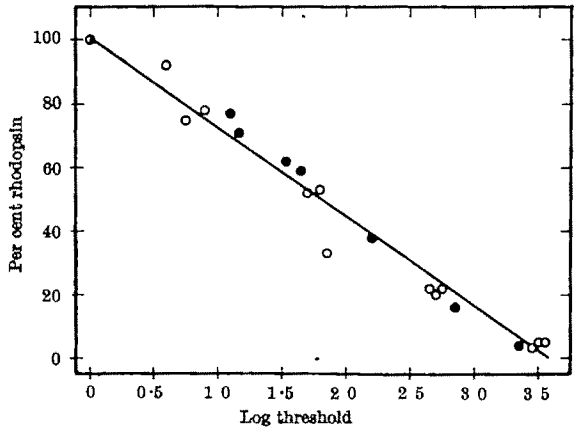

Fig. 3. The relation between rhodopsin content of the retina and the visual threshold in animals dark-adapted after exposure to bright light, and in animals night-blind due to vitamin A deficiency. In both instances, the same relationship is observed: the log threshold rises linearly with fall in rhodopsin concentration ●, Night blindness; ○, dark adaptation

animals, and I_t and R_t are, respectively, the threshold and rhodopsin concentration in vitamin A-deficient or partly dark-adapted animals.

This result is not wholly unexpected. Wald has pointed out the striking qualitative similarity between the synthesis of chicken iodopsin and rhodopsin in solution, and the course of human cone and rod dark adaptation[7]. This comparison is valid only provided that one compares the logarithm of the visual threshold with the concentration of visual pigment. Wald has also offered a theory which may explain such a relation[8].

Recently, Rushton *et al.* have made direct measurements of the rise and fall of human visual pigments in the living human eye during light and dark adaptation[9,10], and these measurements show a striking parallelism between the course of human light and dark adaptation, and the course of bleaching and re-synthesis of the visual pigments. Again, this relationship is evident only when the logarithm of the visual threshold is compared with the concentration of visual pigment[11].

Very recently, Rushton has compared the regeneration of rhodopsin and the course of dark adaptation under the same conditions in a colour-blind subject, and has also found that the logarithm of the threshold falls in parallel with the increase of rhodopsin content in the eye[12].

There have been several previous attempts to correlate the electroretinogram with visual pigment concentration[13–15], all of which have attempted to correlate the increase of visual pigment concentration with the increase in size of the *b*-wave potential elicited with a constant test-flash. As Riggs has pointed out, no simple proportionality exists between magnitude of electroretinogram response and the logarithm of stimulus intensity in the vertebrate eye[2]. Furthermore, the shape of curve obtained by plotting magnitude of response against time in the dark for intensity of a single flash may vary with the luminance of the test-flash selected[16]. As can be seen from Fig. 1, if the test light is too dim, one does not begin to record an electroretinogram until considerable quantities of rhodopsin have accumulated in the retina. This may explain why Granit, Munsterhjelm and Zewi failed to record an electroretinogram in the cat until 40 per cent of the visual pigment had been regenerated[14]. In the rat, as we have seen (Fig. 1), one can record an electroretinogram at any concentration of rhodopsin provided that the test stimulus is bright enough.

On the other hand, if the test stimulus were very bright, large fluctuations in rhodopsin might occur with little effect on the size of the electroretinogram potential. A preferable procedure on all counts is to evaluate the sensitivity of the eye by measuring the light intensities required to evoke a constant potential, perhaps most simply as here the just perceptible electroretinogram.

In summary, following 30 min. of intense light adaptation, the rhodopsin concentration of the eye of the rat is lowered to less than 5 per cent of the dark-adapted level, and the electroretinogram threshold has risen about 3·50 log units (about 3,000 times). With time in the dark, the logarithm of the electroretinogram threshold falls in strict parallelism with the rise of rhodopsin concentration. Both log threshold and rhodopsin content of the eye return to the dark-adapted level in about 100 min.

Distribution of Retinene and Vitamin A in the Eye during Light and Dark Adaptation

On exposure to light, rhodopsin bleaches to a mixture of retinene (vitamin A aldehyde) and the protein, opsin. The retinene may then recombine with opsin, forming rhodopsin again, or it may be reduced to vitamin A. After an intense and prolonged light adaptation, almost all the retinene in the eye is transformed to vitamin A[17].

Several years ago, Wald observed in frogs that the bulk of the vitamin A formed after light adaptation disappears from the retina[17]. More recently it has been shown that the total amount of retinene and vitamin A in the frog's eye does not vary during light and dark adaptation[18]; thus it seemed probable that exchanges of vitamin A occur between the visual cells and the pigmented layers (pigment epithelium and choroid) that lie in contact with them. Probably most, if not all, of these exchanges involve the pigment epithelium, the long processes of which envelop the outer segments of the visual cells. In many animals the pigment epithelium also contains considerable stores of vitamin A, even in the dark-adapted state[17].

Histological evidence for the exchange of vitamin A between retina and pigment epithelium has been obtained by Jancsó and Jancsó[19] and Greenberg and Popper[20], who observed typical vitamin A fluorescence in the pigment epithelium of the rat after light adaptation, which disappeared on dark adaptation. In agreement with the latter observations, I have found that the pigment epithelium of the albino rat contains no detectable stores of vitamin A in the dark-adapted state.

The distribution of retinene and vitamin A during light and dark adaptation has not hitherto been studied quantitatively. The albino rat seemed ideally suited for this purpose, both because in this animal the pigment epithelium contains no vitamin A when dark adapted, and because (unlike the frog) the retina readily separates from the back of the eye in either the light- or dark-adapted condition.

For these experiments, groups of animals (weighing 150–200 gm.) were dark adapted overnight, and then brightly light adapted in a white porcelain pan illuminated with three 100-watt flood lamps. For

The experiments were performed in the following way. Groups of animals were light-adapted for 30 min. in a white porcelain pan, brightly illuminated with three 100-watt flood lamps. At selected times after the lights were turned out, an animal was selected at random and the electroretinogram threshold recorded. Each measurement was made with a fresh animal, anæsthetized with nembutal (10–15 mgm.) 5–10 min. beforehand. To prepare for the first measurement (at 3 min), anæsthetic was given to one animal a few minutes before the end of light adaptation. After an animal was anæsthetized, it could be prepared for the experiment and its threshold determined in about 3 min. Then the electroretinogram was recorded over a luminance-range of 5 log units.

The stimulus was a 1/50 sec. flash of white light, the luminance of which could be varied continuously with circular photographic wedges. The electroretinogram was recorded from the cornea with cotton wick electrodes connected with a Grass *P*-6 amplifier and Dumont oscilloscope fitted with a camera attachment. Capacity-coupled amplification was used to yield a more stable base line.

To measure rhodopsin, the same or other groups of animals were light-adapted as before on the following day. At appropriate times, an animal was anæsthetized, its eyes removed, and the retinas dissected free and dropped into cold 4 per cent alum solution. The retinas were collected pair by pair in this manner throughout the entire experiment. Each pair of retinas was finally washed twice with water, once again in neutral phosphate buffer, and the rhodopsin was extracted overnight with 0·2 ml. of 2 per cent digitonin. The next day, the extract was centrifuged clear, 0·01 ml. of 1 *M* hydroxylamine was added, and the absorption spectrum was run in a Cary recording spectrophotometer. The solution was bleached with white light for 5 min., and the absorption spectrum re-run. The difference in extinction at 500 mμ before and after bleaching indicated the concentration of rhodopsin. Measurements of rhodopsin in rats during dark adaptation have previously been made by Tansley[5] and Lewis[6]. In all, six complete experiments were performed measuring electroretinogram thresholds, and three complete experiments measuring rhodopsin concentration.

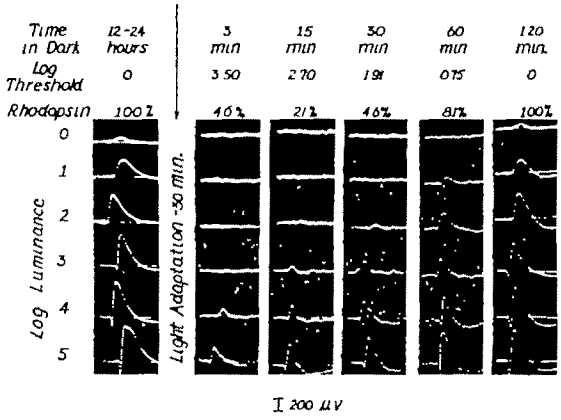

Fig. 1. Electroretinogram responses during dark adaptation in the rat. The top three lines show the time in the dark; the logarithm of the electroretinogram threshold, the lowest luminance necessary to evoke a perceptible electroretinogram; and the rhodopsin content expressed as percentage of the dark-adapted level. The electroretinograms are evoked with 1/50 sec. flashes of white light over a luminance range of 5 log units. The first row of electroretinograms shows the responses of a control animal, dark-adapted overnight. After light adaptation, the electroretinogram threshold is raised about 3·5 log units, and the responses at high luminances are diminished in size. With time in the dark, the threshold returns to normal, and the responses at higher luminances assume the dark-adapted form

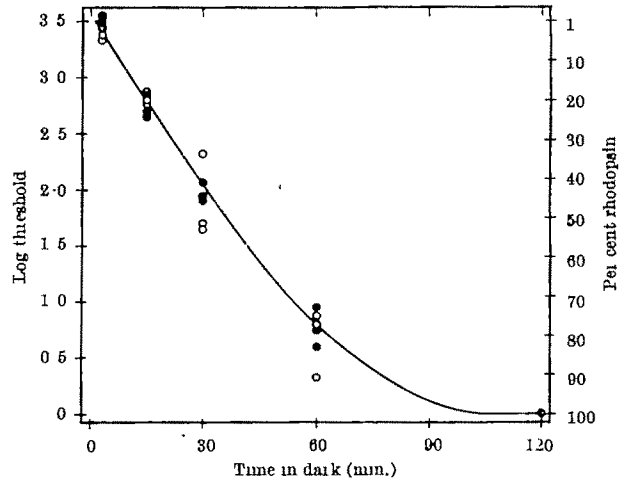

Fig. 2. Dark adaptation in the rat. Following light adaptation, the fall of the logarithm of the electroretinogram threshold parallels the rise in concentration of rhodopsin. Both the threshold and rhodopsin concentration are back to the dark-adapted level in about 100 min. ●, log threshold, ○, rhodopsin

Fig. 1 shows the electroretinogram responses recorded in such an experiment over a range of luminances of 5 log units. At the top of Fig. 1 the time in the dark following light adaptation is shown, and on the next line the logarithm of the electroretinogram threshold, the lowest luminance of light which evoked a perceptible electroretinogram. The normal threshold is set arbitrarily at 1, so that log threshold is 0. The third line shows the rhodopsin content, expressed as percentage of the completely dark adapted level.

The first row of electroretinograms shows the responses of a control animal which had been dark adapted overnight. After 30 min. of light adaptation, the threshold recorded after 3 min. in the dark was raised 3·50 log units (about 3,000 times). The rhodopsin concentration was reduced to 4–5 per cent of the dark-adapted level. With time in the dark, the sensitivity of the eye returned gradually to the dark-adapted state, in parallel with the rhodopsin concentration. Dark adaptation was completed in about 100 min.

Fig. 2 compares the rise in rhodopsin concentration and fall of electroretinogram threshold during dark adaptation. It is seen that the log threshold falls in strict parallelism with the rise in rhodopsin concentration.

Fig. 3 compares the relationship between rhodopsin concentration and log threshold both during dark adaptation and night blindness owing to vitamin A deficiency. It is clear that the logarithm of the electroretinogram threshold, even under these different conditions, rises and falls linearly with the concentration of rhodopsin. This relationship is expressed by the equation:

$$\log I_t/I_0 = 3{\cdot}6\ (R_0 - R_t)/R_0$$

in which I_0 and R_0 are, respectively, the threshold and rhodopsin concentration in dark-adapted control

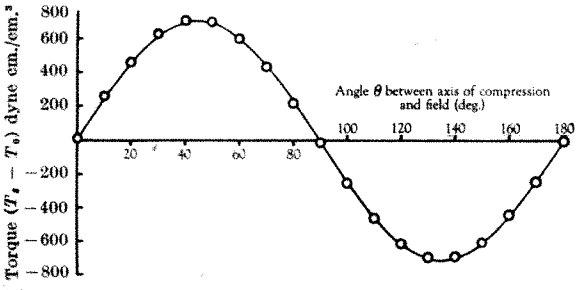

Fig. 1. Torque curve due to a directed stress of 520 kgm./cm.² on a sample of basalt, suspended in a field of 10·6 kilo-oersteds. Circles are experimental points, line is sin 2θ curve

that the application of stress had not produced any permanent anisotropy. Curves of the difference $(T_s(\theta) - T_0(\theta))$ were plotted, showing the expected sin 2θ form (2), as in the example in Fig. 1. The values of λ_s determined from $(T_s - T_0)$ using equation (2) are given in column 3 of Table 1.

Table 1. SATURATION MAGNETOSTRICTIONS OF FIVE ROCK SAMPLES

Rock	$(T_s - T_0)$ dyne cm./cm.³	(λ_s) exp.	I_s e.m.u./cm.³	(λ_s) calc.
Dolerite	150	$0{\cdot}20 \times 10^{-6}$	4·0	$0{\cdot}2_5 \times 10^{-6}$
	150	$0{\cdot}19 \times 10^{-6}$	4·0	$0{\cdot}2_5 \times 10^{-6}$
Basalt	710	$0{\cdot}91 \times 10^{-6}$	11·1	$0{\cdot}6 \times 10^{-6}$
	750	$0{\cdot}97 \times 10^{-6}$	11·3	$0{\cdot}6 \times 10^{-6}$
Monchiquite	630	$0{\cdot}81 \times 10^{-6}$	9·2	$0{\cdot}5 \times 10^{-6}$

The saturation magnetic moments I_s of the rocks were also measured and are given in column 4 of the table. These values were used to make crude estimates of the expected magnetostrictions $(\lambda_s)_{\text{calc.}}$ (column 5) by assuming that magnetostriction is proportional to I_s:

$$\lambda_s = \lambda_{sm}(I_s/I_{sm}) \qquad (3)$$

where λ_{sm} and I_{sm} are values of λ_s and I_s for pure magnetite and are taken as $\lambda_{sm} = 25 \times 10^{-6}$, $I_{sm} = 480$ e.m.u./cm.³. It is reasonable to expect that (3) would be correct for a rock in which the only strongly magnetic mineral is nearly pure magnetite. This is the case with the dolerite specimens, in which 2·0 per cent by volume of the rock is magnetic mineral, approximately half being magnetite with $I_s \sim 400$ e.m.u./cm.³ and half ilmenite, which can be neglected for this purpose. The magnetic minerals in the basalts from Kiama are impure cubic magnetites (L. G. Parry, private communication) for which values of λ_s are not known. However, for the three rock types examined here magnetostriction has the sign and approximate magnitude expected for magnetite-bearing rocks and it is reasonable to take as general the rule that the magnetostriction of a rock may be simply calculated as a weighted sum of the magnetostrictions of its constituent magnetic minerals.

In view of this result, the experiments reported by Stott and Stacey[3,4] show that when an intrinsically isotropic rock is subjected to stress while cooling in a field it acquires thermo-remanent magnetization in a direction deflected away from the field by such an angle that it returns precisely to the field direction when unloaded.

The determination of saturation magnetostrictions of slightly magnetic materials by the method described above could certainly be used, without modification, down to $\lambda_s = 10^{-6}$ and appears to be capable of even further development.

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GEOLOGY

Charnockite in the Making

EXTENSIVE quarrying is being done on the hill slopes west of Kabbal (12° 30′ N., 77° 18′ E., situated about 40 miles south-south-west of Bangalore), and so fresh surfaces were available for examination. Peninsular gneiss is the prevailing rock of this region. It is thinly foliated and often highly contorted. The gneiss is generally biotitic; but there are hornblendic layers and streaks.

In the middle of the light-coloured banded exposures of gneiss there are small irregular or elongated patches of coarse-grained, greasy, brownish-green rock (Fig. 1). The disposition of these patches bears no relation to the foliation direction of the gneiss, and often runs athwart it. Though the fabric has been affected because of coarser crystallization, it is remarkable that in many of these patches the banding of the gneiss can still be recognized to be passing through them. Crystals of hypersthene exhibiting schiller lustre have been developed in these coarse patches.

From the geological map of Mysore State, it can be seen that the main mass of charnockite occurring in the Biligirirangan Hills and eastwards branches into narrow finger-like projections in the Halagur–Satnur region north of the River Cauvery, an area which was formerly mapped as Closepet granite but which is now known to be composed mainly of Peninsular gneiss. Farther northwards, the charnockites are found in patches of varying sizes, and even these isolated occurrences completely disappear near about lat. 12° 30′ N. Kabbal is situated on one such fringe of the huge charnockite massif which includes the Biligirirangan Hills and the Nilgiri Mountains.

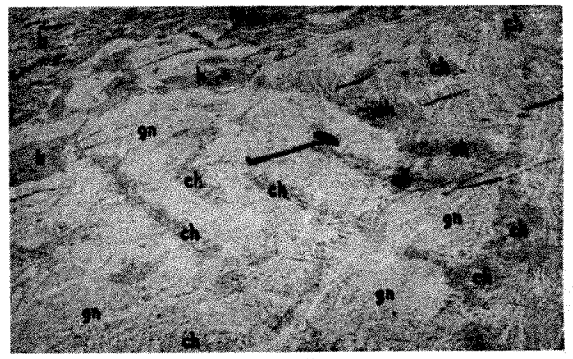

Fig. 1. Photograph of a quarry face showing charnockite patches (*ch*) in Peninsular gneiss (*gn*). The dark areas in the top left hand of the picture are composed of hornblendic inclusions (*h*) of varying sizes

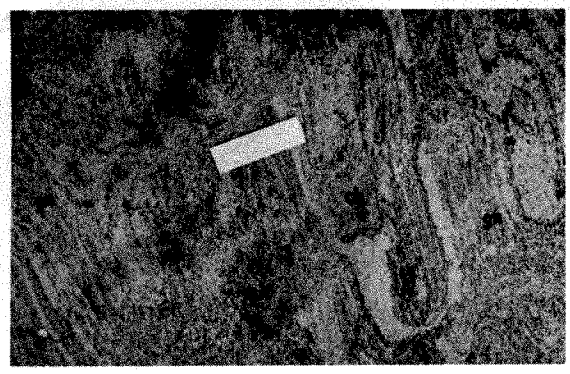

Fig. 2. A close-up photograph showing parts of contorted Peninsular gneiss (*gn*) becoming converted into charnockite (*ch*). The coarse crystallization has resulted in the partial obliteration of the foliation of the gneiss. The protractor-scale is 6 in. long

Figs. 1 and 2 clearly show that portions of the gneisses are becoming converted into charnockites. When recrystallization has advanced, the gneissic foliation is destroyed ; but in the intermediate stages the banding can be traced through the patches getting charnockitized (Fig. 2). In Kabbal, we are apparently on the rim of a charnockitization front where it is possible to have visual demonstration of the successive stages in the transformation of a gneiss to a coarse-grained rock.

The changes can also be followed in thin sections of these rocks. Flakes of biotite in parallel alignment characterize the gneiss. The basic patches are composed mainly of green amphiboles with occasional biotites. When subjected to transformation, a light-green diopside develops from the hornblendes. In the charnockitic patches, coarse hypersthenes with the characteristic pink to green pleochroism have been formed. The amphiboles are brownish-green in colour, and the biotites when present are foxy-red.

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CRYSTALLOGRAPHY

Super-Cell Structure of Semiconductors

THE structures of many compounds and alloys have been shown to be essentially super-lattices on a few basic lattices. Interest in the diamond structure in particular has been stimulated recently by the technological importance of semiconductors. The best known semiconductors—germanium and silicon—have the diamond structure and many semiconducting compounds of interest have the closely related structures of zinc blende and chalcopyrite. Some work[1] has been done recently in an attempt to list the possible super-lattices of the cubic lattices, but the diamond structure has not yet been considered. The aim of this communication is to introduce a new line of attack on this problem of super-lattices.

The diamond structure consists of two interpenetrant face-centred cubic sub-lattices symmetrically spaced. The zinc blende lattice can be thought of as a super-lattice of the diamond structure in which each of these sub-lattices is occupied by a different atomic species. If the distribution of atoms in zinc blende could be randomized the structure would become a 'defect' diamond structure. (For a discussion of the term 'defect' see ref. 2.) Any adamantine material may in like manner be described as a super-lattice on the diamond structure and its unit cell will be related to the unit cell of diamond. Similar families of compounds can be found based on other basic lattices. I propose to call possible unit cells of super-lattices based on a given lattice 'super-cells' of that lattice, and to illustrate the concept here with reference to the adamantine super-cells. In practice the formation of a super-lattice often leads to a distortion of the original lattice. Since, however, this is often slight I shall neglect it in this treatment and assume that pseudo-cubic symmetry is accurately maintained when a super-lattice is formed. Thus I shall assume in discussing the adamantine super-cells that the atomic sites available are exactly those of a diamond structure.

Table 1 lists the simpler adamantine super-cells. The nomenclature chosen (*C* (cubic), *T* (tetragonal) and *O* (orthorhombic)) denotes the external symmetry of the super-cell in question—which is also the highest symmetry class possible for a substance with this as its unit cell. Super-cells within each of these main groups are numbered in order of increasing size. For simplicity certain less-symmetrical super-cells will not be discussed.

At first sight it might be thought that all super-cells would be built up of simple unit cells and thus that the super-cell dimensions would be simple multiples of the *C*1 cell. This is not so, because the conventional unit cell of diamond is not primitive. Thus the *T*1 super-cell may be derived from the normal unit cell (here called the *C*1 cell) by the standard transformation of face-centred tetragonal to body-centred tetragonal. This cell is still not

Table 1. SIMPLER ADAMANTINE SUPER-CELLS

Crystal glass	Cell label	Dimensions	No. of sites	Cell label	Dimensions	No. of sites
Cubic	*C*1	1 1 1	8	*C*4	4 4 4	512
	*C*2	2 2 2	64	*C*5	5 5 5	1,000
	*C*3	3 3 3	216	*C*6	6 6 6	1,728
Tetragonal	*T*1	$1/\sqrt{2}$ $1/\sqrt{2}$ 1	4	*T*19	$1/\sqrt{2}$ $1/\sqrt{2}$ 11	44
	*T*2	$1/\sqrt{2}$ $1/\sqrt{2}$ 2	8	*T*20	$1/\sqrt{2}$ $1/\sqrt{2}$ 12	48
	*T*3	$1/\sqrt{2}$ $1/\sqrt{2}$ 3	12	*T*21	1 1 6	48
	*T*4	$1/\sqrt{2}$ $1/\sqrt{2}$ 4	16	*T*22	$\sqrt{2}$ $\sqrt{2}$ 3	48
	*T*5	1 1 2	16	*T*23	$1/\sqrt{2}$ $1/\sqrt{2}$ 13	52
	*T*6	$\sqrt{2}$ $\sqrt{2}$ 1	16	*T*24	$1/\sqrt{2}$ $1/\sqrt{2}$ 14	56
	*T*7	$1/\sqrt{2}$ $1/\sqrt{2}$ 5	20	*T*25	1 1 7	56
	*T*8	$1/\sqrt{2}$ $1/\sqrt{2}$ 6	24	*T*26	$1/\sqrt{2}$ $1/\sqrt{2}$ 15	60
	*T*9	1 1 3	24	*T*27	$1/\sqrt{2}$ $1/\sqrt{2}$ 16	64
	*T*10	$1/\sqrt{2}$ $1/\sqrt{2}$ 7	28	*T*28	1 1 8	64
	*T*11	$1/\sqrt{2}$ $1/\sqrt{2}$ 8	32	*T*29	$\sqrt{2}$ $\sqrt{2}$ 4	64
	*T*12	1 1 4	32	*T*30	$2\sqrt{2}$ $2\sqrt{2}$ 1	64
	*T*13	$\sqrt{2}$ $\sqrt{2}$ 2	32	*T*31	$1/\sqrt{2}$ $1/\sqrt{2}$ 17	68
	*T*14	2 2 1	32	*T*32	$1/\sqrt{2}$ $1/\sqrt{2}$ 18	72
	*T*15	$1/\sqrt{2}$ $1/\sqrt{2}$ 9	36	*T*33	1 1 9	72
	*T*16	$3/\sqrt{2}$ $3/\sqrt{2}$ 1	36	*T*34	$3/\sqrt{2}$ $3/\sqrt{2}$ 2	72
	*T*17	$1/\sqrt{2}$ $1/\sqrt{2}$ 10	40	*T*35	3 3 1	72
	*T*18	1 1 5	40			
Orthorhombic	*O*1	$1/\sqrt{2}$ $\sqrt{2}$ 1	8	*O*16	$1/\sqrt{2}$ $9/\sqrt{2}$ 1	36
	*O*2	$1/\sqrt{2}$ $3/\sqrt{2}$ 1	12	*O*17	$1/\sqrt{2}$ $\sqrt{2}$ 5	40
	*O*3	$1/\sqrt{2}$ $\sqrt{2}$ 2	16	*O*18	$1/\sqrt{2}$ $5/\sqrt{2}$ 2	40
	*O*4	$1/\sqrt{2}$ $2\sqrt{2}$ 1	16	*O*19	$1/\sqrt{2}$ $5\sqrt{2}$ 1	40
	*O*5	$1/\sqrt{2}$ $5/\sqrt{2}$ 1	20	*O*20	$\sqrt{2}$ $5/\sqrt{2}$ 1	40
	*O*6	$1/\sqrt{2}$ $\sqrt{2}$ 3	24	*O*21	$1/\sqrt{2}$ $11/\sqrt{2}$ 1	44
	*O*7	$1/\sqrt{2}$ $3/\sqrt{2}$ 2	24	*O*22	$1/\sqrt{2}$ $\sqrt{2}$ 6	48
	*O*8	$1/\sqrt{2}$ $3\sqrt{2}$ 1	24	*O*23	$1/\sqrt{2}$ $3/\sqrt{2}$ 4	48
	*O*9	$\sqrt{2}$ $3/\sqrt{2}$ 1	24	*O*24	$1/\sqrt{2}$ $2\sqrt{2}$ 3	48
	*O*10	$1/\sqrt{2}$ $7/\sqrt{2}$ 1	28	*O*25	$1/\sqrt{2}$ $3\sqrt{2}$ 2	48
	*O*11	$1/\sqrt{2}$ $\sqrt{2}$ 4	32	*O*26	$1/\sqrt{2}$ $6\sqrt{2}$ 1	48
	*O*12	$1/\sqrt{2}$ $2\sqrt{2}$ 2	32	*O*27	1 2 3	48
	*O*13	$1/\sqrt{2}$ $4\sqrt{2}$ 1	32	*O*28	$\sqrt{2}$ $3/\sqrt{2}$ 2	48
	*O*14	$\sqrt{2}$ $2\sqrt{2}$ 1	32	*O*29	$\sqrt{2}$ $3\sqrt{2}$ 1	48
	*O*15	$1/\sqrt{2}$ $3/\sqrt{2}$ 3	36	*O*30	$3/\sqrt{2}$ $2\sqrt{2}$ 1	48

The super-cell dimensions are given in units of the simple unit cell parameter '*a*'.

Table 2. SOME TYPICAL ADAMANTINE COMPOUNDS LISTED BY SUPER-CELLS

Super-cell	Adamantine compound
$C1$	C (diamond), Si, Ge, Sn (grey) ZnS (blende) and more than 30 analogues including the III–V, II–VI, and certain I–VII compounds $CdIn_2\square Se_4$ and $Cu_2Hg\square I_4$
$C2$	Cu_3SbS_3 (tetrahedrite), Cu_3SbS_4 and related compounds
$T5$	$CuFeS_2$ (chalcopyrite) and its analogues $Cu_2 Fe SnS_4$ (stannite) Many II $III_2\square VI_4$ compounds
$T16$	Holmes structure for In_4Te_3 (not strictly adamantine) (see ref. 7)
$O2$	Woolley and Pamplin's structure for $In_2\square Te_3$
$O3$	$Ga_2\square Hg_5Te_8$ and $In_2\square Hg_5Te_4$ (possibly)

$\square$ is the symbol for a vacant lattice site.

primitive—the primitive cell of diamond is in fact a rhombohedral one and so not listed in Table 1.

Table 2 shows some typical adamantine materials listed by means of their super-cells. A fuller discussion of the inter-relationship of the adamantine compounds can be found in ref. 3.

A general formula for an adamantine compound can be written thus :

$$A_aB_bC_c \ldots X_xY_yZ_z \ldots$$

where $a,b,c, \ldots x,y,z, \ldots$ are the relative numbers of $A,B,C, \ldots X,Y,Z, \ldots$ atoms in the compound. The elements $A,B,C, \ldots$ come from any of the first four B sub-groups of the periodic table, while $X,Y,Z, \ldots$ come from the remaining B sub-groups (omitting, of course, the rare gases). The formula is valid as a candidate for the diamond structure provided that there are on average four valence electrons per site. This requires that :

$$\frac{\Sigma_i n_i v_i}{\Sigma_i n_i} = 4$$

where n_i is the number of atoms of the ith kind, with v_i electrons in its outer shell. Vacant sites must be counted, and for these v_i is zero. This provides a necessary, but not sufficient, condition for the existence of an adamantine material. It is readily seen that the Mooser and Pearson rule[4] is satisfied, and so all adamantine materials will be expected to be semiconductors.

I have calculated[3] the various classes of intensity of X-ray reflexions which are to be expected from a $C1$ and a $C2$ super-cell in which all the atomic sites are assumed different. The results can readily be applied in the analysis of any new super-lattice which may be described on either of these unit cells. The $C2$ super-cell is especially interesting because it includes the smaller super-cells $C1$, $T1$, $T2$, $T5$, $T6$, $T13$, $T14$, $O1$ and $O3$, and thus embraces most of the common adamantine compounds.

The study of solid solutions between compounds of the zinc blende type has already yielded several new examples of super-lattices. Super-cells may be used to predict compositions at which ordering may occur. Ordering will be possible on a given super-cell only if the number of sites available in that super-cell is correlated with the composition of the alloy. Consider, for example, alloys of two zinc blende compounds MX and NY. A general alloy may be written :

$$M_xN_{1-x}X_xY_{1-x}$$

Ordering on a $C1$ cell is possible for $x = \frac{1}{4}$, $\frac{1}{2}$ or $\frac{3}{4}$. Ordering on a $T3$ or $O2$ cell is possible for $x = \frac{1}{6}$, $\frac{1}{3}$, $\frac{1}{2}$, $\frac{2}{3}$ or $\frac{5}{6}$. Also on a $T4$, $T5$, $T6$, $O3$ or $O4$ cell for $x = \frac{1}{8}$, $\frac{1}{4}$, $\frac{3}{8}$, $\frac{1}{2}$, $\frac{5}{8}$, $\frac{3}{4}$ or $\frac{7}{8}$. Thus the most likely compositions for ordering are $x = \frac{1}{2}$, $\frac{1}{4}$ or $\frac{3}{4}$, while $x = \frac{1}{5}$ (requiring, for example, a $T7$ or $O5$ super-cell) is much less likely to be an ordering composition. If ordering is suspected at a particular composition then a consideration of the possible super-cells enables one to predict the pattern of super-lattice lines which will occur. For example, if $x = \frac{1}{3}$ is thought to be an ordered phase, then the super-lattice powder lines should be indexed at first on a threefold cubic cell ($C3$). From the absences which occur it should be possible to decide between $T3$ and $O2$.

Another use of super-cells is in the examination of alternative structures. Chalcopyrite, $CuFeS_2$, was originally assigned a tetragonal structure based on a distorted $C1$ cell[5]. Fifteen years later Pauling and Brockway[6] showed that the now generally accepted structure based on a $T5$ super-cell gave better agreement with the X-ray data. Many of the recently discovered ordered adamantine materials may perhaps need a similar revision. A systematic examination of the possible adamantine super-lattices is a desirable starting point for a critical survey of the known materials as well as for the prediction of new ones.

Super-cells should also prove useful in discussing the effects of ordering on the properties of a material, because changes in shape of the Brillouin zone due to ordering may be deduced from X-ray intensity calculations.

A fuller discussion including details of the X-ray intensity calculations will be published elsewhere in due course.

I wish to thank Dr. J. C. Woolley and Dr. S. Wallwork for helpful discussions.

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METALLURGY

Determination of Silver in Lead Concentrates by Atomic Absorption Spectroscopy

THE fire assay method is used universally for the determination of silver in ores and concentrator products. This method, which is capable of very high precision, is subject to a loss of silver during cupellation, and corrections for this loss, if made, must be on an empirical basis depending on the conditions of cupellation[1–3]. Walsh[4] showed that atomic absorption spectroscopy offered possibilities as an absolute spectrochemical method freed from the necessity of using chemically analysed standards or synthetic samples the composition of which approximated that of the unknown. Several papers[5–7] on the application of atomic absorption spectroscopy to

the determination of cations in solution have been published. These papers showed that, in general, the atomic absorption technique was free from inter-element effects and required the minimum amount of manipulation. Lockyer and Hames[8] directed attention to the possibility of determining the noble metals by atomic absorption spectroscopy and quoted a limit of detectability of 0·1 p.p.m. for silver.

We have studied the application of this technique to the determination of silver in the lead–silver–zinc ores and concentrator products at the Zinc Corporation Ltd., Broken Hill, Australia. Special emphasis has been placed on the determination of silver in lead sulphide concentrates containing approximately 550 p.p.m. (18·0 oz. per ton) silver.

The apparatus used was basically the same as that described by Box and Walsh[9]. Initially an EEL flame photometer burner giving a 2·5-cm. flame path was used. In order to obtain satisfactory absorption readings it was necessary to use silver concentrations of between 10 and 15 p.p.m. This meant that the silver content of 1 gm. of lead concentrate had to be taken into solution in a final volume of 50·0 ml.

Lead at the concentration of 20,000 p.p.m. was shown to have no effect on the absorption due to silver. It was therefore decided to try to eliminate completely all separations.

A number of unsuccessful attempts were made to devise a method based on complete solution of all components in the sample. Techniques which involved the formation of lead sulphate resulted in a loss of silver by adsorption.

The method finally selected was based on the solution of the lead concentrate in concentrated hydrochloric acid, measurement of atomic absorption being made in a 25 per cent v/v hydrochloric acid, 3 per cent v/v nitric acid solution. The standards used were solutions of pure silver in 25 per cent v/v hydrochloric acid run concurrently with each batch of test samples.

Trouble from two sources was experienced when working at these high acid concentrations and with solutions saturated with lead chloride. The stainless steel inlet capillary of the EEL atomizer corroded rapidly, and at the same time lead chloride was precipitated in it. Substitution of a glass inlet capillary eliminated the trouble due to corrosion. To eliminate the precipitation of lead salts in the capillary it was necessary to adjust the conditions so that the final analysis solution, while having a silver concentration of 10–15 p.p.m., was unsaturated with lead chloride.

Table 1 shows a comparison of the silver results obtained by the fire assay and atomic absorption methods on five samples of lead concentrate. Each atomic absorption run was made on a different day. The fire assay results are the average of four determinations and are uncorrected for silver lost during cupellation.

Table 1. THE SILVER CONTENT (OZ./TON) OF LEAD CONCENTRATES

Sample No.	Atomic absorption Run					Mean	Fire assay
	1 (*a*)	2 (*a*)	3 (*b*)	4 (*b*)	5 (*b*)		
1	18·25	18·23	17·98	17·90	17·90	18·05	17·35
2	16·59	16·73	16·58	16·45	16·55	16·58	16·25
3	17·08	17·03	16·98	16·55	16·70	16·87	16·60
4	17·68	17·84	17·69	17·50	18·05	17·75	17·30
5	17·62	17·62	17·49	16·90	17·60	17·45	16·70

a, Analyst *A*; *b*, analyst *B*.

The standard deviation of the atomic absorption results is 1·14 per cent relative. They indicate that atomic absorption spectroscopy offers a rapid and precise means of determining silver in lead concentrates, giving results approximately 0·5 oz. per ton higher than the uncorrected fire assay result at this level.

A more detailed account of this work will be submitted to the Institution of Mining and Metallurgy and the Australasian Institute of Mining and Metallurgy.

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Cathodic Cleaning of Metals before High-Temperature Oxidation

SINCE metallic oxidation is a surface phenomenon, the preparation of the surface prior to the oxidation experiment is very important. If the method of preparation produces a thin film of oxide or another compound on the surface, the subsequent oxidation may be affected. Thus, Vernon, Akeroyd and Stroud[1] found that the rate of oxidation of zinc below 225° C. was different for abraded, etched or electrolytically polished surfaces. For fundamental work, the ideal is to commence the oxidation with a film-free surface. This was done in the case of iron by Davies, Evans and Agar[2]. The iron was reduced in hydrogen at 480° C., and after this gas had been removed by evacuation, oxygen was introduced. However, it is not possible to carry out this procedure with all metals. Thus the oxide of tin cannot be reduced by hydrogen below the melting point of the metal. The oxidation of solid tin cannot therefore be carried out on an initially film-free surface.

When this is not possible, a method of preparation must be found which is relatively easy to carry out and which also gives reproducible results. One such method is that of cathodic cleaning, with sodium carbonate as an electrolyte, and this has been used in the case of tin. The advantages of the method are: (1) traces of grease are mechanically removed by the hydrogen produced; (2) any oxide film on the surface is reduced to the metallic state. When the specimen is then taken out of the solution, washed and dried, a new oxide film forms on the surface when it is exposed to air. It is reasonable to assume that, provided the specimens have been kept in a desiccator, the thickness of this film is the same each time. Hence the oxidation experiment can be carried out on a surface carrying a thin oxide film of constant thickness.

However, experiments on tin of 99·9999 per cent purity in this laboratory have shown that the mechanism is more complicated than formation in air of a simple film, and can give misleading results. The tin specimen, 5 cm. × 1·6 cm. × 0·01 in. thick, was made the cathode in a 0·1 *M* solution of sodium carbonate with a platinum gauze as anode. A current of 80 m.amp. was supplied from a 12-V. battery for a total time of 14 min. (7 min. each side of specimen facing the anode). The specimen was removed with the current still on, washed with water, then with alcohol and allowed to dry. Such a specimen oxidized at 200° C. for 4 hr. remained bright, whereas an untreated specimen showed mauve interference colours. It is apparent that a film, which interferes with the subsequent oxidation, forms on the tin as a result of the cathodic treatment. The thickness of this film can be determined electrometrically, using a de-aerated solution of 0·005 *M* potassium chromate in the apparatus described by Mills and Evans[3]. The potential of the specimen (cathode) versus a silver–silver chloride reference electrode is measured periodically until the end-point is reached, that is, when the potential changes from that due to oxide reduction to that corresponding to evolution of hydrogen. The number of millicoulombs required for the reduction of the oxide can be taken as a measure of film thickness. The film thickness calculated on this basis is given in Table 1 for specimens oxidized at 200° C. for various times, together with the interference colour.

Table 1. MILLICOULOMBS REQUIRED FOR REDUCTION OF FILM

Time (hr.)	Before treatment	After treatment
1	11 (no interference colour)	4·4 (no interference colour)
2	19 (yellow)	5·9 ,,
3	23·5 (light brown)	7·3 ,,
4	27·5 (mauve)	10·7 ,,

The film thickness on the untreated specimen after 1 hr. at 200° C. is slightly greater than after 4 hr. of oxidation for the treated specimen.

The film thickness before and after cathodic treatment can also be determined electrometrically. It was found to correspond to 3·47 millicoulombs before treatment and to 2·0 millicoulombs after treatment. Thus the thinner film produced as a result of the cathodic treatment has a much greater influence on the subsequent oxidation than the original film, reducing the rate of oxidation by about one-third. It is obvious that the two films are different, and that cathodic treatment of tin before the high-temperature oxidation of the metal gives results which are not characteristic of the metal itself.

It is possible that this applies to the other metals as well. Therefore, the possible effect of cathodic cleaning on the metal should first of all be investigated, in order to avoid producing misleading results in the subsequent oxidation experiments. In the case of tin, the formation of the resistant film during cathodic treatment is dependent on time of treatment, applied voltage and nature of electrolyte.

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CHEMISTRY

Phase Diagram of the System Vanadium Pentoxide - Boron Trioxide

IN a previous communication I reported on the investigation of the system vanadium pentoxide–phosphorus pentoxide[1]. A similar method has been applied in the examination of the system vanadium pentoxide–boron trioxide. The present report describes the liquidus curve of the system vanadium pentoxide–boron trioxide, together with the results of X-ray investigations of the fine structure. The liquidus curve was established by a special differential thermoanalytical apparatus described in detail in a former communication[2]. The heating curves of five samples are presented in Fig. 1. The composition of these samples was as follows—vanadium pentoxide + boron trioxide, percentages by weight: (1) 95 + 5; (2) 90 + 10; (3) 85 + 15; (4) 70 + 30; (5) 55 + 45.

Apart from the melting point, no other maxima indicating conversion or eutectics appear in the heating curves. The melting point decreases with the rise of content of boron trioxide.

X-ray investigations of fine structure were carried out by the Debye–Scherrer method. The structure of eight samples of various composition was examined. The composition of these samples was as follows—vanadium pentoxide + boron trioxide: 95 + 5; 90 + 10; 80 + 20; 65 + 35; 55 + 45; 50 + 50; 45 + 55; 35 + 65.

The boron trioxide used in preparing these samples was crystallized by a method similar to that applied in the heat treatment of the samples. The lines of the powder diagram, established for the crystals of the product obtained in this way, and also the lines of vanadium pentoxide[3], were found in the powder diagrams of all samples examined. Apart from the lines of the two types of crystals mentioned, no

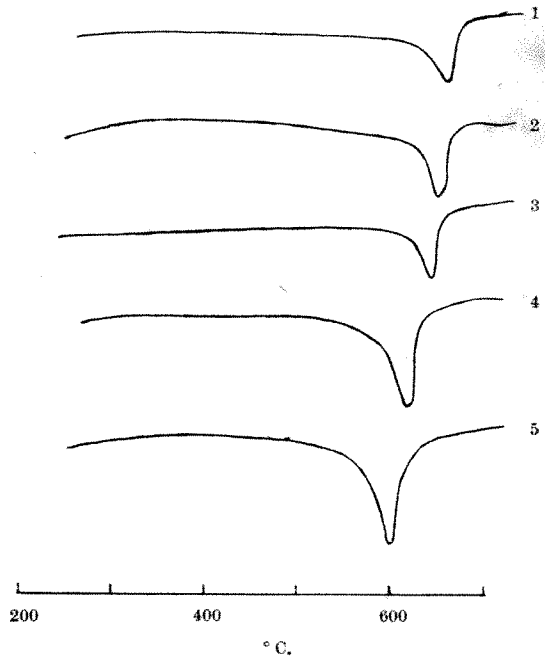

Fig. 1

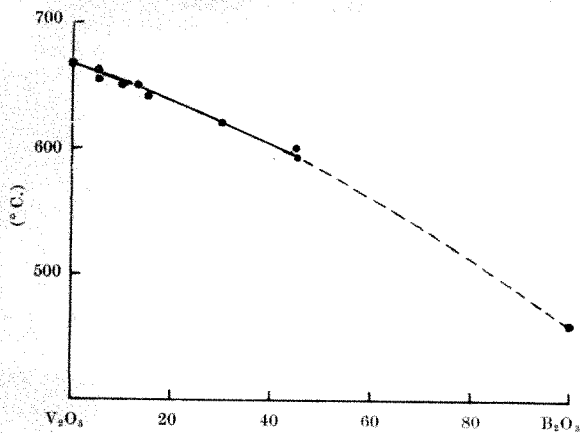

Fig. 2

other interference lines indicating the presence of a third phase were observed.

As the presence of boron trioxide can be detected even in samples containing only 5 per cent of the compound, and as in the sample containing 65 per cent boron trioxide, apart from this compound, only vanadium pentoxide can be detected, the system vanadium pentoxide – boron trioxide cannot be regarded as a eutectic system.

Fig. 2 shows the phase diagram plotted on the basis of the heating curves revealed in Fig. 1, and of the results of the X-ray investigations of fine structure.

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True Reactivity of the Organocadmium Compounds

WHILE studying the chemistry of the organocadmium compounds, evidence was found making necessary a revision of accepted views regarding their reactivity and indicating that a 'salt effect' plays a critically important part as a catalyst in their reactions. Organocadmium compounds are generally considered to be very reactive with acid chlorides, but practically inert towards aldehydes and ketones[1], thus making possible the important 'organocadmium synthesis' of ketones[1,2].

Although twenty-four years have elapsed since the discovery of this synthesis by H. Gilman, there is no record in the literature of any attempt to use isolated, pure organocadmium compounds to effect the ketone synthesis. Without any exception, the *in situ* reaction mixtures, as obtained by the metathetical reaction of the organomagnesium compounds with cadmium salts, have been used. Therefore, I tried to repeat the acetophenone synthesis of Gilman and Nelson[1] with the difference that pure dimethylcadmium[3] was used instead of the *in situ* reaction. The surprising result was that benzoyl chloride did not form acetophenone with pure distilled dimethylcadmium. (Benzene or ether solution, reaction time 2 hr. at 40°.) 92 per cent of the benzoyl chloride remained unattacked as shown by saponification to benzoic acid. Moreover, under similar conditions, only slight reactivity was observed between benzoyl chloride and distilled diethylcadmium, dibutylcadmium and recrystallized (free from magnesium salt) diphenylcadmium, respectively. When distilled diethylcadmium was treated with acetyl chloride (benzene solution, reaction time 20 min. at 28°), 79 per cent of the diethylcadmium remained unchanged.

In all the recorded cases in the literature, mixtures of the organocadmium compounds and the magnesium salts were used to effect the ketone synthesis; hence my negative findings suggest that in Gilman's original experiments[1] as well as in the hundreds of other ketone syntheses described with the use of organocadmium compounds, a hitherto unrecognized 'salt effect' exerted an unintentional, and in many cases indispensable, activating effect. This salt effect could have been caused by the magnesium salts generated in the usual preparation of the organocadmium compounds:

$$2R\mathrm{Mg}X + \mathrm{Cd}X_2 = \mathrm{Cd}R_2 + 2\mathrm{Mg}X_2$$

The activation hypothesis was supported by the finding that benzoyl chloride produced acetophenone in 74 per cent yield on treatment with distilled dimethylcadmium in the presence of one mole of magnesium bromide. Furthermore, diethylcadmium, dibutylcadmium and diphenylcadmium reacted with benzoyl chloride in the presence of magnesium bromide and magnesium chloride, respectively, giving the corresponding ketones in yields of 60–80 per cent (conditions the same as before). The reaction of acetyl chloride (2 mol.) with distilled diethylcadmium (1 mol.) was complete (97 per cent) when two moles of magnesium bromide etherate were present (benzene solution, 20 min. at 28°). With a longer reaction time (3 hr.), this last reaction goes to completion even in the absence of magnesium salts. In contrast, using less reactive organocadmium compounds, the magnesium salts influence not only the velocity but also the direction of the reaction. Thus, an enforced reaction of benzoyl chloride with dimethylcadmium (5 hr. at 82° in benzene) resulted in a complex mixture of products, with only 20 per cent of acetophenone.

The salt effect influences the reactivity of aldehydes also: benzaldehyde showed only 19 per cent conversion with distilled diethylcadmium in ethyl ether (100 hr. at 25°), but 86 per cent conversion (into phenyl-ethyl-carbinol) in 1 hr. using a diethylcadmium solution prepared from ethylmagnesium bromide and cadmium chloride. These results explain the observations of Gilman[1] with regard to the relative reactivities of aldehydes and acid chlorides with organocadmium compounds; salt-free diethylcadmium was employed in the experiment with benzaldehyde, but even after five months the reaction was incomplete; an *in situ* mixture of the organocadmium compounds and magnesium halides was used in the ketone syntheses.

The elucidation of the difference between the reactivity of the genuine organocadmium compounds and the *in situ* mixtures containing magnesium salts means that we should differentiate between organocadmium chemistry, as at present known, and the chemistry of the genuine organocadmium compounds, which still remains to be studied. The reaction of tertiary alkylhalogenides and organocadmium compounds, as my preliminary experiments indicate, are subject to a catalysis by magnesium salts

also. Therefore, the re-evaluation of the results of J. Cason and R. J. Fessenden[4] seems to be desirable.

William G. Dauben and John W. Collette[5] discussed an abnormal organocadmium reaction, proposing a mechanism for the reaction of arylcadmium compounds with acid chlorides in which an internal Lewis-acid type intermediate of the class of the acylonium salts was postulated. Neither this hypothesis nor other speculations regarding the reaction mechanism or organocadmium reactions[6] considered the catalytic role of magnesium salts in the ketone synthesis although invariably present. Cason and Reist[7] suggested, without any experimental proof, that among others perhaps the magnesium salts could influence the reaction of alkylcadmiums with succinyl dichloride. They supposed that the presence of magnesium salts promotes the side-reaction leading to esters, instead of the normally expected ketones. This assumption contrasts with all of our experimental findings, indicating that magnesium salts promote the formation of ketones, thus diminishing the side reaction.

The recognition of this activation effect opens the way to a planned regulation of the reactivity of organocadmium compounds. It is possible to activate an organocadmium compound in a preselected degree, depending on the type of salt employed. H. Gilman[1] tried unsuccessfully to obtain α-keto esters by the reaction of ethyl chloro-oxalate with diethylcadmium :

$$CdR_2 + 2ClCO \cdot COOC_2H_5 = 2RCO \cdot COOC_2H_5 + CdCl_2$$

I tried the same reaction (with R—CH_3 or n-C_4H_9) with lithium bromide as the activator instead of the magnesium salts, which are apparently too active. 8·7 gm. (100 m.moles) of lithium bromide in 35 ml. of tetrahydrofuran was added to 13·7 gm. (100 m.moles) of ethyl chloro-oxalate in 10 ml. of tetrahydrofuran at −30°. 7·1 gm. (50 m.moles) of dimethylcadmium in 20 ml. of tetrahydrofuran was added at − 65° in 1 hr., and stirred another hour at −65°. The tetrahydrofuran was distilled off *in vacuo* at 25°, the residue taken up in water, extracted with ether, the combined ether and tetrahydrofuran solutions freed of solvents, and the residue fractionated at a pressure of 18 mm. mercury. At 52–53°, 5·90 gm. (51 per cent theoretical yield) of ethyl pyruvate was obtained; phenylhydrazone (m.p. 114–115°, mixed melting point with authentic material 115–116°). Similarly, at −40°, substituting dibutylcadmium for the dimethylcadmium, ethyl α-ketohexanoate was obtained in 70 per cent yield. This is the first generally applicable organo-metallic synthesis of this type of compound ; for Stacy and McCurdy[8], using an *in situ* organocadmium solution, obtained only traces of ethyl α-ketohexanoate from the reaction of dibutylcadmium with ethyl chloro-oxalate, although in special cases, with hindered arylcadmium reagents, yields were much better.

As the preparation of pure, distilled organocadmium compounds is somewhat cumbersome, the description of an experiment where this is avoided is given here. From 1·35 gm. of lithium metal and 11·6 gm. of butylbromide, an ethereal solution of butyllithium was prepared at − 30°. The 'double titration' method indicated that 68 m.moles of butyllithium was formed. This was transformed into a dibutylcadmium solution by admixing 9·3 gm. (34 m.moles) of cadmium bromide. After 30 min. stirring at 35°, the ether was distilled off *in vacuo* at room temperature, the residue dissolved in 45 ml. of tetrahydrofuran, and this solution, containing 34 m.moles of dibutylcadmium and 152 m.moles of lithium bromide, treated as above with ethyl chloro-oxalate. Ethyl α-ketohexanoate was obtained in a yield of 68 per cent of theoretical (7·44 gm.).

I have found that magnesium salts exert a similar 'salt effect' in the reaction of the organozinc compounds. Obviously, a potential activation of organometallic reactions could always be considered if salts are present in the systems employed. The Grignard compounds are of special interest : Raymond E. Dessy and co-workers[9] have demonstrated that ethereal solutions of ethylmagnesium bromide contain a complex with the formula $(C_2H_5)_2MgMgBr_2$ (and not the usually considered C_2H_5MgBr). Similarly, phenylmagnesium bromide solutions contain only the species $(C_6H_5)_2Mg.MgBr_2$. The usual higher reactivity of Grignard compounds as compared with the lower reactivity of the R_2Mg type compounds apparently represents another important case of activation of organometallic reactions by magnesium salts.

The mechanism of these reactions is being studied and experiments are being continued to apply the 'selective activation principle' to develop syntheses for other classes of compounds hitherto inaccessible by organometallic synthesis.

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Detection of Iodine Compounds by Paper Chromatography

Kolthoff and Sandell[1] have found that minute amounts of iodine as iodide can be detected and determined by the ceric sulphate–arsenious acid reagent :

$$As^{3+} + 2Ce^{4+} \rightleftarrows As^{5+} + 2Ce^{3+}$$

They have pointed out that the effect of iodides on the reduction of the ceric ion by arsenite is catalytic.

Bowden, Maclagan and Wilkinson[2] have described methods for the detection of inorganic and organic iodine-containing compounds on paper chromatograms using the ceric–arsenious reaction. The positions of iodine-containing compounds were indicated by white spots on a yellow background. A difficulty encountered in this reaction is the fading of the chromatograms after some minutes due to the presence of small traces of atmospheric iodine.

We have overcome these disadvantages by exposing the chromatograms, immediately after development,

to vapours of a 50 per cent phenol solution and then drying in air; the white spots of iodine-containing compounds are fixed and a marked contrast against dark brown background is obtained. This seems to be due to the oxidation of phenol by the excess of ceric sulphate.

Under similar conditions α- and β-naphthols give white spots with a violet tinge, against a yellow background. Unfortunately these spots are not so easily obtained as those of phenol.

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Gas Chromatography of Unesterified Fatty Acids using Polyester Columns treated with Phosphoric Acid

THE gas chromatography of unesterified fatty acids was first reported by James and Martin[1], who used a column liquid phase of silicone oil containing 10 per cent stearic acid. Beerthuis *et al.*[2] extended this work to higher fatty acids (C_{12} and higher) using silicone oil plus β-anthraquinone carboxylic acid and 'Apiezon *L*' grease as liquid phases. With these systems, considerable tailing of the peak occurs and extremely high column temperatures are required. The association phenomenon of the carboxyl group is responsible for the difficulty of the analysis.

More recently, several authors[3–5] have separated fatty acids of lower molecular weight using more polar liquid phases such as dioctyl sebacate plus sebacic acid[3] and polyesters of dibasic acids and glycols[4,5].

The extension of polyester phases to the analysis of higher fatty acids (C_{12}–C_{22}) would be advantageous because unsaturated could be separated from saturated acids at lower temperatures than with other phases. The disadvantages of polyesters are their poor thermal stability and high 'bleed' at temperatures higher than 220° C. Furthermore, the polyesters alone are not acidic enough to overcome completely the association phenomenon of the higher acids.

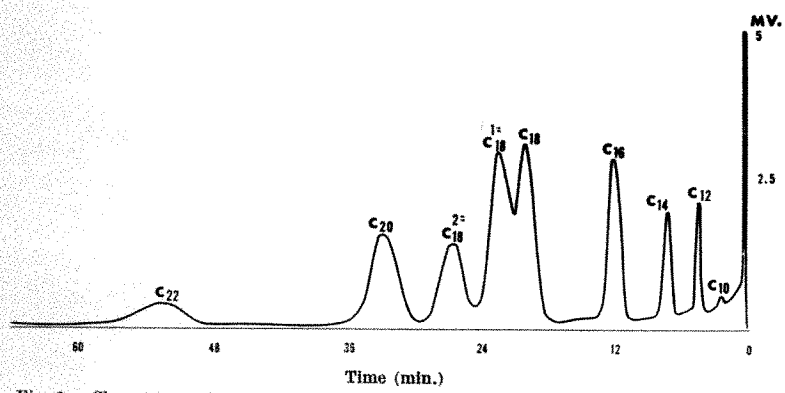

Fig. 1. Chromatographic separation of a mixture of long-chain fatty acids. Flash heater 270° C., column temperature 235° C., helium pressure 16 p.s.i. (45 ml./min.), column 100 cm. × 4 mm., hot-wire detector, sample size 3 μl.

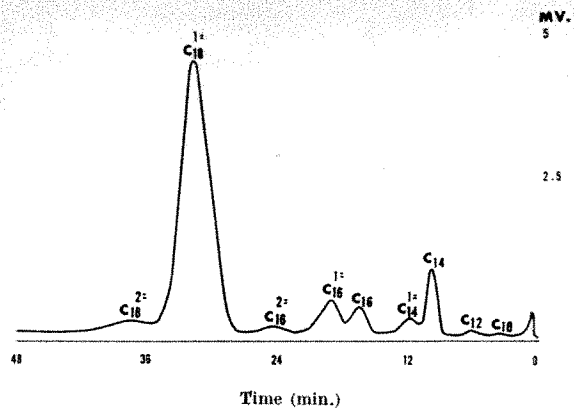

Fig. 2. Chromatographic analysis of a commercial oleic acid. Flash heater 270° C., column temperature 230° C., helium pressure 16 p.s.i., column size 100 cm. × 4 mm., hot-wire detector, sample size 3 μl.

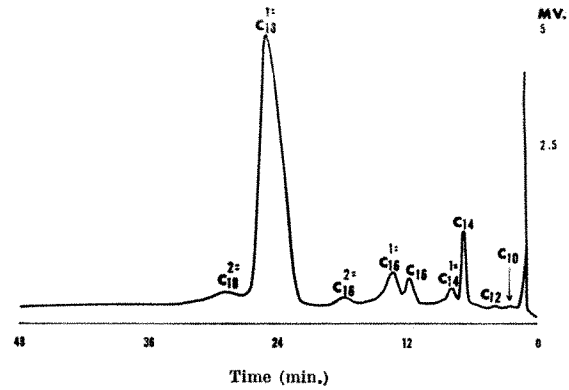

Fig. 3. Chromatographic analysis of the methyl esters of a commercial oleic acid. Flash heater 270° C., column temperature 180° C., helium pressure 16 p.s.i., column size 100 cm. × 4 mm., hot-wire detector, sample size 1 μl.

With a column having a polyester treated with phosphoric acid as the liquid phase, well-defined symmetrical peaks were obtained with C_4–C_{22} acids. Saturated and unsaturated acids were separated from each other. Separations were made at relatively low column temperatures of 220–235° C., and the columns appear to be extremely stable at these temperatures, being usable for several weeks with little loss in efficiency. At 180° C. methyl esters are also separable on the same columns with good peaks.

The column packing was 25 per cent (w/w) diethylene glycol adipate polyester[6] ('Lac-2-*R*-446', Cambridge Industries Co., Inc., 101 Potter Street, Cambridge 42, Mass.) and 2 per cent phosphoric acid (85 per cent H_3PO_4) on 60–80 mesh, acid-washed 'Celite 545'. The polyester was dissolved in chloroform and the 'Celite' added. Then the phosphoric acid was added to the slurry, the chloroform was removed by evaporation on a steam-bath with constant stirring, and the powder was placed in a vacuum oven at 60° C. for 24 hr. The coated

'Celite' was finally vibration-packed in a copper *U*-tube (100 cm. × 4 mm.) and was conditioned for 16 hr. at 220° C. The gas chromatographic instrument was one of my own design utilizing Gow-Mac filaments for thermal conductivity detection.

The separation of a synthetic mixture of fatty acids from C_{12} to C_{22}, including some unsaturated acids, is shown in Fig. 1. The incomplete separation of the stearic and oleic acid peaks typical of this polyester could probably be improved by lengthening the column or by using another treated polyester. Fig. 2 shows the analysis of a commercial oleic acid at 230°, and Fig. 3 the analysis of the methyl esters of the same acid at 180° C. The fatty-acid sample was three times (3λ) as large as the methyl-ester sample (1λ) in order to achieve approximately the same thermal conductivity response.

Table 1. COMPARATIVE GAS CHROMATOGRAPHIC ANALYSIS OF A COMMERCIAL OLEIC ACID AND ITS METHYL ESTER

Acid	Free acid (per cent)	Methyl ester (per cent)
C_{10}	0·2	0·1
C_{12}	0·3	0·1
C_{14}	5·7	4·8
$C_{14}(^{1}=)$	2·7	2·1
C_{16}	4·2	3·9
$C_{16}(^{1}=)$	6·4	5·6
$C_{16}(^{2}=)$	1·2	1·4
$C_{18}(^{1}=)$	75·3	77·2
$C_{18}(^{2}=)$	4·2	4·8

Table 1 compares the analyses calculated from the areas under the peaks in Figs. 2 and 3. The differences in the analyses may be due to differences in thermal conductivity of esters and acids. Further work will be required to relate the peak areas of the free acids to true weight percentages of the various acids in the samples.

The polyester phase treated with phosphoric acid gives excellent separations and symmetrical peaks for the higher fatty acids. It should find many applications in biochemical and plant-control work. These liquid phases seem particularly stable to heat, possibly because of ester formation between phosphoric acid and the hydroxyl groups of the polyester.

This work will be described more fully elsewhere.

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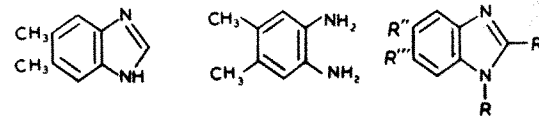
BIOCHEMISTRY

Effect of Some Benzimidazoles on a Vitamin B_{12}-requiring Alga

THE identification of 5 : 6-dimethyl benzimidazole (I) as an acid degradation product of vitamin B_{12} was made in 1949 by Brink and Folkers[1] and independently by Holiday and Petrow[2]. The latter authors also speculated on the biogenesis of vitamin B_{12} and riboflavin, and suggested the possibility of their common derivation from 4 : 5-dimethyl-*o*-



I II III

phenylenediamine (II)—a chemical precursor of (I). Furthermore, both these compounds were shown by Emerson *et al.*[3] to possess vitamin B_{12}-like activity in the rat. McNair Scott, Rogers and Rose[4] tested 49 substituted benzimidazoles on several bacterial systems—including the vitamin B_{12}-requiring *E. coli* 113-3. In particular, they found that —SH and —NO_2 substitution in the 4-position was associated with competitive vitamin B_{12} antagonism. More recently, Timmis and Epstein[5] demonstrated that 4,5,6-trichloro benzimidazole and its corresponding 1-β-D-ribofuranosyl were non-competitive and competitive antagonists respectively in the highly sensitive vitamin B_{12}-dependent flagellated green alga *Euglena gracilis* var. *z*.

A large series of benzimidazoles was synthesized in 1952 by Feitelson *et al.*[6], *inter alia* for the purpose of discovering vitamin B_{12} antimetabolites which might prove of value as chemotherapeutic agents in the treatment of cancer. The object of the present communication is to report the results of some growth-response tests with these compounds on the *E. gracilis* system.

Approximately 140 benzimidazoles were tested using techniques already described[5,7,8]. On preliminary examination, none was found to support algal growth in the absence of vitamin B_{12}, while 20 produced significant inhibition at low vitamin concentrations. The majority of the latter compounds were tested in subsequent assays to determine whether their inhibitory effects could be reversed or partially reversed by massive concentrations of vitamin B_{12}.

As can be seen (Table 1) no example of competitive or reversible antagonism was detected—a finding possibly related to the observation that (I) does not possess a vitamin B_{12}-like effect in *E. gracilis*.

Four benzimidazoles—Nos. 15, 16, 33 and 103—proved to be surprisingly toxic irreversible antagonists and at concentrations of less than 15 μgm./ml.

Table 1. CONCENTRATIONS OF BENZIMIDAZOLES PRODUCING 50 PER CENT INHIBITION OF GROWTH OF *E. gracilis* VAR. *z*

Code No.	(III)				Concentration of drug (μgm./ml.) producing 50 per cent inhibition of growth. Vitamin B_{12} (μμgm./ml.)		
	R	*R'*	*R''*	*R'''*	10	100	1,000
8	Me	H	NO_2	H	118	111	94
39*	H	$C_{12}H_{27}$	NH_2	H	317	221	219
40	H	CH_2Cl	H	H	63	75	72
41*	H	CH_2Cl	H	H	109	101	105
62*	CH_2Cl	H	H	H	170	180	171
68*	H	CH_2Cl	Me	H	463	405	408
76*	H	CH_2Cl	Me(C_4)	H	238	300	265
92	Et	H	Cl	Cl	90	63	56
101*	CH_2CH_2Cl	CH_2Cl	H	H	70	67	58
122	CH_2OH	H	H	H	74	74	72
127	Me	H	Me	H	440	427	377
128	H	Et	Cl	Cl	225	214	213
15	Me	CH_2Cl	H	Cl	2·5	3	2·5
16*	CH_2CH_2Cl	CH_2Cl	H	Cl	11	11	12
33*	CH_2CH_2Cl	CH_2Cl	Cl	H	9	14	13
103*	CH_2CH_2Cl	CH_2Cl	Cl	Cl	1·5	1·5	1·5

* Examined as hydrochloride.

produced 50 per cent inhibition of growth in the presence of up to 1,000 μμgm./ml. of vitamin B_{12}. These compounds generally possess chloroalkyl groups in the 1- and/or 2-positions and chlorine substituents in the 5- and/or 6-positions. It is of interest to note that compound No. 101—designated by Feitelson *et al.*[6] in 1952 as "a novel type of nitrogen mustard"—was afterwards shown by Hirschberg, Gellhorn and Gump[9] to be highly toxic to both human and mouse brain tumour cells in tissue cultures. The enhancement of toxicity associated with progressive chlorine substitution on the benzene ring is strikingly exemplified by a comparison of the activities of compounds Nos. 101, 33 and 103 (Table 1). Since in all probability substitution of this type would lead to increased fat solubility, these differences in biological reactivity may well be associated with differences in the ratios of relative solubilities of these compounds in lipids and water. Such a mechanism has been suggested by Timmis and Hudson[10] in relation to the neutropenic effect of two homologous series of αΩ dimethanesulphonoxyalkanes.

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Enzymatic Transformation of Dehydroascorbic Acid to Diketogulonic Acid

THE conversion of dehydroascorbic acid to diketogulonic acid has been studied in chemical systems[1]; but, as Harris[2] has pointed out, definite evidence is not available for any enzymatically catalysed transformation.

A search by us has shown that cauliflower (*Brassica oleracea botrytis*) and bitter gourd (*Momordica charantia*) possess an enzymatic mechanism for the conversion of dehydroascorbic acid to diketogulonic acid. The technique of investigation consisted in incubating homogenates with dehydroascorbic acid and following the course of reaction by estimating the amount of substrate disappearing and diketogulonic acid formed by the 2 : 4-dinitrophenylhydrazine method[3]. A system made up from heat-treated plant material was run simultaneously as control, and provided data for non-enzymic transformation. The homogenate was prepared by grinding the tissue with cold acetate buffer in a chilled Waring blendor, straining through muslin and making up to 20 per cent (w/v). In a typical assay 10 ml. of the enzyme, or the heat-treated, preparation was incubated with 3,000 μgm. of dehydroascorbic acid, the final volume being made to 30 ml. with buffer after adding any supplements. 5-ml. aliquots of the mixture were analysed at zero time and at the end of 60 min. of incubation at 37° C.

Table 1. ENZYMATIC TRANSFORMATION OF DEHYDROASCORBIC ACID TO DIKETOGULONIC ACID IN CAULIFLOWER AND BITTER GOURD

		Diketogulonic acid formed (per cent)	Dehydroascorbic acid disappearing (per cent)
	Cauliflower		
No. 1	Experimental	12·0	14·8
	Control	6·2	9·9
No. 2	Experimental, with added Mn^{++}, final concentration 0·001 *M*	12·4	13·0
	Control	5·7	5·7
	Bitter gourd		
No. 3	Experimental	8·9	10·1
	Control	2·9	2·9
No. 4	Experimental	17·9	17·9
	Control	9·5	8·3

Results recorded in Table 1 show that whereas spontaneous transformation of dehydroascorbic acid to diketogulonic acid occurred in all experiments, enzymic conversion also occurred, as evidenced by the fact that the transformation in the untreated homogenates was significantly higher than in the heat-treated controls.

We are grateful to the Council of Scientific and Industrial Research, New Delhi, for financial assistance.

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Specific Protein of Legumes which reacts with Animal Proteins

INTERACTIONS of proteins among themselves, except immunological reactions, can be studied by various methods; but only in a few exceptional cases could they be demonstrated, as in the reactions of trypsin inhibitors and of agglutinins of legumes. Whether the *iso*hæmagglutinins in man are the result of immunization or are a direct product of the participation of blood-group genes has not yet been fully settled. But the proteins which are contained in some plants and agglutinate erythrocytes cannot be a result of immunization; they are, so to speak, natural antibodies. An antibody, however, is defined as a substance produced in response to an antigen. In this regard an antibody produced not in response to an antigen is self-contradictory. To avoid such confusion, Boyd[1] proposed the term 'lectin' for such substance as is produced not in response to an antigen but reacts more or less specifically with certain proteins or antigens.

It is already well established that agglutination and the precipitation can be caused by one and the

same antibody. Therefore the agglutinating 'lectin' can probably precipitate appropriate substances, and the distinction between agglutinating and precipitating 'lectin' may not be necessary. However, it is interesting that hitherto observations were made only on the agglutinating 'lectins' of plants. One of the reasons lies probably in the fact that the agglutination of erythrocytes is very sensitive. The second reason might be that such substances can be expected to be used as test substances for blood groups, while no direct application could be expected of a 'precipitating lectin'. On the other hand, observation of a precipitating 'lectin' is not always easy, because the formation of precipitate can also be caused by reactions other than a direct reaction of a protein with other proteins, for example, by the change of *p*H and/or salt concentration and so on.

In any event it was hoped that among the proteins of remote phylogenetic origin, there might be some which bind fairly firmly with each other, although specific reactions of proteins of animal origin among themselves occurred only exceptionally, apart from immunological ones. With the elaboration of 'crossing electrophoresis' developed in our laboratory[2], search was made for plant proteins specific for animal proteins in the extracts of some beans. In Fig. 1 is shown an example of 'crossing diagrams of human serum' against the extract of jack beans. From Fig. 1 it is clearly shown that the extract of jack beans contained a protein which reacted specifically with serum proteins. This specific protein, named provisionally protein *J*, migrated toward the cathode under the usual conditions of electrophoresis of serum at *p*H 8·6. It reacted with α_1-, α_2-, β-globulins and probably also with γ-globulin, but not with albumin.

That the peaks of the crossing diagram, especially those corresponding to α_1, α_2-, and β-globulins, consist of precipitate could be clearly shown by two-dimensional crossing electrophoresis in agar gel, as the thin film of gel was transparent. The precipitation could also be observed by Ouchterlony's method[3] as shown in Fig. 2.

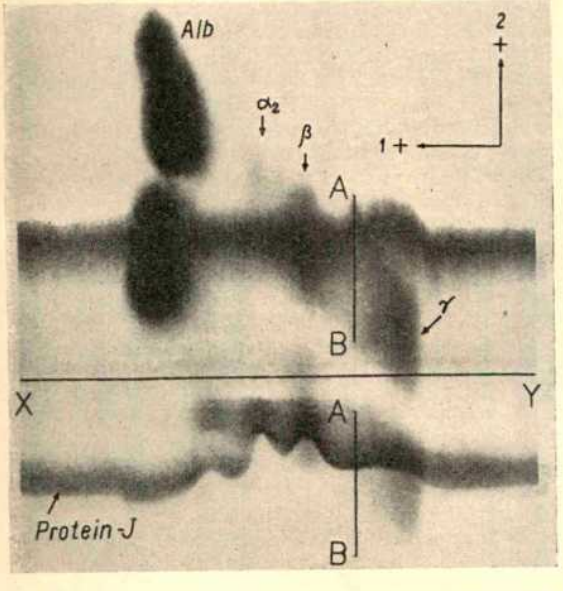

Fig. 1. Crossing diagram of human serum against protein *J* of jack bean. First electrophoresis: 0·003 ml./cm. of human serum was applied on lines *AB* and the first electrophoresis was carried out at 80 V. for 14 hr. Second electrophoresis: after the first one, 0·003 ml./cm. of water extract (5 : 1) of jack bean meal was applied on the line *XY* and the second electrophoresis was carried out at 120 V. for 8 hr. Barbiturate buffer, *p*H 8·6 and ionic strength, 0·05. Filter paper, Tōyō No. 52. Stained with amido-black 10 *B*

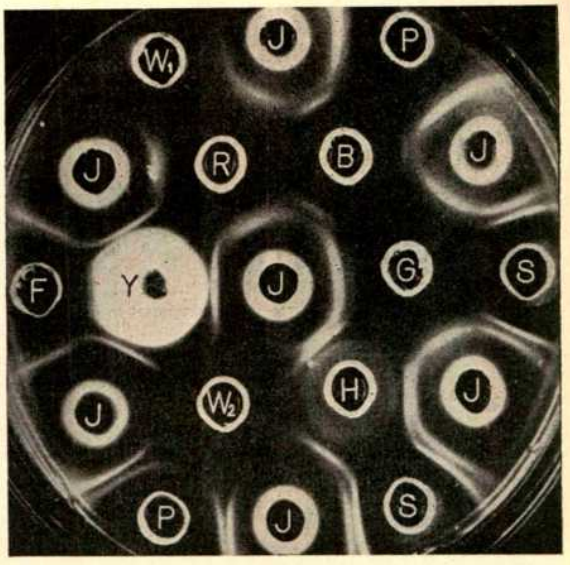

Fig. 2. Lines of precipitate appeared in the agar gel by the reaction of jack bean extract with animal proteins. *J*, Water extract of jack bean meal (5 : 1); *H*, human serum; *G*, guinea pig serum; *B*, bovine serum; *R*, rat serum; *S*, sheep serum; *P*, hog serum; *F*, fowl serum; W_1, egg white diluted with 4 vol. of physiological saline solution; W_2, egg white diluted eight times; *Y*, egg yolk diluted four times

As might be expected, the crossing diagrams of the sera of various animals showed species specificity, and human sera in some diseases showed distinct changes in pattern. Thus it is hoped to utilize the crossing diagrams of the sera against protein *J* for the diagnosis of certain diseases.

Further, protein *J* reacted with proteins of egg white as well as egg yolk. On the other hand, of the legumes hitherto tested, namely, kidney bean (uzura bean, *Phaseolus vulgaris* Linn.), 'torokusun' bean (a variety of the former), adzuki bean (*Adzukia angularis* Ohwi), cow-pea (sasage-bean, *Vigna sinensis* Savi), soy bean, and peanut, it was found that the kidney bean and 'torokusun' bean contained a similar protein, but their content was much smaller. From the crossing diagrams, it was found that they migrated toward the cathode with nearly the same mobility as protein *J* of jack bean and reacted chiefly with α_2-globulin of serum. It is suspected that they are of the same nature and that such proteins might be distributed fairly widely in legumes.

Detailed reports on the species specificity of the crossing diagrams of sera of various animals and the changes in diseases will be published elsewhere.

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Inositol Phosphatide in Peas

SOME properties and analytical data concerning an inositol phosphatide of peas have been reported previously[1,2]. The availability of accurate methods for the determination of inositol in lipids, both by microbiological[3] and chemical means[4,5], has made it possible to conduct further experiments which are reported here.

The quantity of inositol phosphatide fraction obtained by Wagenknecht's modification of Carter's procedure[6] has been reported to increase during storage of raw peas (*Pisum sativum*) at $-17 \cdot 8°$ C. for periods of several days to several months[2]. Since this inositol phosphatide fraction is known to contain impurities it was thought desirable to determine whether the percentage of inositol in the fractions was constant with time over the entire period of frozen storage. Aliquots of the inositol phosphatide fractions obtained from peas of Pluperfect variety were subjected to hydrolysis with 4 *N* hydrochloric acid in sealed tubes at 120° C. for 16 hr. A modification of the periodate oxidation methods of Agranoff *et al.*[5] and Le Baron *et al.*[4] was used to determine inositol content of the hydrolysates. The results (Table 1) indicate that the percentage of inositol in these samples varies with time at $-17 \cdot 8°$ C., but the total weight of inositol in the fractions is relatively invariant over the period from two days to four months of storage.

Table 1. INOSITOL CONTENT OF PEA INOSITOL PHOSPHATIDE FRACTIONS

Duration of frozen storage	Inositol* (per cent)	Inositol phosphatide (mgm.)	Inositol content (mgm.)
0 days	6·4	23	1·5
2 days	1·8	133	2·5
2 months	1·0	229	2·3
4 months	1·0	241	2·4
6 months	1·1	169	1·8

* Determined by modified periodate oxidation procedure (refs. 2, 4 and 5).

An enzymatic liberation of components of the inositol phosphatide fraction had previously been postulated, based on the observation that the inositol phosphatide content of raw (but not of heat-treated) peas increased with time[2]. On the basis of the results presented here it would appear that this increase is caused by the enzymatic liberation, during frozen storage, of inositol-free lipid materials the solubility properties of which are sufficiently similar to those of phosphatidyl inositol to allow them to be extracted with the inositol phosphatide fraction.

Although several components were known to be present in the inositol phosphatide fraction, as was shown by chromatographic methods[2], previous paper chromatographic results gave no evidence for the presence of free inositol. As a further check on the absence of free inositol a sample of the water-soluble intact potassium form, which had been prepared from the calcium–magnesium mixed salt as described in a previous publication[1], was analysed for inositol by the excellent microbiological assay of McKibbin[3], utilizing *Saccharomyces carlsbergensis* strain 4228. The purified potassium salt of the inositol phosphatide fraction was shown to contain less than 1 μgm. of free inositol per milligram.

Paper chromatographic evidence from another laboratory (Benson, A. A., personal communication) indicated that the calcium–magnesium mixed salts of pea inositol phosphatide contained, besides monophosphoinositide, components possessing the R_F values of glycerophosphorylglycerol, phosphatidyl ethanolamine, phosphatidic acid, and some free inositol. The results presented here confirm that the purified potassium salt of the inositol phosphatide fraction contains inositol only in the bound form.

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5-Deoxycytidylic Acid-deaminating Activity in Human Gastric Mucosa and Other Adult Mammalian Tissues

THE enzymatic deamination of deoxycytidylic acid to deoxyuridylic acid in sea urchin eggs and embryos has been demonstrated by Scarano[1] and Scarano and Maggio[2]. Moreover, later results obtained by Scarano and Tallarico[3] on the presence of deoxycytidylic acid-deaminase in livers of rat, chicken, rabbit in various stages of their embryonic development may indicate that this enzymatic activity, in developing or regenerating tissues, is proportional to their growth-rate. This latter view was confirmed in experiments by Maley and Maley[4] on the determination of this enzymatic activity in embryonic tissues, in some spontaneous and experimental tumours and in regenerating livers.

In order to ascertain whether deoxycytidylic acid-deaminase is only characteristic of tissues in evolution or is common to tissues in continuous physiological regeneration, we examined several adult mammalian tissues for this enzyme activity. The tissues and organs investigated have been chosen in view of their active cellular proliferation.

The experimental procedure was essentially that proposed by Scarano[1]. The homogenates were prepared by scrapping of the mucosa surface. The specific activity is referred to as μmoles of deoxycytidylic acid deaminated in 10 min. per 10 mgm. nitrogen of the homogenate (the deamination of 1 μmole of deoxycytidylic acid giving a ΔA_{280} of $-0 \cdot 344$). The human tissues used for the enzymatic assays were collected immediately from surgical operations. Histological examinations were carried out on each of the specimens used.

The results obtained for the human gastro-enteric mucosa and for other mammalian tissues are reported in Table 1.

The results indicate that the rabbit gastric mucosa has a deoxycytidylic acid-deaminating activity although in a lesser amount as compared to the human. This enzymatic activity is not found in other segments of rabbit gastro-enteric mucosa and in testicle, being scarcely detectable in bone marrow. Cat and ox gastric mucosa have also been examined, and a very low deoxycytidylic acid-deaminating activity was found.

Table 1. 5-DEOXYCYTIDYLIC ACID-DEAMINATING ACTIVITY OF ADULT MAMMALIAN TISSUES

Human	stomach	11·05 ± 0 75 μmole/10 mgm. N per 10 min.
,,	ileum	6 66 ,, ,, ,,
,,	colon	10 67 ,, ,, ,,
,,	sigmoid colon	4 48 ,, ,, ,,
,,	rectum	4 39 ,, ,, ,,
Rabbit	stomach	1 57 ,, ,, ,,
,,	ileum	not detectable
,,	colon	not detectable
,,	testicle	not detectable
,,	bone marrow	scarcely detectable
Cat	stomach	scarcely detectable
,,	ileum	not detectable
,,	colon	not detectable
Ox	omasum	scarcely detectable

The failure to detect deoxycytidylic acid-deaminase in some tissues, as in the case of the bone marrow and testicle, does not mean that the enzyme is completely absent. The enzyme might either have been destroyed during the extraction, or be present in too small a concentration to be detected with our assays.

Chromatographic analysis of the deproteinized incubation mixtures confirmed the formation of deoxyuridylic acid in agreement with the spectrophotometric results.

Further investigations, now in progress, indicate the presence of deoxycytidylic acid-deaminase in human blood cells.

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Serotonin in Pineapple

SEVERAL investigators have noted and studied the presence of serotonin and its precursors in fruit, mainly banana and tomato[1–4]. As well as aiding the study of serotonin itself, this has the purpose of warning against the possible misdiagnosis of malignant carcinoid tumours by analysis of urine for elevated 5-hydroxyindoleacetic acid-levels when these are spuriously high following a diet rich in serotonin or its precursors.

During work on urinary 5-hydroxyindoleacetic acid, I noted unusually high peaks of excretion following the ingestion of pineapple juice. A more systematic study was conducted to determine the serotonin content of canned and fresh pineapple juice. Three brands of canned pineapple juice were selected, and samples were taken directly from the cans after shaking well. The fresh fruit was peeled and the skin discarded. The rest was pulped in a vitamizer and stored at about − 7° C. The pulp was centrifuged and the supernatant used for analysis. Analysis was by the colorimetric method of Udenfriend *et al.*[5].

The three brands of canned juice contained 23 mgm. serotonin/l., 25 mgm. serotonin/l. and 25 mgm. serotonin/l. respectively and the fresh juice 12 mgm. serotonin/l. It is almost certain that serotonin exists in the free state in the fresh as well as in the canned juice. The smaller quantity in the fresh juice may be due both to the rather inefficient pulping method used compared with commercial juice extraction and to the possibility that canned juice is concentrated somewhat in the processing.

A study of the urinary excretion of 5-hydroxyindoleacetic acid following ingestion of pineapple juice was also carried out. Two adult male subjects each drank 500 ml. of commercial canned pineapple juice and gave urine samples over the following 6 hr. The samples were analysed for 5-hydroxyindoleacetic acid by the colorimetric method of Udenfriend *et al.*[6]. The method was slightly modified at the final stage, the ethyl acetate being saturated with water at room temperature immediately before use. This ensured that the final volume of aqueous phase was the same, regardless of the atmospheric temperature. Table 1 shows the pattern of excretion.

Table 1

Time	μgm./min. 5-hydroxyindoleacetic acid
Subject 1	
7.15–10.30	1 8
	Pineapple ingested
10.30–11.45	22 1
11.45–12.50	31 2
12.50– 2.15	13 0
2.15– 3.15	7 7
3.15– 4.45	5 9
Subject 2	
7.45–10.30	3 0
	Pineapple ingested
10 30–11.20	8 6
11.20–12.25	30 5
12.25– 1.30	17·7
1.30– 3.00	9 8
3.00– 4.40	3·7

The rate of excretion per hour over this period has increased by approximately ten times.

It would seem, therefore, that pineapple can be added to the list of forbidden fruit in a diet where 5-hydroxyindoleacetic acid analyses are being conducted and may also open another avenue to the study of serotonin.

I wish to acknowledge the help of Mr. R. Horgan with the colorimetric procedures.

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Nitrite Oxidation by *Nitrobacter* in the Presence of Certain Nitrophenols

IT was reported by Simpson[1] that 2,4-dinitrophenol, at a concentration of 1 m*M*, strongly inhibits nitrite oxidation by *Nitrobacter*, although compounds such as ethyl nitrite and nitromethane appeared to have no inhibitory action. Other workers[2] have, however, failed to obtain any inhibition with 2,4-dinitrophenol. We have therefore re-investigated the effect of this compound on nitrite oxidation.

The oxidation of nitrite, at an initial concentration of 10 m*M*, by washed suspensions of *Nitrobacter* was followed manometrically at 30° in the absence of 2,4-dinitrophenol and in the presence of varying concentrations of the compound. All experiments were performed in the presence of 0 05 *M* phosphate buffer *p*H 7·5 and the solution of 2,4-dinitrophenol

used was prepared in this buffer. It was found that the compound is a powerful inhibitor of nitrite oxidation and the inhibition produced by different concentrations is shown in Table 1.

Table 1. INHIBITION OF NITRITE OXIDATION BY 2,4-DINITROPHENOL

Concentration of 2,4-dinitrophenol (m*M*)	Percentage inhibition of oxygen uptake
0·3	16
0·6	23
1·2	64
1·8	80
2·4	94

One possible explanation of the effect of 2,4-dinitrophenol is that, by virtue of its nitro groups, it can compete with nitrite for the nitrite-oxidizing enzyme. However, it was found that variation of the initial nitrite concentration between 6 and 44 m*M* had little effect on the degree of inhibition produced by a given concentration of 2,4-dinitrophenol. It therefore seems unlikely that such a competition between nitrite and 2,4-dinitrophenol occurs.

Another possibility is that 2,4-dinitrophenol inhibits because of its well-known ability to uncouple oxidative phosphorylation[3]. Although it has yet to be proved, it is almost certain that nitrite oxidation by *Nitrobacter* is linked to the production of high-energy phosphate bonds. If this phosphorylation is coupled in an obligatory way, then any uncoupling agent should inhibit nitrite oxidation. The effect on nitrite oxidation of two dyes, janus green and brilliant cresyl blue, both of which have been shown to uncouple oxidative phosphorylation in mammalian systems[4], was therefore tested, but neither had any effect at concentrations up to 10 m*M*. It is possible, however, that neither dye could penetrate to the site of nitrite oxidation within the cell.

The effect on nitrite oxidation of a few compounds related to 2,4-dinitrophenol was also tested, and the results are given in Table 2. All conditions were the same as in the experiments with 2,4-dinitrophenol; each compound was used at a concentration of 1 m*M*.

Table 2. EFFECT ON NITRITE OXIDATION OF SOME COMPOUNDS RELATED TO 2,4-DINITROPHENOL

Compound tested	Percentage inhibition of oxygen uptake
2,5-Dinitrophenol	61
m-Nitrophenol	77
p-Nitrophenol	100
p-Nitroaniline	25
Phenol	7

It is of interest that the nitrophenols produced the greatest inhibition, and it appears that both the phenolic hydroxyl and nitro groups are necessary to give the maximum effect. As in the case of 2,4-dinitrophenol, inhibition may be due to a direct action on the nitrite oxidizing enzyme, or to an uncoupling of oxidative phosphorylation.

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PHYSIOLOGY

Inhibition of Appetite in Dairy Cattle by Certain Intermediate Metabolites

MANNING *et al.*[1] have discussed the applicability of the glucostatic theory of Mayer *et al.*[2] to the regulation of food intake in sheep. Glucose in ruminant animals plays a relatively minor part in energy metabolism, since a major portion of ingested carbohydrates are degraded to volatile fatty acids which are absorbed into the blood stream via the rumen wall[3]. Consequently, a chemoreceptor mechanism of regulation of intake in ruminants may depend on any of several metabolites. The objective of this experiment was to examine several major intermediate metabolites for their effect on appetite.

Sodium acetate (adjusted with acetic acid to *p*H 7), glucose, acetic, propionic, valeric, hexanoic and lactic acids were administered intravenously by constant drip over the same 8-hr. period during each of three consecutive days. In each trial, identical twin cows of the Guernsey, Holstein-Friesian or Jersey breed were injected. One twin received the metabolite in three litres of physiological saline and the other received an equal amount of physiological saline. The injections were made into the jugular vein through a small polyethylene catheter inserted previously that remained in place throughout each trial. The catheter was firmly attached to the shoulder of the animal, thus allowing all manipulations to be made at that position. This technique permitted the elimination of any restraining apparatus other than a halter, to which the animals were already accustomed. The injection procedure and experimental manipulation apparently did not affect intake, since the control twins consumed the same amount of feed during the three-day injection period as they did during the three days prior to injection. The effect on appetite was determined by comparing the voluntary hay intake of chopped alfalfa of the control twin (saline injected) with that of the treatment twin (metabolite injected). The relative amounts of each metabolite administered are shown in Table 1. These amounts are expressed as a percentage of body maintenance requirement[4]. So far as possible, the higher levels of organic acids used were those corresponding to what would seem to be equal to, or in excess of, the actual amounts absorbed from the gastro-intestinal tract during an 8-hr. period.

Administration of glucose did not elicit a reduction in daily intake. This is in agreement with the observation of Vallance and McClymont[5] during injection of 4 kgm. of glucose over a 48-hr. period, and that of Manning *et al.*[1] following intravenous administration of 50 per cent glucose to sheep. In the case of the higher (25 per cent) level, concentrations of blood glucose were raised from approximately 40 mgm. per 100 ml. to approximately 100 mgm. per 100 ml., or about 2½ times normal. From these results, it is clear that raised levels of blood glucose have little or no effect on the appetite of dairy cattle.

The administration of the higher level of acetic acid and sodium acetate resulted in a highly significant reduction in feed intake during the 8-hr. injection period; with both metabolites consumption was negligible. Consumption during the other 16 hr. of the three injection days approached normal. However, the 24-hr. feed-intake values during the three days were significantly lower for the treatment

Table 1. EFFECT OF INTRAVENOUSLY ADMINISTERED METABOLITES ON CONSUMPTION OF FEED BY IDENTICAL TWIN COWS

Metabolite	Level*	No. of trials	Average intake during 8-hr. injection period, 3 days. Treated twin (lb.)	Average intake during 8-hr. injection period, 3 days. Control twin (lb.)	Average 24-hr. intake including 8-hr. injection period, 3 days. Treated twin (lb.)	Average 24-hr. intake including 8-hr. injection period, 3 days. Control twin (lb.)
Glucose	4 0	2	8 2	9 2	19 5	18 8
Glucose	25 0	2	5 8	6 4	16 4	15 8
Sodium acetate	12 5	2	0 5§	8 4	14 0†	20 2
Acetic acid	12 5	1	0 8§	6 3	3·1‡	17 9
Acetic acid	4 0	1	14 8	14 1	27 1	28 6
Acetic acid	3 5	1	6 8	9 3	18 1	16 6
Propionic acid	12 5	2	2 1§	10 0	15·1‡	23 6
Butyric acid	6 25	2	14 7	14 7	27 6	28 0
Valeric acid	6 25	2	15 4	18 8	30 4	32 8
Hexanoic acid	6 25	2	12 0	12 6	28 8	29 6
Lactic acid	6 25	2	19 8	20 4	32 2	34 6

* Percentage of body digestible energy maintenance requirement. † Significant ($P < 0\ 05$). ‡ Significant ($P < 0\ 01$). § Significant ($P < 0{\cdot}005$).

twins than for the control twins. Administration of propionic acid resulted in significant reductions in intake during the 8-hr. and 24-hr. periods. There was very little carry-over effect from acetate, acetic or propionic acid injections, since eating began very soon after cessation of each 8-hr. injection period.

None of the other metabolites mentioned above caused a significant reduction in feed intake. Valeric acid and lactic acid injection resulted in a small mean reduction in intake, but the results were variable and exhibited no definite trend.

The results of this series of trials strongly suggest the existence of a chemoreceptor response to changes in blood constituents. Apparently, one of the possible mechanisms of regulation of intake involves the absorption of acetic acid and propionic acid or, as indicated by the experiment using sodium acetate, the acetate and propionate ions, into the blood stream which, at threshold-levels, would elicit a chemoreceptor response inhibiting intake. Acetic and propionic acid inhibition of feed intake may account for the observation that dairy cattle consume less forage in the form of silage than in the form of hay, since silage contains significant amounts of these acids.

The level of feed consumption (highly variable in ruminants) is of the utmost importance, since gross efficiency of milk production is limited by voluntary intake of nutrients. From the results of this experiment, it is postulated that rations tending to promote the production of metabolites serving as energy sources that do not inhibit nutrient consumption could greatly enhance the gross efficiency of animal production by promoting an increase in voluntary intake of nutrients.

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Electrical Inexcitability of the Synaptic Membrane in the Frog Skeletal Muscle Fibre

VARIOUS types of evidence indicate that the endplate potential of frog twitch muscle fibres is an electrically inexcitable synaptic activity[1,2]. Electrical inexcitability of the synaptic membrane has been demonstrated most clearly in cells in which electrically excitable activity is lacking, for example, the electroplaques of marine electric fishes[3] and slow muscle fibres of frog[4]. Electrical inexcitability of synaptic membranes in other cells has also been demonstrated[1,2]. Hitherto, however, it has not been shown that the chemically excitable[5] synaptic membrane of twitch muscle fibres is also unresponsive to electrical stimuli. The junctional region is small, and there is intermingling of membrane of greater and lesser chemical sensitivity[5].

Experiments described here demonstrate that sites of the junctional membrane do not develop an inward current when a directly evoked spike is propagated through the endplate region. These are also the sites with the largest and most rapidly rising externally recorded spontaneous miniature endplate potentials.

Most of the work was done on whole sartorius muscles of frog (*Rana pipiens*). A few experiments were performed on isolated single nerve–muscle fibre preparations from the semitendinosus muscle, the results being identical in both series. The preparations were bathed in hypertonic saline, made by doubling the sodium chloride of a standard frog Ringer's solution. Hypertonicity served two functions: decreasing the contraction of the muscle[6] and increasing the frequency of spontaneous miniature endplate potentials[7]. The latter effect aided location of synaptic sites, which appear to be distributed as small patches in the junctional region[5].

Superficial nerve endings to a neuromuscular junction were visualized, and a recording micro-electrode was inserted into this region of the muscle fibre. Spikes were elicited by depolarizing pulses which were applied through another intracellular electrode in the same muscle fibre at some distance away from the junction. An external recording micro-electrode was used to explore the endplate region for discrete areas of spontaneous sharply rising external negativities. The potentials were recorded with direct coupled amplifiers.

When the external micro-electrode was localized at a site which yielded rapidly rising outside-negative miniature endplate potentials, the potential recorded during the spike was purely positive (Fig. 1*A*). On moving the micro-electrode in the long axis of the fibre less than 5μ from this site a brief dip developed in the positivity (Fig. 1*B*). The dip became larger when the electrode was moved slightly farther away (Fig. 1*C*). Negativity developed on moving the electrode another 30μ (Fig. 1*D*). Further displacement of the electrode by about 100μ resulted in a potential with a very large negativity (Fig. 1*E*). This last was the potential usually recorded outside the muscle fibre at non-synaptic regions.

Invasion of the junctional region by the directly evoked spike was confirmed by the records obtained with the intracellular micro-electrode (Fig. 1*F*). The externally probed site which gave the purely positive potential of Fig. 1*A* was shown to give rise to spontaneous negativities both before and after the spikes

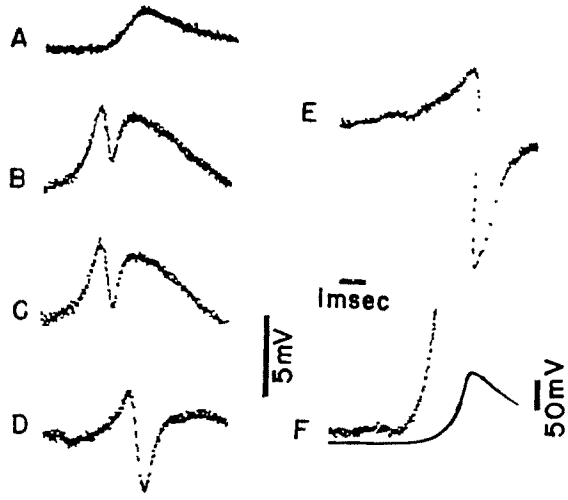

Fig. 1. Potentials at different sites outside endplate of single semitendinosus muscle fibre (*R. pipiens*) during passage of directly evoked spike. Latter is shown (*F*) as recorded intracellularly at endplate region with low amplification and simultaneously at gain used for extracellular recordings (*A–E*). The spikes were elicited by long, weak intracellular depolarization, to minimize stimulus artefact. Accordingly, latency varied in different records. *A*, positivity recorded at endplate site which also yielded maximal, steeply rising, externally negative miniature endplate potentials *B–E*, changes produced on moving external micro-electrode away from this site, as described in text. Amplitudes in different records cannot be compared, since they depend on closeness of micro-electrode to surface of membrane. Records retouched

were elicited, thus demonstrating the undamaged state of the recording site. Large negativities associated with spikes were never recorded from sites producing rapidly rising miniature end-plate potentials. At non-junctional regions external positivities were seen only in grossly damaged fibres.

The potential recorded by a closely placed external electrode is proportional to the membrane current[5], a negative potential indicating inward current and activity of the region probed by an external micro-electrode. Thus, the purely positive potentials recorded at restricted sites of the synaptic region indicate that these sites remained inactive during passage of the impulse while sites less than 100μ away were excited by the initial outward depolarizing local circuit current and gave rise to large external negativity. The brief dips in the positivity recorded at intermediate sites reflect the distribution of current flows in regions near both active and inactive membranes.

The same regions that are inactive during passage of a spike are capable, however, of becoming active, passing an inward current and generating the externally negative miniature end-plate potentials. The regions in which the external miniature end-plate potentials are largest and steeply rising are also the sites which are most sensitive to ionophoretic applications of acetylcholine[6]. It may be reasonably concluded, therefore, that the sites of the junctional membrane which generate miniature end-plate potentials and which respond by depolarization to chemical excitants are also the neurally excitable synaptic sites of the neuromuscular junction. They are electrically inexcitable, at least by stimuli representing a change in membrane potential of more than 120 mV., the spike amplitude of the muscle fibre.

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Absorption and Excretion of Copper in Mice

THE marked elevation of tissue copper that occurs in Wilson's disease is generally thought to be due to an increased absorption of copper from the gastro-intestinal tract[1,2]. In the work reported here, this concept was re-examined.

Swiss albino mice, 5–7 weeks of age, were kept on a diet providing 45–75 μgm. copper a day per mouse. Various amounts of copper, to which copper-64 was added, were then given orally or intravenously. Intravenous injections were given in a 3–5 sec. period; in oral administration, 0·2 ml. of the copper solution was passed into the stomach through a polyethylene catheter. Three mice from each group given a specific copper dose were bled at intervals for organ and serum radiocopper assays and at least 5 mice were used for collection of urine and fæces.

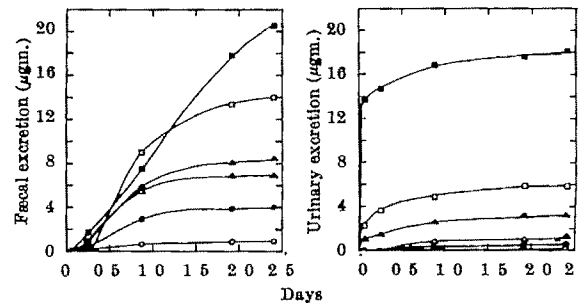

Fig. 1. Cumulative fæcal and urinary excretion of a copper dose after intravenous injection. ○, 1·7 μgm.; ●, 6·3 μgm.; △, 11 μgm.; ▲, 15·5 μgm., □, 25 μgm.; ■, 48 μgm.

The fæcal excretion of a copper dose after intravenous injection of amounts from 1·7 μgm. to 48 μgm. is shown in Fig. 1. The larger the dose of copper given, the greater was the amount of copper excreted; 96 μgm. injected under these conditions was lethal to half the mice within 1 hr. Since, after intravenous administration, copper appears in fæces principally through biliary excretion[3], it would seem that the amount of copper excreted in bile by the normal animal increases with increasing copper loads. In accord with this, following the injection of 0·15, 1·1, 3·2, 11 and 48 μgm. copper, at least 0·05, 0·63, 1·7, 6·7 and 15 μgm. respectively were found in the liver 10 min.–7 hr. after administration; hepatic

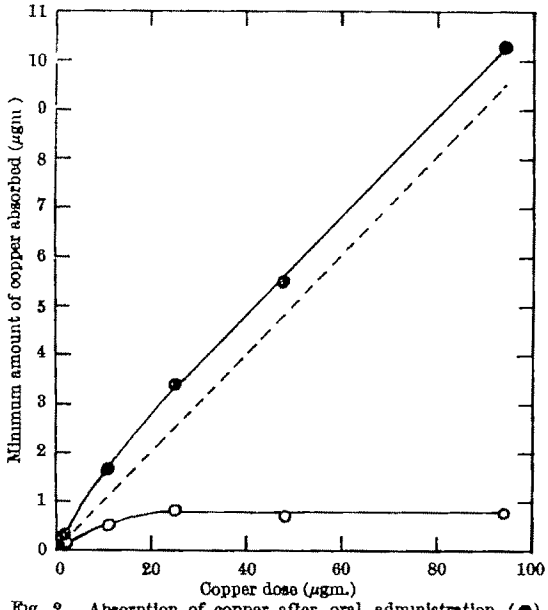

Fig. 2. Absorption of copper after oral administration (●). Dashed line passing through origin and parallel to absorption curve at doses of 25 μgm. or more represents hypothetical first-order process; ○, total absorption curve less the first-order absorption process

radiocopper then decreased and was afterwards found in the fæces. The concentration of copper in several bile samples obtained from animals killed 21 hr. after injection was found to increase with the size of the dose. In contrast, the concentration of copper in bile in Wilson's disease is in the normal range despite the presence of a markedly increased hepatic copper pool[2,3].

When mice were given 46 μgm. copper intravenously once a day for 6 days, the fæcal excretion of the last dose was similar to that of the first dose. Since only part of each dose was excreted before injection of the next, all preceding doses added to the total copper excretion. Thus, even with continued copper administration, the larger the copper load, the greater was the fæcal copper excretion.

With intravenous doses of copper of 0·15–11 μgm., only a small fraction of the dose appeared in the urine (Fig. 1). With 48 μgm., almost 30 per cent of the dose was excreted within 90 min.

The maximum amount of copper present in the body at one time represented the minimum amount of copper absorbed, and was estimated by subtracting the radiocopper present in the gastrointestinal contents from that in the total body. The results are shown in Fig. 2. It can be seen that the larger the dose the greater was the amount of copper absorbed. There appeared to be at least two processes involved in absorption: one appeared to be first-order and the other suggested an enzymatic mechanism.

When mice were injected with 46 μgm. stable copper intravenously or 92 μgm. stable copper subcutaneously once a day for 6 days prior to the oral administration of 1·7 μgm. labelled copper, the absorption of labelled copper was 75 and 58 per cent of normal, respectively. This finding is the converse of that found in Wilson's disease and is in accord with a dilution of the oral copper in the copper excreted into the intestinal tract from the injected load.

The results presented in this communication suggest that the elevation of tissue copper in Wilson's disease is probably due to a defect in biliary copper excretion rather than an increase in copper absorption.

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Growth of Mouse Femurs during Continual Centrifugation

THE size and shape of various parts of an organism are believed to be influenced by gravity[1]. One would expect the relative size and cross-section of supporting structures to increase with either an individual's height or the intensity of the environmental gravity.

Gray and Edwards first experimentally demonstrated such a gravitational influence on the cross-section shape of a growing structure by continual centrifugation of wheat coleoptiles[2]. Smith and his co-workers found that this would increase the size of chicken legs[3]. This report deals with the greater size and altered shape of mouse femurs.

This is one aspect of a long-range programme designed to study the influence of gravity on development. In this particular work, the *NLW* strain of five-week-old white mice were exposed to continual centrifugation at four times the Earth's gravity (4*g*). Duration of exposure was for periods of 1–8 weeks. The diet consisted of 'Purina' laboratory chow for mice and uncooked potatoes. These potatoes served as the only source of water. The centrifuge is described elsewhere[4]. A number of anatomical and physiological measurements were performed at the termination of exposure. The details of these determinations will be described later. The effect on the femurs of female mice was more striking than many other effects.

As can be seen from Fig. 1, experimental animals first lost mass and then continued to grow. At the end of one week they had returned to approximately initial body mass. The femurs, on the other hand, continued to grow just as fast, if not faster, than the controls. At later developmental stages, this rapid growth of experimental bones is not as pronounced. The femurs also assumed a more circular cross-section. Other factors being equal, such a change would give a supporting structure more strength with which to support gravity.

There are at least two possible explanations for the faster bone growth as compared to total experimental growth: mechanical stress and moderate starvation. Wolff's law proposes that mechanical force will evoke growth of the stressed portion of the bone[1]. The artificial increase in the force of weight during centrifugation could certainly cause such stresses. The initial decrease in body mass can be largely attributed to a lowered food consumption during the first week of centrifugation. In cases of moderate starvation, bone developmental responses demonstrate a lag, being in most cases among the last organs to show growth retardation[5]. Further work

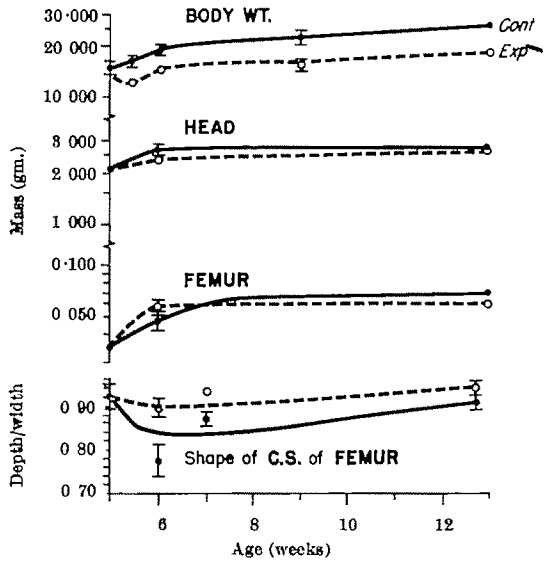

Fig. 1 Growth of various structures of the female white mouse during centrifugation at 4*g*. The experimental points at one week and eight weeks of exposure represent determinations with nine and seven animals respectively. These animals were killed at the appropriate time. Body masses at zero time are based on the averages for these 16 animals. Other values from zero time were for five mice which were killed at five weeks of age. Control values are from individual litter mates of the experimental animals. These animals grew in cages identical to those placed in the centrifuge. The index for shape of the femur cross-section is calculated by dividing the shorter thickness (depth) by the greater thickness (width). Solid lines are for control curves and broken lines for experimental curves. Standard errors are indicated by the extent of the vertical lines above or below the experimental points When these errors are not shown for the animals at two and four weeks it is because results are based on less than three measurements. In other cases the extent of the error is less than the extent of the points

is necessary to demonstrate the actual cause or causes for the relative increase in size of femur. Starvation alone does not seem a very plausible explanation for change in cross-section. The shorter axis of the bone shaft, being mechanically weaker, should be the most susceptible to a growth-enhancing stress, thus producing greater roundness.

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Evidence of a Specific Action on the Central Nervous System by the Esters of Some Plant Growth Regulator Acids

THE pharmacology of plant-growth regulator acids has been little studied; nevertheless, these substances which react in minute traces in green plants possess intense biological activity. We have prepared various esters of these acids with the intention of studying their action on the central nervous system. Dimethylaminoethanol was chosen as the agent of esterification because Pfeiffer *et al.*[1] had demonstrated that this amino-alcohol has stimulating effects. We have synthesized the dimethylaminoethylic esters of the following acids: phenoxyacetic acid and some of its derivatives substituted on the aromatic nucleus (4-chloro-, 4-fluoro-, 2,4-dichloro-, 2-methyl-4-chloro-compounds), naphthalenic acid, α- and β-naphthoxyacetic acid, 3-indolylacetic acid, phenylpropionic acid.

The method of preparation and the physical constants of these products have already been described[2].

Pharmacological study of these different substances has shown that they possessed a specific action on the central nervous system, principally at the level of the hypothalamus[3]; this property is not due exclusively to dimethylaminoethanol since it can be substituted by other amino-alcohols; but on the other hand the acidic group seems to be the important part of the molecule. Among the compounds studied, the dimethylaminoethylic ester of *para*-chlorophenoxyacetic acid (which we term 235 *ANP*) was particularly active.

The oral *L.D.*50 of 235 *ANP* is 1,750 mgm./kgm. Rats treated chronically at 400 mgm./kgm. a day during three months and longer tolerate this dose without any blood, hepatic or renal troubles.

(*a*) The specific action on the central nervous system was shown in the following experiments:

Fish (*Cyprinus vulgaris*, *Phoxinus phoxinus* Linné) immersed in a 0·5/1,000 solution of the 235 *ANP* in water exhibit convulsive seizures and dilation of chromatophores. The Siamese fighting fish, even in the absence of a male congener, develops its fins, expands its chromatophores, and attains a fighting temperament.

In mice, autographic records showed that after administering 150 mgm./kgm. subcutaneously of 235 *ANP* for ten days a significant increase in spontaneous activity could be observed.

In the rabbit, 100 mgm./kgm. of 235 *ANP* injected intravenously significantly lowered the threshold for seizures from intravenously infused metrazol.

(*b*) The specific effect of 235 *ANP* on the hypothalamus was demonstrated with the help of B. Minz's method[4].

It is known that the application of a piece of filter paper of 5 mm.^{2}, steeped in adrenaline solution (5/100), on the fronto-parietal cortex of a female rabbit causes arterial hypertension and uterine contractions, due to the secretion of hypertensive and oxytocic substances by the hypothalamus[5].

The same reactions occur in a hypophysectomized animal; but they are suppressed if the hypothalamus is destroyed[6].

We have confirmed the correctness of this method, which permits us to study the effect of psychotropic drugs on the hypothalamus[7].

We have observed that the 235 *ANP* provokes a considerable stimulation of the hypothalamic area (Fig. 1).

The other compounds, derived from plant-growth regulator acids which were prepared, are still being studied; so far we have already examined the effect of the substances on the chromatophores of fish, on glycæmic regulation and their relationship with catecholamines and serotonin.

Already the results achieved suggest research on the manner in which the esters of plant-growth

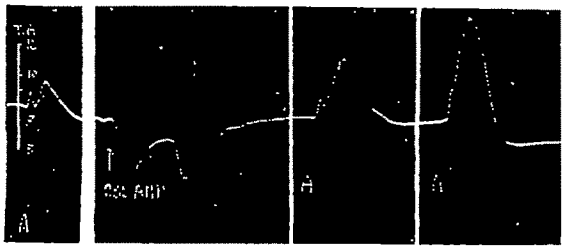

Fig. 1. Blood pressure record *A*, Application of adrenaline on the fronto-parietal cortex of a rabbit. After intravenous injection of 235 *ANP* (50 mgm./kgm.) one can observe a considerable increase of the hypertensive reaction

regulator acids exert their stimulation. So far three possibilities have been examined.

(*a*) The potentialization of the central action of adrenaline by a stimulation of the cerebral cortex induced by the drug. (*b*) Direct action on the hypothalamus and hypophysis or on the level of catecholamines and serotonin, which are found in great quantities in this region. (*c*) Regularization by 235 *ANP* of the metabolic activity of the hypothalamic region could explain some of the powerful actions of the drug.

Pharmacological and biochemical studies are now being carried out with the view of explaining the mechanism of action of 235 *ANP* and other esters of plant-growth regulator acids, which seem to act as metabolic regulators at the level of the hypophyseal-hypothalamic region.

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HÆMATOLOGY

Glutathione Stability Test in Hæmoglobin *E* – Thalassæmia Disease

HÆMOGLOBIN *E* – thalassæmia disease represents a double heterozygous state with reference to genes for hæmoglobin *E* and thalassæmia. Studies on glutathione stability which have recently provided valuable information regarding the cause of hæmolysis as it occurs in drug-induced hæmolytic anæmia and in hereditary non-spherocytic hæmolytic anæmia have not so far been done in hæmoglobin *E* – thalassæmia disease. In the present communication, 20 cases of hæmoglobin *E* – thalassæmia disease were investigated with reference to the behaviour of their erythrocytically reduced glutathione-level when incubated *in vitro* with acetylphenylhydrazine. The relevant features of these 20 cases are given in Table 1.

Table 1. RELEVANT FEATURES OF TWENTY CASES OF HÆMOGLOBIN *E* – THALASSÆMIA DISEASE

	Mean	Range
Age (yr.)	5·8	1–28
Hæmoglobin (gm. per cent)	6·44	3·4–9·28
Hæmoglobin *F* (per cent)	23·8	13·0–50·0
Reticulocytes (per cent)	8·1	2·1–17·0

The method employed was essentially the same as originally evolved by Beutler[1]. In order to increase the sensitivity of the test, 4 mgm. of glucose was added to 1 ml. of blood as suggested by Szeinberg *et al.*[2] and later adopted by Beutler[3]. With this method, the range of reduced glutathione destruction in the normal Bengalee population varied from 1 to 10 mgm. per 100 ml. of erythrocytes. Two apparently normal persons, however, showed unstable glutathione-level, indicating that a certain proportion of Indians has such glutathione instability similar to the state of instability reported first in people of negroid origin[5,6] and later in those of Syrian, Iranian and Jewish[7] extraction. In contrast to the normal findings, the pattern in hæmoglobin *E* – thalassæmia disease was different (Table 2). In 12 out of 20 cases, the glutathione destruction exceeded 30 mgm. per 100 ml. of erythrocytes and in 9 the post-incubation level was lower than 30 mgm. In all the patients, both sensitive and non-sensitive, glucose-6-phosphate dehydrogenase activity of red cells was, however, found to be high.

Table 2. RESULTS OF GLUTATHIONE STABILITY TEST IN NORMALS AND IN HÆMOGLOBIN *E* – THALASSÆMIA DISEASE

	No. of subjects	Reduced glutathione-level in mgm. per 100 ml. of erythrocytes			
		Range		Mean	*S.E.*
Non-sensitive normals	20	Before	47–95	65·05	2·1483
		After	40–89	61·60	2·6173
Non-sensitive hæmoglobin *E* – thalassæmia	8	Before	19·6–92	54·48	8·0291
		After	17·6–92	51·70	7·4065
Sensitive hæmoglobin *E* – thalassæmia	12	Before	41·5–82	63·275	1·8039
		After	0–50	27·5	5·2448

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Blood Groups of Selected Aboriginal and Indigenous Populations

THE Laboratory of Physical Anthropology at Yale is investigating the distribution of the following genetic traits in various populations of Primates, including man: the blood groups, the serum transferrins (β-globulins), haptoglobins, and hæmoglobin

variants. This is a report of the blood types in three of the human populations investigated.

(*A*) *Kapauku Papuans*. Seventy samples of venous blood were obtained from the inhabitants of the West Central Highlands of New Guinea. These people occupy an area between 135° 25′ and 137° longitude and 3° 25′ and 4° 10′ south latitude. They are referred to as *Kapauku* by coastal inhabitants of Netherlands New Guinea and call themselves *Me*. The frequencies are reported in Table 1. The discovery of two Diego-positive individuals is not wholly unexpected for this area. It has not, however, been reported before. The frequencies of the ABO(H) blood types are different from those published for other Papuan groups by Sanger *et al.*[1] and Bijlmer[2-4]. No attempt was made to select a random sample, since our research is aimed at relating the social structure of aboriginal human groups to gene frequencies. Therefore, blood samples are taken, when possible, from individuals that are related to one another by some network of social relations. Thus, the fact that the ABO(H) frequencies differ radically from others reported from Papua, particularly in the unusually low frequency of type A, may be due to our deliberate attempt to select related individuals. However, the Kapauku are an isolated people, a factor which must be considered.

Table 1. KAPAUKU PAPUANS

A_1	7	K+k+	1
O	52	K−k+	69
B	11	Di^a+	2
M	1	CCDee	50
N	52	CcDEe	13
MN	17	CcDee	4
Fy^a+	70	ccDEe	1
U+	70	ccDee	1
P+	25	C^wcDEe	1
Kp^b+	70		

Nijenhuis[5] reports the presence of the Henshaw (He) antigen among Papuans. Fifty-one of our samples were tested with an He reagent. All were Henshaw-negative.

(*B*) *Indigenes of Providencia Isla, Colombia*. Providencia is an island off the coast of Colombia. Forty-two samples of venous blood were drawn and typed. The results are reported in Table 2. The population is a mixture of Indian, Negro and White. All C-positive bloods were C^w negative. Published frequencies of blood types from Colombia report only Indian populations, thus comparisons are not possible at present.

Table 2. INDIGENES OF PROVIDENCIA

A_1	3	K+k+	1
A_2	2	K−k+	41
O	23	Kp^b+	42
B	14	ccDee	20
M	12	CcDee	13
N	9	ccDEe	4
MN	21	ccddee	2
Mg−	42	CCDee	1
P+	39	CcDEe	1
Fy^a−	42	$ccD^{u}ee$	1
Di^a−	42		

(*C*) *East Africans*. One hundred and eighty-nine bloods from several Kenya tribes were tested. Table 3 reports the frequencies found in the entire group, which consisted of Masai, Wakamba, Luo, Kikuyu, Giriama and Pokomo tribesmen. The Masai samples were drawn at Kajiado Hospital, which serves the Masai tribe. The Wakamba samples were drawn at the village of Mulutui, near Kibwezi railroad station. The rest were drawn from patients at the George VI hospital in Nairobi and the Coast Province Hospital in Mombasa.

Table 3. EAST AFRICANS

Blood types	Wakamba	Masai	Coast tribes Pokomo, Giriama	Upland tribes Luo, Kikuyu
A_1	7	17	7	2
A_2	5	3	1	0
O	21	38	21	8
B	16	24	11	1
A_1B	0	0	1	0
A_2B	1	4	1	0
ccDee	37	62	27	8
CcDee	7	10	4	2
ccDEe	5	9	7	0
$ccD^{u}ee$	1	0	0	0
Ccddee	0	1	0	0
CcDEe	0	1	2	1
ccDee	0	2	0	0
CCDee	0	1	0	0
ccddee	0	0	2	0
M	14	37	11	3
N	8	10	9	4
MN	28	39	22	4
K−k+	50	86	40	11
K+k+	0	0	2	0
P+	48	84	40	9
P−	2	2	2	2
Fy^a+	0	2	4	0
Fy^a−	50	84	38	11
U+	50	86	42	11
Di^a−	50	86	42	11

The frequencies are generally similar to those reported by Foy *et al.*[6] and Allison *et al.*[7]. The number of A_2B samples seems unusually high and cannot be explained by our non-random method of sampling. Each A_2B individual is clearly unrelated to the others. All C-positive bloods were tested and found to be C^w negative.

The co-operation of colleagues at the Nairobi Medical Research Laboratories, Dr. L. M. J. Couvee of Bialk, New Guinea, and Dr. Alvarao Garcia N. of San Andres, Colombia, is gratefully acknowledged. Dr. Fred Allen, Boston Blood Grouping Laboratory, provided the anti-Mg sera, and Dr. M. Layrisse of Caracas, Venezuela, provided the anti-Di^a sera. This research is supported by *RG* 6053 of the United States Public Health Service, and was aided by the Wenner-Gren Foundation and United States Atomic Energy Commission Grant *AT*-(11-1)-405 to the University of Michigan.

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Interrelations of Serum Protein Fractions in Normal Humans

RECENT advances in the study of protein–protein interactions[1], including the haptoglobin–hæmoglobin[2] and protamine–fibrinogen[3] complexes, have stimulated interest in serum protein abnormalities such as macroglobulin aggregation[4]. Although the serum proteins frequently undergo significant alterations with the onset of disease and yield characteristic patterns on electrophoretic separation, little is known about their interdependence in the healthy state. The present report describes an electrophoretic examination of interrelations between protein fractions in the course of variations within the normal human range.

Blood was obtained from 100 healthy persons between the ages of sixteen and seventy-two. There were equal numbers of males and females. Serum proteins were separated by cellulose acetate electrophoresis and stained with lissamine green. The dyed fractions were eluted, and the concentrations of albumin and α_1-, α_2-, β-, and γ-globulins then calculated by comparing the quantity of eluted dye with the known dye uptakes of standard preparations. Since for each sex the means between the corresponding fractions were not significantly different, the two groups were combined. Table 1 summarizes the results.

Table 1. MEANS AND STANDARD DEVIATIONS OF SERUM PROTEIN FRACTIONS OF 100 NORMAL PERSONS

	Albumin	Globulins α_1	α_2	β	γ
Mean (gm /100 ml)	4 07	0·30	0 78	0 92	1·29
± Standard deviation	0·37	0 04	0·11	0 12	0 23

The five fractions were approximately normally distributed and, using standard statistical procedures, the partial correlation coefficients of the ten possible pairs were determined. Table 2 indicates that the most significant values were obtained for the pairs derived from the α_1-, α_2-, and β-globulins. It is noteworthy that the least significant values are those of pairs involving γ-globulin of reticulo-endothelial origin with the other proteins of hepatic origin.

Table 2. PARTIAL CORRELATION COEFFICIENTS OF NORMAL SERUM PROTEIN FRACTIONS

	Globulins α_1	α_2	β	γ
Albumin	−0 183	−0·145	0 210	0 031
α_1-Globulin		0 987	0·317	0 067
α_2-Globulin			0 247	−0·046
β-Globulin				0 029

The virtually perfect correlation between α_1- and α_2-globulins is explicable in terms of similarity of constitution. Both fractions comprise glycoproteins and lipoproteins, and have sedimentation rates close to 3 Svedberg units[5]. Similarly, the α_1-globulin–β-globulin correlation can be considered to result from the lipid moiety common to each; both sediment at 5 S[5]. The lower correlation between α_2- and β-globulins may be attributable to the glycoproteins and lipoproteins contained in each. Both sediment in the ultracentrifuge at 7 and 12 S[6].

The most significant negative correlation was found for albumin–α_1-globulin. In this connexion Schultze[7] has noted that some α_1-globulin is carried by albumin under paper electrophoretic conditions, while Tata[8] has demonstrated the existence of a prealbumin–α-globulin complex. Of interest is the present finding that the albumin–γ-globulin relation is not inverse as it frequently is in disease. It is certain that the behaviour of some protein fractions as dependent variables is, like their distribution[9], governed by experimental conditions.

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PATHOLOGY

A New Factor in the Use of Antibiotics

NEW clinical problems have arisen from the intensive use of antibiotics during the past twenty years. During this time, several aspects of those problems have been studied in an attempt to elucidate the various mechanisms related to the sensibility, resistance and dependence of micro-organisms as well to the mode of action of antibiotics.

When observations are made, not *in vitro*, but in host organisms, the interpretation of the phenomenon becomes more confused due to the many variables taking part in the problem and to the effect of antimicrobial activity added to humoral defensive responses of the host against the pathogenic agent. In these responses, both the drug effect breaking down the equilibrium of normal phagocytic activity and the formation of antimicrobial antibodies are often found.

Irregularities in the activity of antibiotic suspensions have been observed by us between serum of patients having different levels of antibiotic and their specific antimicrobial activity, as well as when looking at the behaviour of bacteria against the antibiotics or their associations. Certain irregularities were found in associations of antibiotics of known *in vitro* bactericidal activity when this activity was greatly reduced *in vivo*, during treatment of the parasitized organism. In spite of adequate dosing, sera of various patients with analogous symptoms and under the same treatment showed differences in their antimicrobial activity, which could not be explained satisfactorily.

These abnormalities could not be easily explained either by differences of antibiotic absorption or by different physiological responses of the human body, either by sex or by age, constitution, etc. It becomes necessary to consider a very representative factor common to the characteristics of previous treatments.

These observations lead us to think of the existence of antagonistic substances, not natural, but of a circumstantial origin in the host organism and capable of being formed as a response to an external stimulus promoted by the drug.

According to this hypothesis, experiments were carried out with various antibiotics, 'Kanamycin' being the first studied. This substance was injected into rabbits through peritoneal and endovenous routes at regular intervals for one month. Doses were steadily increased from 10 to 200 mgm. At the end of each treatment, a total amount of 450 mgm./kgm. had been injected into each rabbit, 12 animals having been used in each lot. The doses of 'Kanamycin' used were not toxic to the rabbits.

Checks of anti-'Kanamycin' activity of normal fresh serum were provided, using samples of blood extracted by heart-puncture from the test animals in advance of their treatment.

The technique used for studying the anti-'Kanamycin' activity of sera was as follows: 0·2 ml. of rabbit serum was placed in small test-tubes of about 1·2 ml. capacity and another 0·2 ml. into 400 ml. solution of 'Kanamycin' was added. A series of two-fold dilutions followed until a 0·097 concentration of 'Kanamycin'/ml. was obtained. Therefore, concentrations of the antibiotic in the assay ranged from 200 to 0·097γ. For each series a 'time of contact' was established (Fig. 1). Parallel tests using sera from untreated rabbits were performed for every series as control of normal sera activity. The series were finally completed—at the end of every conventional 'time of contact'—with 0·2 ml. of a bacterial suspension of *Staphylococcus aureus* Heatley (Oxford 657). The bacterial suspension, a 10^{-5} dilution from an 18-hr. culture in nutrient broth at 37° C., was prepared according to techniques already described (Portolés, 1960). Experiments were repeated three times and the results are recorded in Fig. 1.

As seen in Fig. 1, the results have been expressed as the minimum inhibitory concentration of 'Kanamycin' per ml. required to avoid the development of *S. aureus*. From these results it is concluded:

(*a*) That growth of *S. aureus* was inhibited by 0·28γ ml. of 'Kanamycin' using nutrient as substrate. 0·28γ ml. was taken as the standard value of 'Kanamycin' activity; (*b*) that normal rabbit sera had a bacteriostatic activity which was equivalent after proper calculations to 0·19γ ml. of 'Kanamycin'; (*c*) that the series of dilutions of 'Kanamycin' in normal rabbit sera gave an inhibition of *S. aureus* at concentrations ranging from 0·097γ to 0·12γ ml.; (*d*) that the series of dilutions of 'Kanamycin' in immuno-sera obtained from rabbits previously treated with the antibiotic decreased the inhibitory effect of *S. aureus* development. The experiments showed that in this case greater amounts of 'Kanamycin' were required to obtain an effect similar to that of 0·28γ ml. in nutrient broth. The values increased with the 'time of contact' from 6 35γ ml. after 4 hr. to 24·63γ ml. after 24 hr.

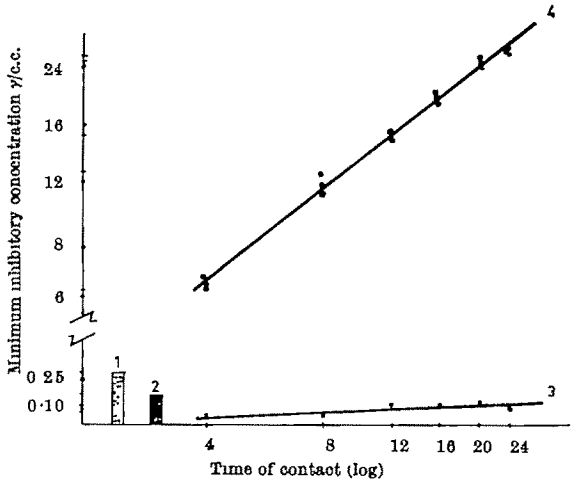

Fig. 1. Susceptibility of *S. aureus* Heatley (Oxford 657) (1) to 'Kanamycin' in nutrient broth; (2) to normal rabbit serum; (3) to 'Kanamycin' diluted at various concentrations in untreated rabbit serum; (4) to 'Kanamycin' diluted at various concentrations in rabbits' sera obtained from animals previously injected with 450 mgm./kgm. of 'Kanamycin' at regular intervals during one month

Intradermic tests were also made in the treated animals, using 0·15 ml. standard solutions of the antibiotic at 40·0, 20·0, 10 0, 5·0, 1·25, 0·62 and 0·31γ ml. in distilled water, pyrogen-free, as well as 0·15 ml. of saline solution. All tests were negative.

From these results it seems conclusive that in the sera of rabbits previously treated with 'Kanamycin' there exists a substance which specifically inactivates the antibiotic. The substance apparently acts proportionally to the 'time of contact', for the antibiotic activity of 'Kanamycin' on *S. aureus* is remarkably reduced. The nature of the agent responsible for this blocking action against the antibiotic is not understood. Experiments made up to the present have demonstrated, however, that it cannot be included in the group of precipitins, but more precise results have been obtained by deviation complement tests. The latter results have shown the presence of certain specific anti-'Kanamycin' antibodies at 1/5 sera dilutions against concentrations of 10 mgm. 'Kanamycin' per ml.

The presence of this new factor in the sera of animals treated with an antibiotic suggests the importance of considering in the therapeutics of antibiotics the close interrelationship between the antibiotic and host-organisms as well as the possible influence of the latter relationship in the so-called 'resistance' to antibiotics.

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A Rapid Method of preparing Pure Serum Gamma-Globulin

IN the course of investigating various methods of isolating skin-sensitizing antibodies from human allergic serum, a procedure has been devised which could be applied to the rapid preparation of other 7*S*-type gamma-globulins in a high degree of purity. The technique employs diethyl amino ethyl cellulose anion exchanger, prepared according to the method used by Peterson and Sober[1], to adsorb out of the serum all proteins other than 7*S*-type gamma-globulins. For this purpose, a batch process has proved superior to the more widely used column chromatography, because of its greater speed and ease of manipulation.

A small portion (2·5 ml.) of human serum, previously dialysed for 16 hr. at 4° C. against 1 litre of sodium phosphate buffer (*p*H 7·5, 0·01 *M*) containing 0·015 *M* sodium chloride, is added dropwise with continuous stirring to moist diethyl amino ethyl cellulose (17 gm. wet weight) which has been equilibrated and mixed with 2·5 ml. of similar buffer

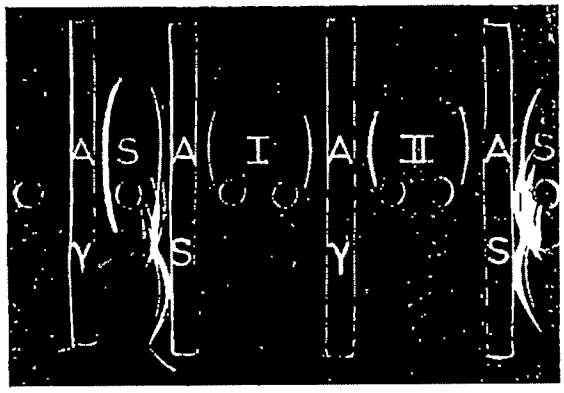

Fig. 1. Immunoelectrophoretic patterns of human serum (*S*) and purified gamma-globulin fractions (I and II) after testing with rabbit anti-human serum (*A/S*) and anti-human gamma-globulin (*A/γ*)

pre-cooled to 4° C. After the mixture has stood at 4° C. for 5 hr., a further 5 ml. of buffer is added with stirring and the resultant slurry is centrifuged in a cooled tube at 3,000 r.p.m. for 15 min. The supernatant (fraction I) contains highly pure gamma-globulin in a concentration of the order of 100–200 mgm./100 ml. (comprising a yield of approximately 50 per cent). A slightly less pure preparation (fraction II) is obtained by a repeat rinse of the exchanger with a further 5 ml. of phosphate buffer (0·01 *M*), still at *p*H 7·5.

The immunoelectrophoretic patterns shown in Fig. 1, obtained by testing with rabbit anti-human serum and anti-human gamma-globulin, reveal fractions I and II to be composed entirely of gamma-globulin. Small amounts (1–3 per cent) of a beta-globulin contaminant—probably siderophilin—can be detected, however, by testing with a more potent specific antiserum against alpha- and beta-globulins.

Quantitative gel-diffusion precipitin analyses with specific rabbit-antisera against alpha$_2$-glycoprotein and 19*S*-type gamma-globulin (kindly carried out by Dr. J. F. Soothill) demonstrated that the gamma-globulin fractions I and II were completely free from these high-molecular weight proteins. This finding was substantiated by *iso*-agglutinin titrations, employing type A and type B cells, which failed to detect any activity in either fraction although the initial serum possessed a 1/32 titre against type *A* cells and a 1/16 titre against type *B* cells.

As seen in Fig. 2, analytical ultracentrifugation in a Spinco model *E* machine also failed to reveal any 19*S*-type component (in fraction I and II solutions containing approximately 300 mgm. protein/100 ml.).

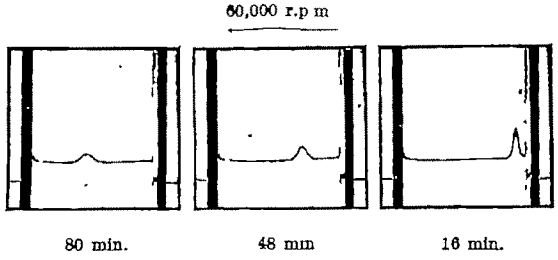

Fig. 2. Ultracentrifugal patterns of gamma-globulin fraction I concentrated two-fold by ultrafiltration. Protein concentration, approximately 300 mgm./100 ml., solvent, sodium phosphate buffer (*p*H 6·9, 0·06 *M*) containing 0·15 *M* sodium chloride; speed, 60,000 rev./min., temperature, 20° C.; $S_{20,w}$ = 6·9*S*

It is also interesting to note the absence of 10*S*-type component, which often appears in gamma-globulin preparations obtained by low-temperature procedures with ethanol and ether; nor could any 4·5*S* component be detected.

The batch process outlined above can be speeded up by omitting the initial overnight equilibration of serum with buffer, although this results in the sacrifice of a slight degree of purity of the gamma-globulin obtained. This modification offers an additional advantage, however, in that the whole procedure can then be more readily carried out under aseptic conditions. Such an adaptation has proved most useful in the preparation of skin-sensitizing antibody fractions (unpublished work), which have to be assayed by passive transfer into human recipients.

Summarizing briefly, the method described provides a convenient way of obtaining small quantities of purified gamma-globulin quickly and with minimum manipulation by a relatively mild treatment. It seems probable that it could be extended to preparations on a considerably larger scale.

I acknowledge the interest Prof. J R. Squire has taken in this work. Ultracentrifugal analyses were carried out by Miss P. Ratcliff on a machine generously provided by the Rockefeller Foundation, New York.

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Inhibition of Ehrlich Ascites Tumour Growth by Surface-active Agents

A RECENT communication by Townsend, Morgan and Hazlett[1] suggests that admixture of 10-hydroxy-Δ^2-decenoic acid with tumour cells will prevent growth of the cells on inoculation into mice. Similar results have been obtained by this group with other dicarboxylic acids[2]. In the course of work on the action of surface-active agents on tumour cell membranes[3], we have noted similar inhibition of growth of Ehrlich ascites tumour cells.

Ehrlich ascites tumour was grown in Swiss mice and removed after seven days. The cells were washed in sterile 0·15 *M* saline and resuspended in the same solution. Surfactant was added to the desired concentration, an aliquot removed for counting[4], and portions of the remainder used to inoculate mice. The final concentrations of surfactants were those known to foster 100, 99, 90 or 50 per cent staining by nigrosin. Groups of five mice were used for each concentration. The survivals of mice injected with our strain of Ehrlich ascites, untreated, are shown in Table 1.

Table 1. SURVIVAL OF MICE INOCULATED WITH GRADED NUMBERS OF UNTREATED EHRLICH ASCITES CELLS

Log No. cells	No of mice (tumours/inoculated)	Days to death from tumour*
1	0/7	†
2	0/10	†
3	0/10	†
4	3/5	23–80 (42)
5	5/5	15–21 (18)
6	5/5	15–21 (19)

* Figures in parentheses are averages.
† Survivors killed at 85 days and no tumour found.

Table 2. SURVIVAL OF MICE INOCULATED WITH GRADED NUMBERS SURFACTANT-TREATED EHRLICH ASCITES CELLS

Surfactant	Log No unstained cells*	% Staining	No. of mice (tumours/inoculated)	pH	Days to death from tumour‡
None	6	0	8/8	6 6	13–30 (20)
Sodium lauryl sulphate	–	100	0/5	6 5	†
	4	99	0/5	6·4	†
	5	90	0/5	6·5	†
	5·7	50	3/5	6·4	25–46 (35)
'*DM*-710'	–	100	0/5	6·2	†
	4	99	0/5	6 2	†
	5	90	0/5	6 1	†
	5·7	50	0/5	6 2	†
Lauryl pyridinium chloride	–	100	0/4		Toxic
	4	99	0/4		Toxic
	5	90	0/4		Toxic
	5 7	50	0/4		Toxic

* Log total cells = 6. † Killed at 68 days and no tumour found ‡ Figures in parentheses are averages.

As is apparent from Table 2, admixture of sodium lauryl sulphate caused an inhibition of tumour formation which is roughly comparable to the increased ability of the cells to take up dye, although there is more than a ten-fold difference in the minimum number of unstained ('viable') cells necessary to produce ascites. In contrast, when the non-ionic surfactant 'Igepal *DM*-710' (a polyoxyethylated nonylphenol of molecular weight approximately 1300) was employed, no tumours were observed at the end of 68 days, even when the final concentration of unstained cells was 500,000. Cells treated with lauryl pyridinium chloride proved toxic to the animals. 10-Hydroxydecenoic acid, in citrate buffer of *p*H 5·5, permits only 37 per cent of the cells to pick up dye (acid concentration 3 mgm. per ml.).

At *p*H 4·3 in phosphate buffer, initially 10 per cent of the cells stained. The figure was not changed immediately by addition of 10-hydroxydecenoic acid, but after 20 min. 70 per cent of the cells exhibited staining. Morphologically, there was no lysis. The cells were wrinkled yet intact as compared to the loss of cytoplasm after treatment with sodium lauryl sulphate or 'Igepal *DM*-710'. Details of these changes will be reported elsewhere.

Attempts were made to inhibit tumour-growth *in vivo* by intraperitoneal administration of sodium lauryl sulphate and '*DM*-710'. Mice were injected with 10^6 cells. One week later all the ascitic fluid obtainable was removed by syringe aspiration. Each mouse was injected with 1 ml. 0·014 *M* surfactant. Samples of ascitic fluid were withdrawn 24 hr. later, and nigrosin uptake determined. The controls and animals treated with sodium lauryl sulphate showed 3 per cent dye uptake; the '*DM*-710' treated, 12 per cent. The control animals died in an additional eight days (average), those treated with sodium lauryl sulphate in four, and those treated with '*DM*-710' in two. All had typical tumour at autopsy.

In view of the results obtained to date, it appears that while inhibition of tumour growth can be obtained with a number of agents, the mode of action of these substances differs. One might speculate that some agents act by altering the cell surfaces, while others may complex vital proteins, inhibit enzymes, or interfere with fatty acid metabolism. It is obvious that alterations in the ability of cells to take up dye are not always correlated with death of the cells[5].

This work was supported in part by grants from the U.S. Public Health Service (*CY*-3475(C2)), Damon Runyon Memorial Fund (*DRG*-426*A*) and the Leukemia Society, Inc. Surfactants were gifts from E. I. DuPont de Nemours and Co., Antara Chemicals and Hooker Chemical Co. The 10-hydroxydecenoic acid was a gift from Prof. Butenandt of Munich.

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ANATOMY

Intracellular Canals in Human Sweat Glands

HIBBS[1] has demonstrated the existence of intercellular canaliculi in human eccrine sweat glands by electron microscopy and found them to be situated in the coiled secretory portion of the glands only. He was unable to recognize intracellular canaliculi, however. These intercellular canaliculi can be seen from his illustrations to be lined by a plasma membrane which shows many micro-villi projecting into the lumen. This lumen contains a moderately homogeneous matrix of low density and several indistinct granular profiles, possibly in the nature of a secretion.

The present communication describes the finding of structures resembling intracellular canaliculi in human eccrine sweat glands. As in Hibbs's cases these were found in the coiled secretory portion of the gland. But in contrast to those in his cases, which were from adult Negro volar skin, they were found in the abdominal skin of a 5-year-old white girl; the biopsy being taken immediately on making the incision for a nephrectomy.

The appearances of these structures are exemplified by that shown in Fig. 1. The lumen (*X*) can be seen to be surrounded by a plasma membrane folded into many micro-villi. It also contains a low-density matrix and several more dense but ill-

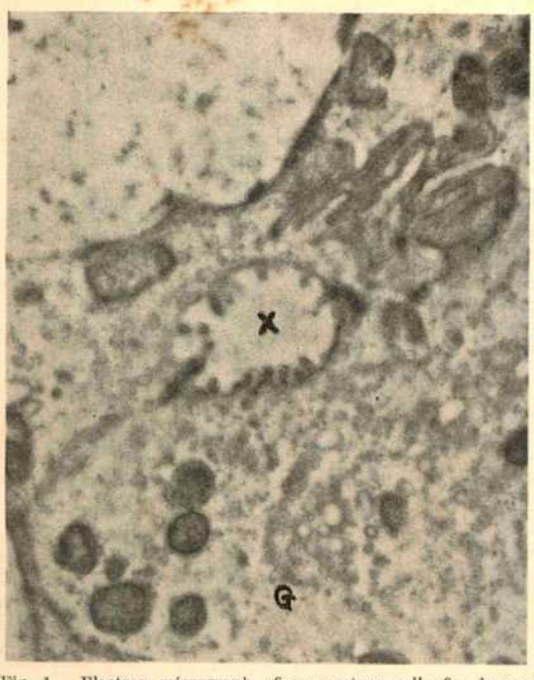

Fig. 1. Electron micrograph of a secretory cell of a human eccrine sweat gland (abdominal skin). The structure (*X*) shows the typical appearances of an intercellular canal, but lies wholly within the cytoplasm. The adjacent structure (*G*) is the Golgi complex. (Palade's osmium tetroxide fixative. × 10,800)

defined granular profiles. These appearances are virtually identical with those reported by Hibbs. It can also be seen from the illustration that the structure lies wholly within one cell. That is to say, cell boundaries are not seen anywhere near it, nor more importantly, are any contiguous with its limiting membrane. It is of interest, and may also be of significance, that it is lying close to the vesicular profiles of the Golgi complex (*G*).

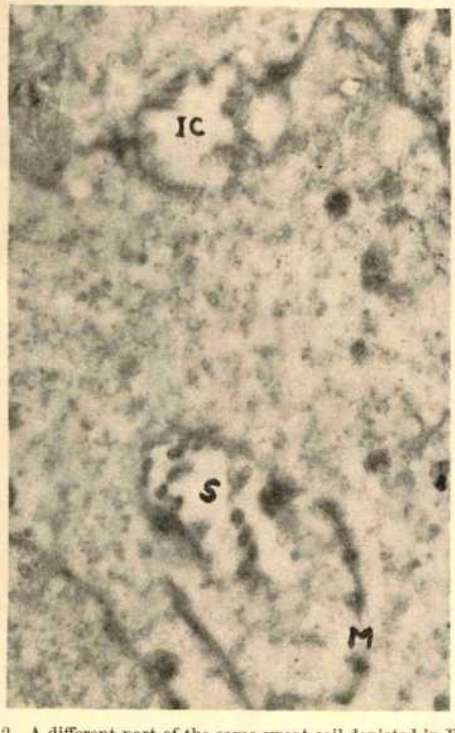

Fig. 2. A different part of the same sweat coil depicted in Fig. 1. *IC*, intercellular canal; *S*, intracellular sinus or canal; *M*, double membrane with desmosomes. (Palade's osmium tetroxide fixative. × 13,400)

In Fig. 2 can be seen an intercellular canaliculus (*IC*) together with a similar structure (*S*) apparently lying entirely within the cytoplasm of the cell. That this is not a true intracellular canaliculus is suggested by its close proximity to the double cell membrane (*M*), which can be seen to possess desmosomes.

By definition a canaliculus must commence and end somewhere. It may be that the structure described here joins two intercellular canaliculi or joins an intercellular canal to the lumen of the coil. On the other hand, it might take the form of a blind sinus, communicating at one end with the lumen or with an intercellular canal, the blind end lying wholly within the cytoplasm.

It has not yet been possible to decide whether these structures are intercellular canaliculi or merely blind sinuses, or whether they are permanent or temporary.

I wish to thank Dr. I. Friedmann and the Institute of Otology, University of London, for putting the facilities of their electron microscope at my disposal.

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Lymph Node Reactivity to Homografts of Cancellous Bone

N. A. MITCHISON[1] first showed that the power to transfer immunity caused by lymphosarcoma *6C3HED* to non-susceptible mice is confined to the lymph nodes draining the site of implantation. Billingham *et al.*[2] also found that in mice the tissues of the host which have the power to transfer immunity to skin homografts are the regional nodes and to a lesser degree the spleen. Gallone[3] and his colleagues had previously shown that an increase in pyronin-staining cells occurred in the lymph nodes draining skin homografts. This work was confirmed and extended by Scothorne and McGregor[4], who showed that in rabbits a considerable increase in weight occurred in lymph nodes draining homografts, but not autografts, of skin. Further, they showed that after homografting, great accumulations of 'large lymphoid cells' appeared in the cortex and to a lesser extent in the medullary cords of the draining lymph nodes. The cellular response waned rapidly with the onset of graft destruction, and within two days the nodes were largely depleted of pyroninophilic elements. Radici and Piredda[5], also using rabbits, have described how, five days after a skin homograft, the reticular cells of the medullary cords of the first regional node are in large part replaced by pyroninophilic cells. Craigmyle[6], however, using cartilage, was able to show that the weight changes and cytological alterations in the regional lymph nodes occurred, but only in response to second-set homografts and first-set heterografts of cartilage. He concluded that cartilage in the rabbit is only mildly antigenic.

The reaction of the first regional lymph node to a constant weight (95–100 mgm.) of fresh cancellous bone removed from the ilium of five albino rabbits

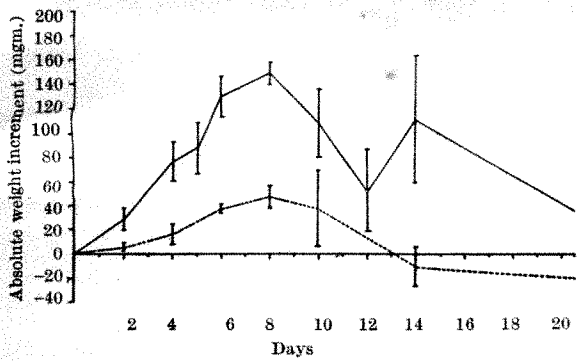

Fig. 1. Graphs of the mean weight increments, with standard errors, of the first regional lymph nodes after homografts (——) and autografts (– – –) of cancellous bone

and inserted into the subcutaneous tissue of the ear in fifty-one Flemish Giant rabbits has been investigated. Control animals were provided by nineteen Flemish Giants which received autografts of cancellous bone into the subcutaneous tissue of the ear. The animals were killed at intervals of 2–21 days after operation. The first regional lymph nodes on both sides were removed, weighed and fixed in Carnoy's fluid, embedded in paraffin, cut at 6μ and stained with methyl green-pyronin.

The mean weight increments and standard errors of the first regional lymph nodes for the homografted and the autografted animals at various time-intervals after grafting are shown in Fig. 1. An overall test of the difference between the homograft nodes on one hand, and the autograft nodes on the other, has been made by combining the values of P for each time-interval, using the method described by Fisher[7]. This test of significance gave $P < 0{\cdot}005$, showing that overall, the difference in mean weight increments of the homografted and the autografted nodes was highly significant.

Histological examination of the lymph nodes reacting to bone homografts has revealed great numbers of pyroninophilic large and medium lymphoid cells in the diffuse cortical tissue and in the medullary cords. Further analysis of the nodes has shown a sectoral distribution (Fig. 2) of these pyroninophilic cells which is probably due to the entry of the 'homograft factor' to that particular part of the cortex. To put this probability to the test, 0·1 ml. indian ink was injected subcutaneously into the ear on the ventral aspect in two rabbits, 1 centimetre from the external auditory meatus. The first regional lymph nodes were removed ½ hr. later, fixed, embedded and sectioned. Indian ink was found to be distributed to only one side of the nodes. Hence the conclusion that the sectoral distribution of the large and medium lymphoid cell response is due to the localized entry of antigenic material from the bone homograft to a particular part of the lymph node appears justified.

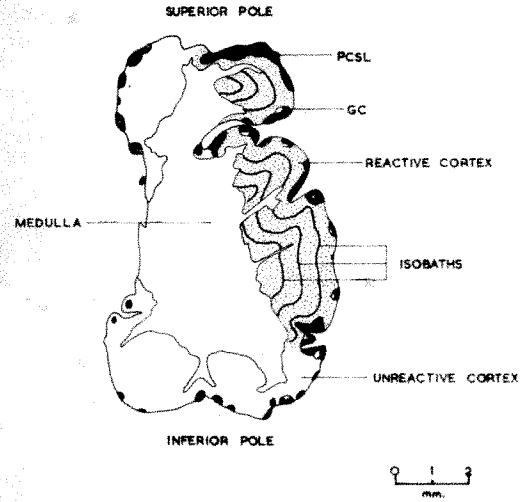

Fig. 2. Camera lucida tracing of a section from a first regional lymph node removed four days after homografting. The distribution of large and medium lymphoid cells in the cortex is shown by stippling. The method of selective sampling of the reactive cortex is indicated by the isobaths. (GC = germinal centre; $PCSL$ = peripheral collection of small lymphocytes)

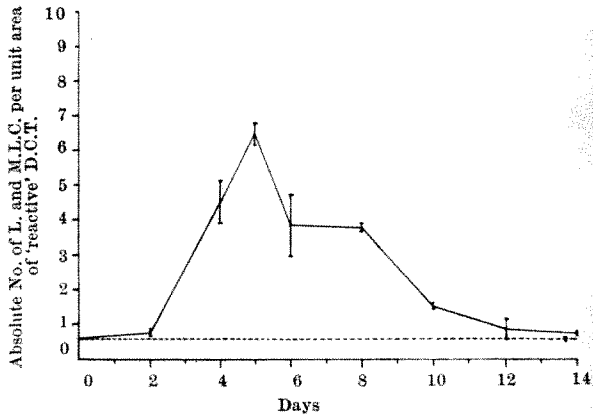

Fig. 3. Graphs of the means, with standard errors, of the counts of large and medium lymphoid cells in the reactive diffuse lymphoid tissue of the cortex from normal (– – –) and homografted (——) lymph nodes

A quantitative analysis of the large and medium lymphoid cell response has been attempted in the reactive sectors of the diffuse lymphoid tissue of the cortex in twenty-four nodes removed 2–14 days after homografting. Counts have been made in three different sections from each node in fields of 57μ^2, using × 10 eyepieces and a × 100 oil immersion objective. The counts were made two graticule divisions apart on lines (or isobaths) four, eight and less frequently twelve, graticule divisions from the surfaces of the nodes (Fig. 2). The mean number of large and medium lymphoid cells per unit area of reactive cortex for three nodes at each time-interval has been found to rise rapidly and reach a maximum between the fourth and sixth day after homografting (Fig. 3). A more gradual decline then ensues, the count returning to a normal level by the fourteenth day after insertion of the graft.

A more detailed account of these results will shortly be published together with the results of an immunological examination of the sera of these animals.

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BIOPHYSICS

Automatic Equipment for the Collection and Processing of Data from Geiger-Müller Counters

DURING a radioisotopic investigation of ion accumulation processes in marine algae it became apparent that a considerable amount of data required to be collected over extended periods of time. Automatic equipment was therefore devised both for the collection and preliminary processing of the information.

Geiger counters (type *GM*4) with their aluminium end-windows protected by epoxy-resin paint are fixed directly above algal sections contained in shallow cavities through which seawater incorporating the radioisotope being studied is rapidly circulated. (A description of the section holder and circulator assemblies is being submitted for publication elsewhere.) The voltage pulses from probe units to which sets of the Geiger counters are sequentially connected are recorded on a standard tape recorder at a tape speed of $1\frac{7}{8}$ in. per sec., the frequency response at this speed being adequate to record without loss of counts from a probe unit with 500 μsec. paralysis time. The number of Geiger counters in a sequence, the periods for which counts are taken and the interval between successive count periods can be pre-set on a programming unit. As the tape recorder motors are switched on only for a duration determined by the programming unit (in practice 1 min. longer than the count period) a single spool of tape can accommodate large numbers of count periods, for example, a 2,400-ft. spool can permit the recording of more than 120 sets of counts of 1-min. duration on each of its two tracks. Originally the reproduction of this data in usable form was a time-consuming task despite the utilization of a playback speed eight times that of recording, but recently a simple data-processing machine has been completed.

The pulses replayed from the two tracks of the magnetic tape are fed into two scalers each provided with dividing circuits, the division ratios corresponding to the times for which the original counts were recorded. The scalers thus indicate directly the counts per minute on their main registers. Each scaler has a subsidiary register on which the dead-time correction factor is automatically computed. On receipt of a signal which is recorded on the tape at the end of each count period and which is isolated by a two-stage frequency-selective network, a read-out and print-out sequence is initiated. In addition to printing out the counts per minute and the dead-time correction factors, a solenoid-operated calculating machine also prints the starting count per minute for each Geiger counter selected in the original sequence together with counter identification numbers. The calculating machine can perform simple operations on the data being printed out such as producing automatically a difference between the newly determined count per minute and starting count per minute. In the majority of cases, this difference is sufficiently satisfactory for direct graphical representation to indicate the course of an experiment without the application of the dead-time correction factor though, if required, the data for dead-time correction are immediately available without reference to tables. On completion of the print-out sequence the scaling and computing circuits are automatically reset.

This simple computing equipment, while designed specifically to deal with tape-recorded data, can be used with advantage for routine Geiger counting wherever large numbers of samples have to be dealt with and is thus felt to be of wider interest.

I am grateful to the Extra-mural Research Section of the United Kingdom Atomic Energy Authority for financial assistance in the construction of the equipment and for permission to publish this description.

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Identification of Ultracentrifugal Components in Human Plasminogen Preparations

SAMPLES of human plasminogen, prepared according to the method of Kline[1], have been subjected to ultracentrifugal analysis[2]. The patterns observed contained two sedimenting peaks. The slower peak constituted approximately 70 per cent of the total area and had a sedimentation constant, $s_{20,w}$, of 4·28 *S*, extrapolated to infinite dilution. The faster peak, which was much broader and resolved poorly from the main component, had a sedimentation constant of about 7–10 *S*. It was merely assumed that plasminogen was to be identified with the 4·3 *S*-component, and on this basis, along with other data, molecular size and shape were estimated. We now report direct evidence to substantiate this assumption.

The proteolytic activity was measured by casein assay, essentially according to Remmert and Cohen[3], except that the casein concentration was 2 instead of 4 per cent. The concentration of protein in the sample being assayed was measured by light absorption at 2800 Å., using 14·0 as extinction coefficient[2]. The activity is therefore expressed as casein units/mgm. protein.

Sedimentation studies were made in a Spinco model *E* ultracentrifuge, using an analytical cell with a 2° sector to minimize the volume required, and a standard fixed-partition cell for separation of components. These runs were made on samples that had been dialysed against acid-saline (0·15 *M* sodium chloride + 0·01 *N* hydrochloric acid, *p*H 2).

In an early separation experiment, a solution at 1·4 per cent concentration was run in the separation cell until the fast component had apparently gone past the partition. After terminating the run, samples were obtained from the top compartment ('Top') and the bottom compartment ('Bottom'), 0·2 ml. each, and diluted with 1·5 ml. of acid-saline. These dilutions were measured for protein content and assayed on casein. A sample of the initial solution was allowed to stand at room temperature during the run ('Warm control') and another solution was kept refrigerated ('Cold control'). These were similarly diluted and assayed. The results are shown in Table 1. This experiment is adequate proof that the proenzyme is to be associated with the slow component. If it were in the fast peak, the activity in 'Top' should be considerably reduced, although not to zero, since the boundary is quite broad; instead

Table 1. PROTEOLYTIC ACTIVITY OF HUMAN PLASMINOGEN AND ULTRACENTRIFUGAL FRACTIONS

Sample	Specific activity (units/mgm.)
Cold control	3·9
Warm control	3·5
Top	6·6
Bottom	3·9

Table 2. PROTEOLYTIC ACTIVITY AND ULTRACENTRIFUGAL ANALYSIS OF HUMAN PLASMINOGEN AND ULTRACENTRIFUGAL FRACTIONS

Sample	Specific activity (units/mgm.)	Relative amount of 4·3 *S*-component (per cent)
Warm control	4·4	70·2
Top	7·8	93·6
Bottom	7·1	88·8

it is increased, as would be expected from removal of inert proteins.

The experiment was repeated, however, with results that were equivocal, as was true in several additional trials. The problem seemed to be due to the difficulty of judging the proper degree of dilution to avoid a protein-level that was too low (poor sensitivity) or too high (non-linearity) for the casein assay. I decided to perform a series of separation runs, in order to pool the respective products. There would thus be enough material to be checked by analytical ultracentrifugation. A group of six separation runs were pooled and yielded 1·96 ml. of 'Top' and 1·07 ml. of 'Bottom'. The sedimentation pattern of the initial sample is shown in Fig. 1. On re-examining the fractions, at similar concentrations, sedimentation patterns as in Fig. 2 were observed. The measured proportions for these samples are shown in Table 2, along with the assay data. It can be seen that 'Top' does contain considerable enrichment of slow peak, and even 'Bottom' shows a similar enrichment. Both fractions show an increased specific activity, fully in accord with the first experiment. In fact, if one plots casein activity for these three samples against percentage of 4·3 *S*-component, a quite acceptable straight line is observed. One can conclude, therefore, that the fast peak represents an inert contaminant. In addition, it is seen that a purification of about 1·8-fold can be achieved by ultracentrifugation. Studies of fractionation with ammonium sulphate, leading to similar conclusions, as well as to electrophoretic identifications, will be published elsewhere.

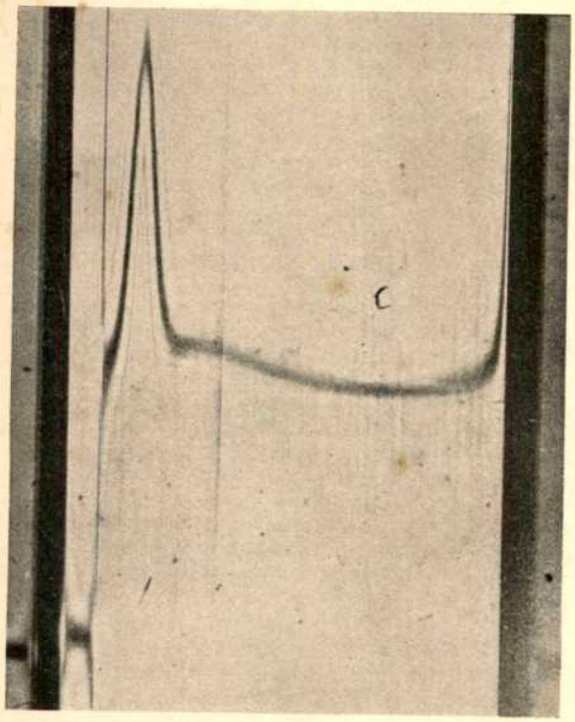

Fig. 1. Ultracentrifugal pattern of human plasminogen (by Kline method). Concentration of protein, 0·80 per cent; bar angle, 40°; photograph at 16 min.; rotor speed, 59,780 r.p.m.

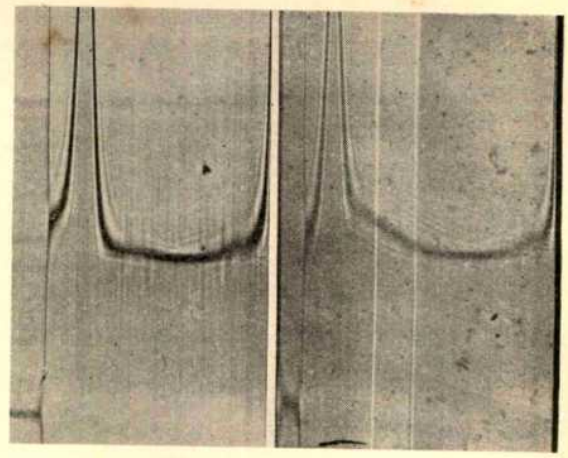

Fig. 2. Ultracentrifugal pattern of human plasminogen fractionated in separation cell. 'Top' fraction on left. Concentration of protein, 0·88 per cent; bar angle, 40°; photograph at 20 min. 'Bottom' fraction on right. Concentration of protein, 0·80 per cent; bar angle, 40°; photograph at 20 min.; rotor speed, 59,780 r.p.m.

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BIOLOGY

Surface of a Parasite and the Hæmocytic Reaction of its Host

EXPERIMENTS recorded in a recent paper[1] have shown that the hæmocytic reaction of insects to parasites and other foreign bodies in their hæmocœle is stimulated by properties of the surfaces of those objects. In an article[2] the publication of which has been delayed, I have brought together observations which suggest that the hæmocytes of an insect react to any surface which lacks specific properties of the surfaces which they themselves lay down, or contribute to, about the organs and tissues of the insect of which they form part.

If that hypothesis is correct, a foreign body that has caused a reaction and has been encapsulated by blood cells might be expected thereby to have acquired a surface that would render it immune to further reaction from the same or a similar host. That this is so was demonstrated[1] by implanting an object in the hæmocœle of an insect and, after it had been encapsulated, transferring the object and the unbroken capsule about it to another host. Objects thus transplanted to individuals of the same species evoked no visible response; those transplanted to hosts of a different kind stimulated another hæmocytic reaction which led to the encapsulated object being enveloped in a second capsule formed by the blood cells of the second host.

The hypothesis has recently been tested in the reverse way, by altering a surface that confers immunity to the reaction and finding that the reaction then takes place. It is well known that living larvæ of the parasitoid *Nemeritis canescens* stimulate no reaction on the part of the hæmocytes of their normal host, *Ephestia sericarium*, so long as their surface is unbroken; although, if their surface is minutely perforated, as by the mandibles of a competing parasite, hæmocytes of the host congregate locally about the wound. These larvæ therefore provide suitable material for examination of an immune surface. When first-instar larvæ of *Nemeritis* were put individually into a variety of fluids, removed and washed for some hours in insect saline, and then implanted in *Ephestia*, two groups of significant results were observed. After immersion in some fluids, the implanted parasites evoked no reaction, but fed and developed normally in their new hosts. After immersion in other fluids, however, the implanted living parasites provoked a hæmocytic reaction in their normal hosts and were found completely covered in a thick layer of hæmocytes. Within that layer they were still alive and moving vigorously as though attempting to divest themselves of the hæmocytic covering.

Various fluids have been used in experiments of this pattern, the period of immersion in them being adjusted to allow survival of the parasite larvæ. So far as the experiments have yet gone, all the fluids found to have the second result, that is, to expose the parasite to encapsulation in its normal host, have been solvents of fats. Octane has been found especially efficient. It appears from these observations that the removal of a lipid constituent of the surface of *Nemeritis* larvæ also removes the specific properties that provide its immunity to the hæmocytic reaction of *Ephestia*.

A few parallel experiments have been carried out using testes of *Ephestia* for implantation. As is common knowledge, if these organs are removed from an insect and implanted in another individual of the same species, they evoke no general hæmocytic reaction; but if implanted in quite different hosts they are encapsulated. When entire *Ephestia* testes were immersed in fluids found to be effective in the experiments with *Nemeritis* larvæ, washed in saline, and implanted in other *Ephestia*, they were encapsulated. These experiments give direct support to the hypothesis put forward, but are not as critical as those involving parasite larvæ because it is not easily possible to observe whether the encapsulated testes are sound and healthy. It is the fact that larvæ of *Nemeritis* can be retrieved from *Ephestia* alive and vigorous although encapsulated that makes them so useful as experimental objects for examining the surface properties that confer immunity to insect parasites in their normal hosts.

A full account of this and related work will be published elsewhere.

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Gestation Time for Delayed Birth in the Quokka

SHARMAN[1] has established that normal gestation time for the Rottnest Island quokka (*Setonix brachyurus*) is twenty-seven days. He has further shown that, in delayed birth in this species, the unilaminar blastocyst stage at which development is arrested occurs about three days after copulation. It is of interest to assess the time necessary from resumption of development of the blastocyst to parturition after the impetus to growth, that is, removal of the initial joey, is applied.

A sample of 40 females with pouch young were caught on Rottnest Island. The joeys were removed and the females taken to the mainland where they were retained in isolation from males. The pouches were examined for the presence of a second joey on the days indicated in Table 1. From Table 1 it is seen that three joeys were born twenty-five days after the removal of the initial joeys, but the majority of births occurred on the twenty-sixth day. Taking twenty-six days as the further gestation time of the blastocyst, which had taken three days to achieve the stage at which development was arrested, it appears that the total gestation time for the 'delayed' joey is twenty-nine days. Since normal gestation time is twenty-seven days, it seems that two days are necessary for resumption of development of the quiescent blastocyst.

Table 1. INTERVAL IN DAYS BETWEEN THE REMOVAL OF THE INITIAL JOEY AND THE BIRTH OF THE 'DELAYED' JOEY

Day	23	24	25	26	27
No. of pouches examined	35	37	40	36	22
No. of joeys found	0	0	3	14	0

During the course of this experiment and other work data were collected on the sex of the initial joey and that of the subsequent 'delayed' joey. Table 2 shows no significant association between the sex of the initial and 'delayed' joeys. This is presented in confirmation of Sharman's finding that the 'delayed' joey is the result of a separate ovulation, and no process analogous to twinning occurs.

Table 2. RELATIONSHIP BETWEEN THE SEX OF THE INITIAL JOEY AND THAT OF THE 'DELAYED' JOEY

		Initial joeys		
		Males	Females	Total
'Delayed' joeys	Males	3	7	10
	Females	5	8	13
		8	15	23

This work was supported financially by grants from the University of Western Australia and the Commonwealth Scientific and Industrial Research Organization.

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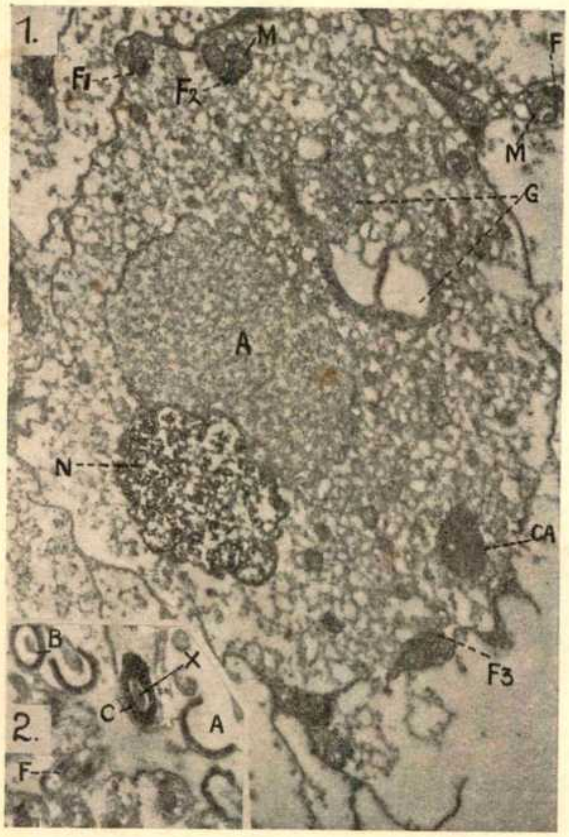
Electron Microscopy of Thysanuran Spermiogenesis

IN a recent discussion[1,2] on the position of the acrosome and centriole in the thysanuran spermatozoon, the necessity for electron microscopy was stressed. In Fig. 1, the Golgi body (acroblast; *G*) is lying to one side of the very large acrosome (*A*). Below is the nucleus (*N*). The flagellum has grown out inside the cell and is cut across in three places (*F*1–3). On the right is a constantly occurring body (*CA*), which at present is considered to be a centriole adjunct, as in other micrographs it is found near the centriole. Cross-sections of the ripe or nearly ripe sperms are shown in Fig. 2. The anteriorly situated acrosome has become a scoop-shaped body (*A*), which passes back to form a tube (*B*), which joins the nucleus (*C*), which passes back to join the flagellum (*F*). No adnuclear thread or flagellum is found on the tubular nucleus, but there is an intranuclear body (*X*), which projects up into the funnel of the acrosome. This is probably what is seen with the light microscope in the form of an intra-nuclear flagellum. This body, however, does not possess the flagellar ultrastructures.



Figs. 1 and 2

A fuller account of this spermiogenesis, and that of *Lepisma*, will be published elsewhere. I thank M. Jean André of the Electron Microscopy Department of the Institut de Recherches sur le Cancer, Villejuif (Seine), for taking the micrographs.

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Influence of Amino Triazole on the Chloroplast Pigments of Wheat Seedlings

3-AMINO-1,2,4-TRIAZOLE is a chemical which has several effects on higher plants. It is a growth inhibitor, and has been used on cotton plants as a defoliant[1]. Hall *et al.* demonstrated that tissues formed subsequent to application of this chemical have a decreased chlorophyll content, while the chlorophyll-level of already mature tissues is unaffected. It was not entirely clear to these investigators whether the observed effect of amino triazole on chlorophyll content is due to chlorophyll destruction or to interference with chlorophyll synthesis. The structural similarity of the triazole ring to the pyrrole rings of chlorophyll prompted the suggestion that amino triazole brings about a block in chlorophyll synthesis prior to the protochlorophyll stage by a competitive inhibitory mechanism[1]. This concept was somewhat strengthened when it was found that levels of catalase, which has a similar structure, were also decreased in both plants and animals by treatment with amino triazole[2,3].

Experiments with *Elodea canadensis* further served to localize the effect of amino triazole as influencing chlorophyll synthesis rather than chlorophyll destruction, but microscopic observations clearly indicated interference with plastid development[4]. This suggested the possibility that the influence of amino triazole on chlorophyll content might be secondary to an effect on the development of the plastid as a whole. According to Pyfrom *et al.*[3], "a small amount of amino triazole interferes with the plastids during leaf formation or differentiation, and chlorophyll *as well as other plastid pigments* are always low in these leaves".

In an effort to secure further insight into this situation, wheat grains were germinated and seedlings were grown in Petri dishes containing filter paper, moistened with water or with various concentrations of amino triazole. The conditions of growth were identical with those described by Haber and Luippold[5] with 400–500 ft.-candles of white light during a 16-hr. day. Analyses for chlorophyll *a*, chlorophyll *b*, and total carotenoids were performed according to the technique of Röbbelen[6]. After preliminary trials with various concentrations of amino triazole, a concentration of 10^{-4} *M* was selected, which permitted about 70 per cent of normal growth during a 12-day period, yet reduced the chlorophyll content to a value approximating 5 per cent of normal.

Wheat seedlings were germinated in darkness, in either 10^{-4} *M* amino triazole or in water. After 6 days, the etiolated seedlings were placed under a light source of the type described by Withrow and

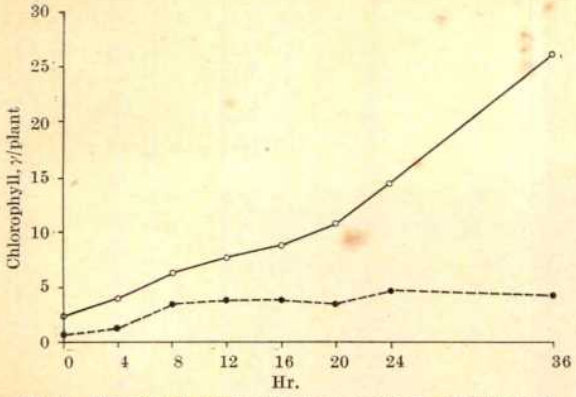

Fig. 1. Greening of 6-day old wheat seedlings, as influenced by 10^{-4} *M* amino triazole. ——, Control; – – –, amino triazole

Elstad[7], which provided a light intensity of 1,000 ft.-candles. Determinations of total chlorophylls (*a* plus *b*) were made at intervals during the subsequent 36 hr. The results (Fig. 1) indicate that normal greening was drastically inhibited by this concentration of amino triazole.

In another type of experiment, wheat seedlings were grown in water under the usual 16-hr. photoperiod. After 6 days, the water in some of the dishes was replaced by 10^{-4} *M* amino triazole, and all the plants were placed in darkness. Chlorophyll estimations were made at 2-day intervals over a period of 10 days. The findings (Fig. 2) indicate no difference in the rate of chlorophyll disappearance in darkness as a result of treatment with amino triazole.

Wheat seedlings were grown in water under a 16-hr. photoperiod for 6 days, and were then transferred to 10^{-4} *M* amino triazole. When such plants were continued under the 16-hr. photoperiod, their subsequent appearance was very striking. The basal portion of the leaves was a normal green in colour. Distal to the green area was a colourless zone about 1 cm. in length, while the portions of the leaves produced after treatment with amino triazole were a reddish-purple in colour, owing to the abundant production of an anthocyanin pigment, which was not detected in untreated plants. Further, this effect was not noted in plants treated similarly, but placed in darkness following treatment with amino triazole.

Wheat grains were germinated in the presence of amino triazole in concentrations ranging from 1×10^{-5} *M* to 2×10^{-4} *M*. After 12 days of growth under the usual 16-hr. photoperiod, analyses for total carotenoids and chlorophyll were made. The results (Table 1) indicate that the reduction in chlorophyll content resulting from treatment with amino triazole is accompanied by reductions of similar magnitude in the carotenoid pigments.

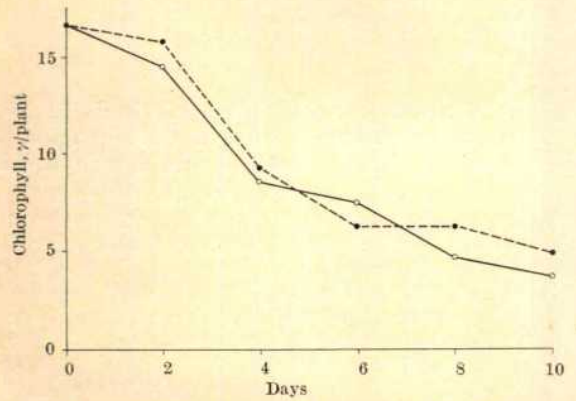

Fig. 2. Disappearance of chlorophyll from 6-day old wheat seedlings, in darkness, as influenced by 10^{-4} *M* amino triazole. ——, Control; – – –, amino triazole

Table 1. Pigment Content of Wheat Seedlings grown for 12 days in Various Concentrations of Amino Triazole

Concentration of amino triazole	Height (mm.)	Chlorophyll/plant (γ)	Carotenoids/plant (γ)
0 (Control)	105·2	56·6	12·7
1×10^{-5} *M*	98·9	46·8	11·0
2×10^{-5} *M*	93·8	26·8	6·7
4×10^{-5} *M*	77·5	7·3	1·3
1×10^{-4} *M*	72·1	2·0	0·5
2×10^{-4} *M*	38·3	1·7	0·3

In summary, the greening experiment indicates that the net rate of chlorophyll synthesis (excess of synthesis over destruction) is drastically reduced by amino triazole. There would appear to be no direct action of amino triazole on the rate of chlorophyll destruction, at least in darkness. Considered together, these findings would appear to add further evidence to that of earlier investigators[1,4] localizing the effect of amino triazole on the synthesis of chlorophyll. But since amino triazole has a similar influence on the levels of both carotenoids and chlorophyll: (1) the hypothesis of Hall *et al.*[1] which considers amino triazole as a competitive inhibitor of chlorophyll synthesis is incorrect, and (2) it would seem reasonable to suppose, confirmatory of earlier findings[3,4], that the effects of amino triazole on plastid pigments are secondary to an effect upon the plastid itself.

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Complex Particles in *Hevea* Latex

Latex freshly tapped from *Hevea brasiliensis* is known to contain particles other than rubber. By high-speed centrifugation, Cook and Sekhar[1] parted such latex into a top fraction and a bottom fraction with serum between. Both fractions are visibly heterogeneous, and Moir[2] has recently distinguished no less than eleven zones in centrifuged latex. Only three types of particle have been described in the literature so far. These are the rubber particles, often pear shaped, found in the top fraction, the Frey Wyssling particles[3], which are yellow bodies found mostly in the lower part of the top fraction, and the 'lutoid' particles of Homans and van Gils[4]. The term 'lutoid' was originally applied to large irregularly shaped islands of a yellowish colour consisting of mainly non-rubber material and seen in whole fresh latex. Ruinen[5] detected a particulate structure in these islands and uses the term to describe individual globules seen therein. Schoon and Phoa[6] mention that "inside the lutoid vacuoles, in a few cases very

small particles are to be observed in Brownian motion". Up to date, no photographs of this phenomenon have been published.

I am at present carrying out an examination by microscopy of latex fractions separated after high-speed centrifugation. The technique of collection and centrifugation described by Moir[2] is used, the latex being tapped directly into a glass container surrounded by melting ice and the temperature kept below 5° C. throughout the preparative procedures. In such material from both mature and young trees, I have observed a distinct type of particle occurring abundantly in the bottom fraction from high-speed centrifugation, and forming the bulk of Moir's zone 8[2].

In the initial and intact state they are spheres of 2–10μ diameter. They have an external membrane which in a medium of suitable refractive index can be made transparent. The interior is fluid and contains very many smaller particles, in size from 1μ down to the lower limit of visibility. These small captive particles are in vigorous motion and can be seen to strike the containing wall frequently and to be deflected back into the interior (Fig. 1).

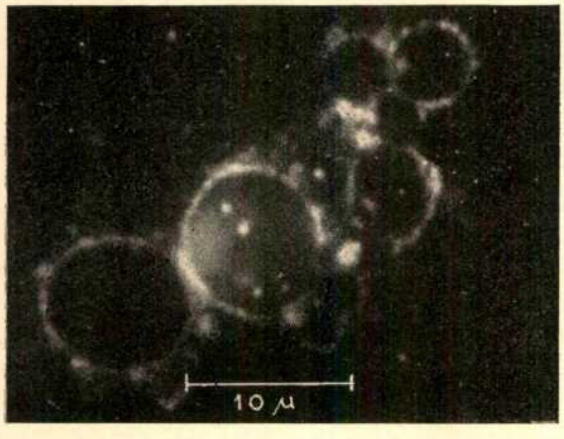

Fig. 1. A group of complex particles, slightly aggregated after centrifugation at 54,000*g*, resuspended in viscous ammonium polymethacrylate–water medium of refractive index 1·371. Photographed with Leitz 'Multblitz' electronic flash illuminant at 300 joules to arrest internal motion, using Reichert anoptral phase 100 × oil objective matched to Reichert variable phase condenser 'Polyphos'

After tapping, the particle membranes soon show signs of disintegration. Before this goes very far, the independent motion of the captive particles usually stops; they migrate to the walls and stick there. The membranes themselves readily adhere to each other to form loose agglomerates which later lose their definite internal structure and appear as confused irregular shaped masses.

These particles have also been observed in preparations of whole latex using an electron microscope (Fig. 2). This work was done in Germany using the following procedure to get a supply of fresh *Hevea* latex. A section of the trunk of a 3½-year-old clonal bud-grafted rubber tree (*RRIM* 603), approximately 1 m. long and 10 cm. diameter, was cut in Malaya and the ends were waxed. The specimen was sent by air to Germany sealed in polythene to reduce losses of moisture. Latex could be tapped for 10 days after the original cutting. Carl Zeiss (Oberkochen) provided laboratory facilities and the use of their Zeiss/*AEG EM*8 electron microscope.

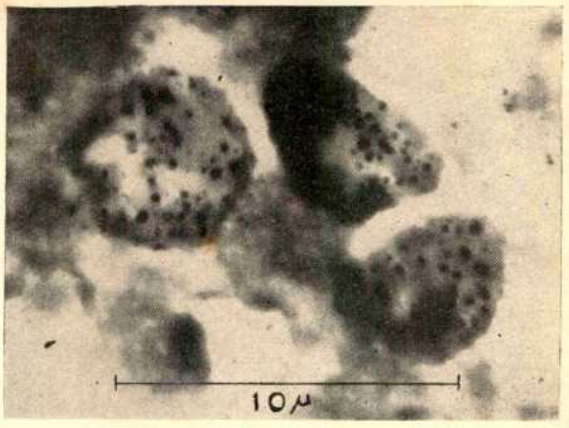

Fig. 2. Electron micrograph of a carbon pseudo replica from a smear preparation of latex taken with the Zeiss/*AEG* electron microscope at low magnification. An attempt was made to remove rubber particles by washing with benzene

The nature and function of these complex particles are not yet understood and are the subject of further investigation. Their appearance tallies with the description of Schoon and Phoa[6] for a type of lutoid; but in this case they are much more abundant than was supposed. Suggestions that rubber synthesis takes place within a plastid have long been current. For example, Milanez[7] described 'galactoplastids' in sectioned stained plant material from *Hevea brasiliensis*. Whether or not the particles now seen are related to the galactoplastids of Milanez, the existence of large numbers of such complex particles in latex has an important bearing on the controversy as to whether latex is whole cytoplasm or vacuolar sap and favours the first proposition.

I am indebted to Dr. Grehn and his co-workers at Leitz G.m.b.H., Wetzlar, for their invaluable advice on optical methods, also to Dr. Mahl of Carl Zeiss, Oberkochen/Württ., for his help with the electron micrograph, and to W. G. Wren and P. De Jonge for the preparation of the tree sample for dispatch to me in Germany.

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A Comparison of Three Methods for the Assessment of Fungal Colonization of Seedling Roots of Leek and Broad Bean

IN recent years several methods have been devised for the isolation of fungi from root tissues. The Harley and Waid serial washing technique[1] has already provided valuable data on fungi closely associated with plant roots[2,3], but it has been suggested that the plating of washed root segments in this method does not always allow the isolation of slow-growing forms (such as Basidiomycetes), these being unable to compete with the faster growing fungi. Methods such as root maceration[4] and root fragmentation[5] have been claimed to provide a more

complete picture of root mycofloras. The experiments described here compare these three methods for the isolation of fungi from healthy seedling roots of leek (*Allium porrum* L.) and broad bean (*Vicia faba* L.).

Plants of both species were grown under greenhouse conditions in a grassland soil (*p*H 5·8) and were sampled 30–35 days after sowing. Before any isolations of fungi were attempted the roots were thoroughly washed, first in tap water to remove all visible soil particles and then in sterile water. Preliminary tests had shown that ten 2-min. washings with sterile water allowed efficient washing of the roots.

From this washed root material, isolation of fungi was attempted by the three aforementioned methods (plating of root segments, root maceration and root fragmentation). In all cases isolation of fungi was effected from similar lengths (20 cm.) of healthy root material. The three methods were applied in a manner which in all essential details was the same as that described by their respective authors[1,4,5]. For all methods Czapek-Dox + yeast extract agar (*p*H 5·0) was used as the isolation medium and all isolation plates were first incubated at 25° C. for three days and thereafter kept at room temperature, during which time isolation and identification of fungi were effected, and counts made of the number of fungal colonies arising from unit amounts of root material.

Table 1. NUMBER OF FUNGAL ISOLATES, PER UNIT LENGTH OF ROOT, OBTAINED BY THE USE OF DIFFERENT ISOLATION METHODS

Leek			Broad bean	
Root segment plating	Root maceration	Root fragmentation	Root segment plating	Root maceration
34	9	5	70	85
39	12	12	—	117

Results given in Table 1 indicate that, with leek, both root maceration and root fragmentation give fewer isolates from root material than does the direct plating of root segments. However, with broad bean this effect is not seen; in fact, root maceration provides more isolates than does the direct plating of root segments.

The results with leek (*Allium porrum* L.) are similar to those obtained by Timonin and Thexton[6] with roots of onion (*A. cepa* L.) and garlic (*A. sativum* L.). These authors attempted isolation and enumeration of root surface micro-organisms by plating dilutions of a suspension of root material obtained by shaking roots in sterile water containing glass beads (maceration of the root surface layers occurred). Their results showed that the number of fungi thus obtained was much less than those from dilution plates prepared from the rhizosphere soil of the same two plants.

It is possible that, with leek, chemical substances (possibly diallyl sulphides) possessing fungicidal or fungistatic properties are released during maceration or fragmentation; while the direct plating of root segments, which only causes a small amount of damage to the roots, causes little or no release of these substances. The results with broad bean show no evidence of any such inhibitory effects resulting from root maceration, although an unidentified substance fungicidal to *Aspergillus niger* has been reported[7] to be present in the stem and root of broad bean.

These results provide support for the suggestion[8] that maceration or fragmentation techniques, while probably useful for the isolation of fungi from the roots of many species, should be used with caution in view of the possible release of toxic substances during the disruption of the root tissues.

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ENTOMOLOGY

Number of Nymphal Instars of the Sugar-cane Froghopper

THERE was some disagreement among earlier authors as to the number of nymphal instars of the sugar-cane froghopper, *Aeneolamia varia saccharina* Distant (Homoptera, Cercopidae). Urich[1] and Williams[2] considered that there were four instars. Gough[3] and Kershaw[4] both stated that there are five instars; but from their descriptions it would appear that they each recognized a different series.

There are in fact five nymphal instars. This statement is based on the following evidence: (1) measurements of the head-widths of nymphs of all stages collected during one season in the field fall into five distinct groups; (2) the antennæ of nymphs in the five different head-width categories differ in size and structure; (3) more than 50 newly hatched nymphs were examined and were found to correspond to the first stage as determined by criteria (1) and (2); (4) two moults have been observed between the true first and second stages.

Table 1. SUMMARY OF CHARACTERS DISTINGUISHING THE FIVE NYMPHAL INSTARS OF *A. varia saccharina*

Instar	Total length (mm.)	Head-width (mm.)	Length of antenna (mm.)	No. of antennal segments
I	1·0–1·5	0·28–0·30	0·14	6
II	1·5–2·0	0·45–0·55	0·22–0·25	6
III	2·5–3·5	0·70–0·80	0·38–0·42	6
IV	4·0–5·5	1·15–1·25	0·60–0·75	6 or 7
V	6·0–8·0	1·65–1·75	1·25–1·40	6, 7 or 8

The characters which distinguish the five instars are summarized in Table 1.

Total length refers to the distance from the tip of the labrum to the tip of the abdomen. It varies with the state of development of the instar and is given here only as a general indication of size. Head-width is the distance between the outer lateral margins of the compound eyes. There are basically six antennal segments, but in the 4th instar the 5th segment, and in the 5th instar the 5th and 6th segments (counting from the base), are usually sub-divided each into two segments. The sub-division of these antennal segments may occur in one but not the other antenna of a single specimen.

Wing pad development may also be used to distinguish most of the stages, as the following key indicates.

(1)	No wing pads present	I and II instars
	Wing pads present	2
(2)	Wing pads on mesothorax only	III instar
	Wing pads on both meso- and meta-thorax	3
(3)	Wing pads scarcely longer than wide at the base	IV instar
	Wing pads distinctly longer than wide at the base	V instar

The five instars described here probably correspond to those recognized by Kershaw[4] although he did not give any detailed descriptions. Neither Williams[2] nor Urich[1] distinguished between the true first and second stage nymphs. Their descriptions of "second", "third" and "fourth" correspond to the true third, fourth and fifth instars. Gough[3] arrived at five instars by splitting the true fifth instar into two separate stages. He was probably misled by a change of appearance in the fifth instar a few days before moulting, due to the development of the adult cuticle and pigments within the nymphal exoskeleton.

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Decreasing Photoperiod inhibiting Metamorphosis in an Insect

Anthrenus verbasci (L.) (Col. Dermestidae) has a two-year life-cycle (semivoltine) under outdoor temperature conditions in southern England, spending the first winter as a young larva and the second as a fully grown larva[1]. Under constant conditions in the laboratory larvæ may be either uni- or semivoltine according to temperature. The percentage of larvæ with a univoltine life-cycle increases from 0 at 15° C. to 100 at 25° C. The larvæ have been shown to possess an endogenous and persistent rhythm controlling the onset of diapause[2]. Each cycle of the rhythm consists of a period of active growth (with moulting and/or pupation) followed by diapause. Under constant conditions the length of the cycle is about 44 weeks, but this is extended to an annual cycle, under outdoor conditions, by the insertion of a period of dormancy after the completion of diapause.

The nature of this dormant period, and the agencies controlling it, were examined by rearing isolated larvæ: (1) under outdoor temperature conditions in a Stevenson screen and (2) under constant temperature conditions (20° C.). In both (1) and (2) 80 larvæ were kept in natural daylight and 80 in continuous darkness. There were two levels of relative humidity, 30 per cent and 70 per cent (with imperfect control when the temperature fluctuated). There were also two regimes of observation; half the larvæ were examined fortnightly and the ecdysed skins noted, while the other half were only examined immediately prior to the expected time of pupation. After this time, that is, from about the 20th week, both groups were examined weekly until the end of the experiment. The above differences in humidity and in frequency of observation did not affect the main result. Altogether 320 isolated larvæ were observed, but only those which successfully completed development are recorded in Fig. 1.

These experiments demonstrated the following points. First, under outdoor conditions, temperature was the important factor controlling the time of pupation—light appeared to play no part (Fig. 1 *A* and *B*). Secondly, under conditions of constant temperature and natural daylight the earliest pupations were delayed by periods up to about 13 weeks. This is shown by reference to the control experiments (Fig. 1 *D*) in which pupation commenced at the 64th week, whereas larvæ exposed to light (Fig. 1 *C*) were inhibited until the 76th week—the difference between *C* and *D* (13 weeks) is indicated by line *a*. (The narrowness of the range of pupation times in *A* and *B* compared with *D* reflects the fact that diapause was completed by all individuals in *A* and *B* before the temperature rose sufficiently to stimulate pupation. *C* can be regarded as intermediate in this respect.)

It would seem, therefore, that towards the end of a two-year cycle, larvæ which would in the absence of light pupate in October are inhibited from pupating until the following January, if they are exposed to natural daylight. Day-length is decreasing during this period, and this is thought to be the stimulus responsible for the inhibition of pupation.

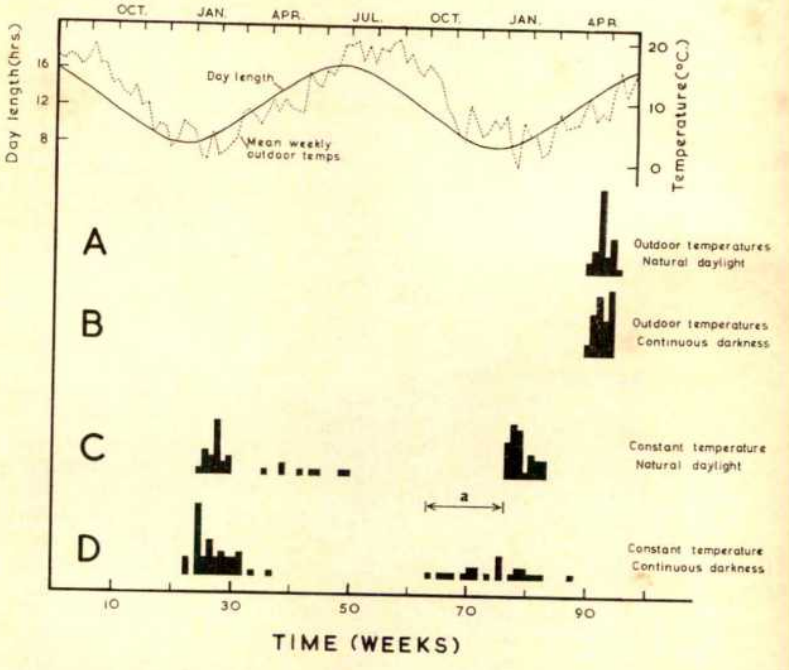

Fig. 1. Frequency of pupation times when larval development has taken place under various combinations of light and temperature. *C* and *D*, constant temperature (20° C.). (An accident occurred, and for this reason *D* represents a combination of two controls, running simultaneously.) One black square marks the time of pupation, to the nearest week, of one individual. Observations were made weekly

This type of response is of considerable ecological significance particularly in a semivoltine species. Since the amount of growth that takes place during an active period of the cycle is directly dependent on the temperature, larvæ developing over a period of two years, in habitats of widely different mean temperature, might reach the fully grown stage at almost any time of the year. A seasonal signal is therefore required to restrict emergence to the spring. Synchronized emergence is important for *A. verbasci*: since the adult life is relatively short, it greatly increases the chances of mating. This must be of considerable importance in areas where the population is small or thinly dispersed.

Anthrenus verbasci (L.) is the first insect in which it has been shown that metamorphosis is prevented during a period of decreasing day-length. Corbet[3] showed that diapause in the emperor dragonfly (*Anax imperator* Leach) was prevented by an increasing photoperiod. These two examples seem to be the only ones in which insects have been shown to be sensitive to a changing photoperiod rather than to one of fixed length.

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GENETICS

Evidence for a Gm^{ab} Allele in the Gm System of American Negroes

RHESUS-POSITIVE [Rh(+)] red blood cells coated with selected incomplete anti-D sera may be caused to agglutinate by serum from selected patients with rheumatoid arthritis[1]. The agglutinating activity of the rheumatoid arthritis serum may be inhibited by sera from some normal individuals[1]. Inhibiting normal sera are called Gm(+), non-inhibiting normal sera are called Gm(−). Four Gm factors detected by different pairs of rheumatoid arthritis and anti-D sera have been reported. They are Gm^{a} [1], Gm^{b} [2], Gm^{x} [3] and Gm-like [4].

In Europeans Gm^{a} and Gm^{b} are due to co-dominant alleles, *Gm* and Gm^{b} [2]. A third dominant allele at this locus, Gm^{ax} [3], determines the factors Gm^{a} and Gm^{x}. Table 1 lists the presumed genotypes for the phenotypes thus far observed among white populations. Family studies[2,3] support the postulated genotypes. The fourth factor, Gm-like, is absent or rare in Whites[4]. It occurs in American Negroes[4] and in Negroid populations from Java and Africa; but it has not been observed in pure Mongoloid populations[5]. Its genetic relation to Gm^{a}, Gm^{b} and Gm^{ax} is unknown[4].

Table 1. PHENOTYPES AND POSSIBLE GENOTYPES FOR Gm^{a}, Gm^{b} AND Gm^{x} IN CAUCASOIDS

Phenotypes	Presumed genotypes
Gm(a + b + x +)	Gm^{ax}/Gm^{b}
Gm(a + b − x +)	Gm^{ax}/Gm^{ax} ; Gm^{a}/Gm^{ax}
Gm(a + b + x −)	Gm^{a}/Gm^{b}
Gm(a + b − x −)	Gm^{a}/Gm^{a}
Gm(a − b + x −)	Gm^{b}/Gm^{b}

While only 56·96 per cent of 2,635 Europeans were found to be Gm(a +) (summarized from various reports in ref. 4), 95 per cent of 74 Eskimos[1], 100 per cent of 110 Negroids (Javanese, Djuka Negroes, Micronesians and West Africans)[5], 100 per cent of 105 Mongoloids (Eskimos, Athabascans, Oyana and Carib Indians)[5], and 100 per cent of 449 natives of Dakar[6] were found to be Gm(a +). Since Gm^{b} is an allele of Gm^{a} one would expect Gm^{b} to be absent among Negroids and Mongoloids with no white ancestry and rare among those with white ancestry. This communication is a report of our tests of this expectancy.

Sera from Baltimore populations of Negroes and Whites were tested at Johns Hopkins Hospital; sera from Cleveland populations of Negroes and Whites were tested at Western Reserve University. All tests were done on slides by the method reported by Harboe and Lundevall[3], with concentrations adjusted to suit the reagents used. The reagents are listed in Table 2. All tests were done with homozygous Rh(+) cells.

Table 2. REAGENTS USED TO TEST FOR Gm^{a} AND Gm^{b}

Laboratory	To test for	RA	Anti-D
Johns Hopkins	Gm^{a}	B785	D4
	Gm^{b}	B30	D8
Western Reserve	Gm^{a}	Kimb.	Bowers
	Gm^{b}	Ham.	Bomb.

The results of the tests on the Negro and White populations are shown in Table 3. The phenotypic distributions in the samples from the two institutions agree within statistical limits ($P > 0·5$, for the serum samples from Negroes, and $P > 0·05$ for the serum samples from Whites).

Table 3. TESTS OF SERUM FROM AMERICAN NEGROES AND AMERICAN WHITES FOR Gm^{a} AND Gm^{b}

A Negroes

Laboratory	No. tested	Gm(a + b +) No.	Gm(a + b +) %	Gm(a + b −) No.	Gm(a + b −) %	Gm(a − b +) No.	Gm(a − b +) %
Johns Hopkins	252	240	95·2	7	2·8	5	2·0
Western Reserve	371	353	95·1	7	1·9	11	3·0
Total	623	593	95·2	14	2·2	16	2·6

B Whites

	No. tested	Gm(a + b +) No.	Gm(a + b +) %	Gm(a + b −) No.	Gm(a + b −) %	Gm(a − b +) No.	Gm(a − b +) %
Johns Hopkins	143	61	42·6	14	9·8	68	47·6
Western Reserve	106	60	56·6	9	8·5	37	34·9
Total	249	121	48·6	23	9·2	105	42·2

The unexpected result is that the combined data of the two institutions show that 95 per cent of American Negroes are Gm(a + b +). That this observation is not due to technical errors is shown by the data for American Whites, which agree with those previously reported for European Whites[4]. Unpublished data of Steinberg, Stauffer, Fudenberg and Blumberg indicate that Mongoloid populations are also essentially 100 per cent Gm(a + b +).

There is no reason to suppose that the Gm^{a} and Gm^{b} factors are not genetically determined in coloured peoples, but a direct test of this is not possible with the available samples. Assuming genetic determination, the genotypic alternatives are that nearly all coloured individuals are heterozygous for Gm^{a} and Gm^{b} with heterozygosity maintained by a system of balanced lethals, or that coloured populations are homozygous for an allele, Gm^{ab}, which determines both Gm^{a} and Gm^{b}. The former alternative requires that 50 per cent of all conceptions end in death to maintain heterozygosity and is therefore untenable. We accept the latter alternative.

The phenotypes and their possible genotypes (assuming a Gm^{ab} allele) for the Gm^a and Gm^b factors in Negroes are shown in Table 4. From this table it may be seen that the Gm(a + b −) and the Gm(a − b +) individuals are homozygotes, hence the square roots of their frequencies provide estimates of the frequency of the alleles Gm^a and Gm^b, respectively, in American Negroes. These values (from the combined samples) are $0{\cdot}150 \pm 0{\cdot}020$ for Gm^a, and $0{\cdot}160 \pm 0{\cdot}020$ for Gm^b.

Table 4. PHENOTYPES AND POSSIBLE GENOTYPES FOR Gm^a AND Gm^b IN NEGROES

Phenotypes	Possible genotypes
Gm(a+ b+)	Gm^{ab}/Gm^{ab} ; Gm^{ab}/Gm^a ; Gm^{ab}/Gm^b ; Gm^a/Gm^b
Gm(a+ b−)	Gm^a/Gm^a
Gm(a− b+)	Gm^b/Gm^b

If we make the reasonable assumptions that the Negro ancestors of the American Negro were homozygous for Gm^{ab}, and that the alleles Gm^a and Gm^b in American Negroes were derived from White ancestors, the sum of their frequencies (0·310) is a measure of the proportion of the genotype of American Negroes which has been derived from these White ancestors. This value agrees with the value derived by Glass and Li[7] (0·306) on the basis of the R^0 allele of the Rh groups and thus reinforces their conclusion that White ancestors have contributed some 30 per cent of the genotype of American Negroes.

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Chromosome Number in the Blue Fox (*Alopex lagopus* (L.))

THE materials examined consisted of testes from five farm-bred blue foxes (*Alopex lagopus* (L.)) which were killed by electrocution during the breeding season. The testes were immediately removed, teased in distilled water where they remained for about 10 min. and then the pieces were put in either aceto-orcein or 50 per cent acetic acid. From the aceto-orcein coloured preparations, temporary slides were made by the usual squash methods. The preparations fixed in 50 per cent acetic acid were squashed in the same manner and coloured by the Feulgen method[1].

The testicular material under observation contained numerous spermatogonial cells undergoing division. Careful counts of only those metaphase plates which seemed to be intact gave 50 chromosomes as the diploid number (Fig. 1*a*). The diploid complex was remarkable for its comparatively small chromosomes.

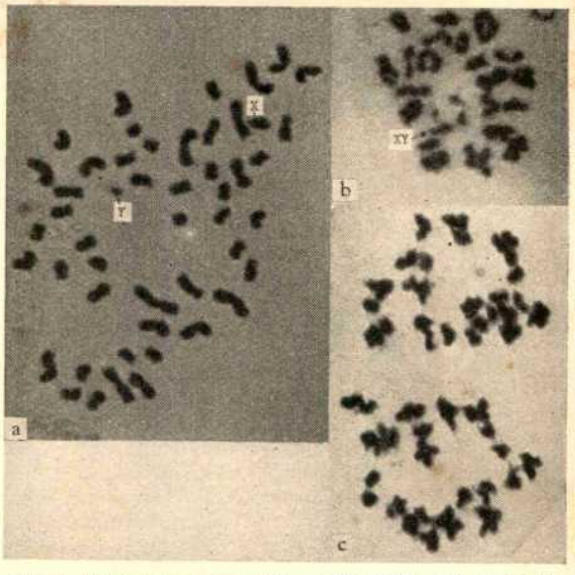

Fig. 1. Chromosomes of the blue fox (*Alopex lagopus*). *a*, Mitotic metaphase with 50 chromosomes. The *X* and *Y* chromosomes are indicated; *b*, first meiotic metaphase with 25 bivalents. The *X*—*Y* complex is indicated; *c*, the second meiotic division. (× *c*, 950)

Because of this the identification of the different chromosomes presented some difficulties. It was found, however, that the diploid complex consisted of 38 meta-centric or sub-metacentric, 11 teleocentric and one dot-like chromosome where the centromere could not be identified. This dot-like chromosome was remarkably smaller than the other ones and apparently has no counterpart. It seems justifiable to consider this to be one of the sex-chromosomes. The other element of the sex-chromosomes seemed to be a rod-shaped chromosome of medium size.

Counts from both the first and the second meiotic division confirmed the number given. The metaphase of the first meiotic division showed 25 bivalents (Fig. 1*b*). Here it was difficult to distinguish the *X*—*Y* complex. It seems that more than one pair of chromosomes have precocious condensation. The second meiotic division was in most cases difficult to count as the chromosomes were small and often lumped together and were diffuse in appearance; but also here 25 chromosomes were found (Fig. 1*c*).

The results obtained in this investigation show that the diploid number of chromosomes in the male blue fox (*Alopex lagopus*) is 50. This is not in agreement with results described earlier. Andes[2] has reported that the number of chromosomes in the blue fox (*Vulpes lagopus*) is approximately between 50 and 60 diploid. He found also 26 tetrads in the first meiotic division. He was, however, unable to distinguish the sex-chromosomes. Wipf and Shackelford[3] agreed with the counts of Andes. They found 52 chromosomes diploid. Neither could these authors find sex-chromosomes on the basis of heteropycnosis, differences in size or other morphological characters.

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FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, October 10

INSTITUTION OF CHEMICAL ENGINEERS (at the Royal Institution, Albemarle Street, London, W.1), at 3 p.m.—Symposium on "Surface Effects and Liquid Behaviour".

UNIVERSITY OF LONDON (at the Institute of Education, Malet Street, London, W.C.1), at 5.15 p.m.—Dr. J. M. Tanner (Institute of Child Health): "Physical Development".*

Tuesday, October 11

UNIVERSITY COLLEGE (in the Anatomy Theatre, Gower Street, London, W.C.1), at 1.15 p.m.—Prof C. W. Allen: "Eclipses of the Sun".*

SOCIETY OF CHEMICAL INDUSTRY, PESTICIDES GROUP (joint meeting with the AGRICULTURE GROUP, at 14 Belgrave Square, London, S.W.1), at 2.45 p.m.—Mr. O. S. Rose, Dr. S. N. Adams, Dr. R. Hull and Dr. R. A. Dunning. "Sugar Beet—Cultivation and Pest Control Measures".

ZOOLOGICAL SOCIETY OF LONDON (at the Zoological Gardens, Regent's Park, London, N.W.1), at 5 p.m.—Scientific Papers.

CEMENT AND CONCRETE ASSOCIATION (at the Institution of Civil Engineers, Great George Street, London, S.W.1), at 5.30 p.m.—Mr. L. A. Ashton and Mr. S. C. C. Bate: "Fire Resistance of Prestressed Concrete Beams".

INSTITUTION OF ELECTRICAL ENGINEERS, MEASUREMENT AND CONTROL SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. C. G. Garton: "Time and Insulation" (Chairman's Address).

ROYAL SOCIETY OF MEDICINE, EXPERIMENTAL MEDICINE AND THERAPEUTICS SECTION (at 1 Wimpole Street, London, W.1), at 5.30 p.m.—Discussion on "The Kinetics and Control of Erythropoiesis".

UNIVERSITY OF LONDON (in the Main Lecture Theatre, New Physics Building, Imperial College of Science and Technology, Prince Consort Road, London, S.W.7), at 5.30 p.m.—Prof. R. Nevanlinna (Helsinki): "Absolute Analysis".*

ILLUMINATING ENGINEERING SOCIETY (at the Royal Institution, Albemarle Street, London, W.1), at 6 p.m.—Dr. W. S. Stiles, F.R.S.: "Lighting and Research" (Presidential Address)

Wednesday, October 12

UNIVERSITY OF LONDON (at the Postgraduate Medical School of London, Ducane Road, London, W.12), at 2 p.m.—Prof. G. H. Lathe: "Biochemical Basis of Liver Function Tests".*

BRITISH COAL UTILIZATION RESEARCH ASSOCIATION (at the Institution of Civil Engineers, Great George Street, London, S.W.1), at 5.30 p.m.—Dr. F. J. Dent: "The Hydrogenation of Coal to Methane" (Ninth Coal Science Lecture).

CHALLENGER SOCIETY (at the Linnean Society, Burlington House, Piccadilly, London, W.1), at 5.45 p.m.—Dr. Jacques Piccard. "With the *Trieste* in the Challenger Deep".

INSTITUTION OF ELECTRICAL ENGINEERS, EDUCATION DISCUSSION CIRCLE (at Savoy Place, London, W.C.2), at 6 p.m.—Discussion on "Laboratory Work for the Part III Examination", opened by Dr. P. F. Soper.

BRITISH INSTITUTION OF RADIO ENGINEERS, ELECTRO-ACOUSTICS GROUP (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6.30 p.m.—Prof. Colin Cherry: "Electro-Acoustics for Human Listeners" (Inaugural Meeting).

ROYAL INSTITUTE OF CHEMISTRY, LONDON SECTION (at the Royal Institution, 21 Albemarle Street, London, W.1), at 7 p.m.—Prof. V. N. Kondratiev (U.S.S.R. Academy of Sciences): "Energy Exchange in the Interaction of Particles under Electric Discharges" (Second Humphry Davy Lecture).

SOCIETY OF CHEMICAL INDUSTRY, PESTICIDES GROUP (joint meeting with the BIOLOGICAL METHODS GROUP of the SOCIETY FOR ANALYTICAL CHEMISTRY, at the Chemical Society, Burlington House, Piccadilly, London, W.1), at 7 p.m.—Dr. J. H. Hamence, Mr. P. H. Needham, Mr. J. G. Reynolds and Mr. R. Goulden: "Biological Assay of Insecticidal Residues".

WOMEN'S ENGINEERING SOCIETY (at "Hope House", 45 Great Peter Street, London, S.W.1), at 7 p.m.—Mr. J. Rice: "The Use of Microwaves in Telecommunications".

Thursday, October 13

LINNEAN SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Prof. H. B. Rycroft: "Proteas of the South Western Cape"; Dr. L. E. Richdale: "The New Zealand Mutton Bird".

UNIVERSITY OF LONDON (at the Royal Veterinary College, Royal College Street, London, N.W.1), at 5 p.m.—Prof. C. W. Emmens (Sydney): "The Biological Assay of Œstrogenic and Anti-Œstrogenic Activity". (Further lecture on October 20.)

INSTITUTION OF ELECTRICAL ENGINEERS, UTILIZATION SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. J. M. Ferguson: "Developments in Electrical Plant for Industry" (Chairman's Address).

SOCIÉTÉ DES INGÉNIEURS CIVILS DE FRANCE (joint meeting with the INSTITUTION OF STRUCTURAL ENGINEERS, at 11 Upper Belgrave Street, London, S.W.1), at 6 p.m.—M. Jean Bellier and M. Max Tourasse: "Pre-stressed Concrete Pressure Vessels for Nuclear Reactors at Marcoule".

CHEMICAL SOCIETY (in the Large Chemistry Lecture Theatre, Imperial College of Science and Technology, South Kensington, London, S.W.7), at 7.30 p.m.—Prof. R. A. Raphael: "Recent Studies on Many-Membered Rings" (Tilden Lecture).

RADAR AND ELECTRONICS ASSOCIATION (at the Royal Society of Arts, John Adam Street, Adelphi, London, W.C.2), at 7.30 p.m.—Mr P. S. Carnt: "Colour Television".*

Friday, October 14

ASSOCIATION OF APPLIED BIOLOGISTS (in the Lecture Hall of the British Museum (Natural History), Cromwell Road, South Kensington, London, S.W.7), at 10.45 a.m.—Symposium on "Soil Fauna in Relation to Soil Formation and Fertility".

ANTIQUARIAN HOROLOGICAL SOCIETY (at 35 Northampton Square, London, E.C.1), at 6.30 p.m.—Opening and House-Warming, followed by Mr. Cecil Clutton. "Two Constant-Force Chronometers".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

LECTURER IN ORGANIC CHEMISTRY, and an ASSISTANT, Grade A, FOR GENERAL CHEMISTRY at Birkenhead Technical College—The Director of Education, Birkenhead Education Committee, 63 Hamilton Square, Birkenhead (October 12).

METEOROLOGICAL OFFICERS (with a first- or second-class honours degree (or equivalent) in physics or mathematical physics or mathematics or engineering or degree (or equivalent) in meteorology) in the Irish Meteorological Service—The Secretary, Civil Service Commission, 45 Upper O'Connel Street, Dublin (October 14).

ASSISTANT EXPERIMENTAL OFFICER (with at least two subjects at advanced level to include chemistry, zoology or biology, and preferably a knowledge of French and/or German), for work which includes scanning and abstracting scientific literature—The Director, Pest Infestation Laboratory, Agricultural Research Council, London Road, Slough, Bucks (October 15).

ASSISTANT EXPERIMENTAL OFFICERS (2) (with at least two scientific subjects at advanced level, or equivalent) AT THE AGRICULTURAL RESEARCH COUNCIL'S PEST INFESTATION LABORATORY, one for work on insects attacking stored foodstuffs, and the other for work on mycological problems connected with food storage—The Director, Pest Infestation Laboratory, Agricultural Research Council, London Road, Slough, Bucks (October 15).

HEAD OF THE DEPARTMENT OF SCIENCE, Grade III—The Academic Registrar, Hatfield Technical College, Hatfield, Herts (October 15).

HOSPITAL BIOLOGIST (with a first- or second-class honours (B.Sc.) degree in biochemistry or physiology or similar qualifications), for routine and research investigations involving bioassays and chemical procedures—The Deputy Director, Vincent Square Laboratories of Westminster Hospital, 124 Vauxhall Bridge Road, London, S.W.1 (October 15).

LECTURER (with an honours degree in science, preferably in chemistry) FOR WORK ON METHOD IN SCIENCE, to help undergraduate students of science and engineering to clarify their attitudes to science through using discussion and other methods of teaching which have already been developed in the college—The Registrar, Brunel College of Technology, Woodlands Avenue, Acton, London, W.3 (October 15).

LECTURERS (2) (with an honours degree in chemistry, with teaching and research or industrial experience) IN THE DEPARTMENT OF CHEMISTRY, one for Organic and one for Inorganic Chemistry—The Principal, Whitehaven College of Further Education, Whitehaven, Cumberland (October 15).

PRINCIPAL OF THE INSTITUTE OF AGRICULTURE, Moulton—Chief Education Officer, County Education Offices, Northampton (October 15).

READER IN MATHEMATICS—Prof. Titchmarsh, Mathematical Institute, The University, Oxford (October 15).

SENIOR LECTURER (with high academic qualifications and preferably industrial and research experience) IN PHYSICAL CHEMISTRY—The Registrar, Lanchester College of Technology, Priory Street, Coventry (October 15).

LECTURER IN PHYSICS AND/OR CHEMISTRY—The Principal, Bede College, Durham (October 22).

LECTURER IN STATISTICS—The Registrar, University College of North Staffordshire, Keele, Staffs (October 24).

ASSISTANT LECTURER (with special qualifications in genetics, cytology or taxonomy) IN BOTANY—The Secretary, The Queen's University, Belfast (October 31).

LECTURER/ASSISTANT LECTURER (preferably with a good honours degree in either agricultural science or veterinary science, suitable research and teaching experience, and previous practical experience in animal husbandry, including the breeding, feeding and management of farm livestock, preferably under tropical conditions) IN ANIMAL SCIENCE at the University of Malaya, Kuala Lumpur—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Malaya and London, October 31).

PRINCIPAL OF ABERDEEN COLLEGE OF EDUCATION—The Principal, The College of Education, St. Andrew Street, Aberdeen (October 31).

CHAIR OF ANATOMY—The Registrar, University College of South Wales and Monmouthshire, Cathays Park, Cardiff (November 5).

LECTURER IN ORGANIC CHEMISTRY at the University of Adelaide, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, November 7).

RESEARCH FELLOWS (with interests in the following fields: (a) geomorphology, (b) biogeography (including plant ecology), or (c) social or economic geography) IN THE DEPARTMENT OF GEOGRAPHY, Research School of Pacific Studies, Australian National University—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, November 7).

CHAIR IN PLANT SCIENCE—The Registrar, Massey Agricultural College (University of New Zealand), Palmerston North, New Zealand (November 30).

DEMONSTRATORS (preferably with an honours degree) IN INORGANIC AND PHYSICAL CHEMISTRY at the University of New England, Armidale, New South Wales, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, November 30).

LECTURER IN METALLURGY at the University of Otago, Dunedin, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand and London, November 30)

LOGAN CAMPBELL CHAIR IN FOOD TECHNOLOGY—The Registrar, Massey Agricultural College, University of New Zealand, Palmerston North, New Zealand (November 30).

SENIOR LECTURER or LECTURER IN MINING at the University of Dunedin, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C 1 (New Zealand and London, November 30).

SCIENTIFIC OFFICER (honours graduate in zoology), for work on plant parasitic nematodes—The Secretary, Rothamsted Experimental Station, Harpenden, Herts (November 30).

WALTER CLARKE BUCHANAN CHAIR IN AGRICULTURAL ECONOMICS AND FARM MANAGEMENT—The Registrar, Massey Agricultural College (University of New Zealand), Palmerston North, New Zealand (November 30).

LECTURERS or ASSISTANT LECTURERS (2) (with at least a good honours degree in zoology or equivalent qualification, experience in teaching and research, and preferably with a special knowledge of entomology or arthropod zoology in general for one of the two posts) IN THE DEPARTMENT OF ZOOLOGY at the University of Malaya, Kuala Lumpur—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Kuala Lumpur and London, December 1).

ASSISTANT, Grade B (graduate, preferably with teaching and/or research and/or industrial experience, capable of taking classes to B.Sc. (General) degree and H N.C. level, and preferably a member of the Royal Institute of Chemistry), IN CHEMISTRY—The Clerk to the Governors, Mid-Essex Technical College and School of Art, Market Road, Chelmsford, Essex.

ASSISTANT LECTURER, Grade B (with an honours degree in zoology with subsidiary botany or a general degree in botany and zoology, and prepared to teach zoology to B.Sc. General and botany and zoology to G.C.E. advanced level standard) IN BIOLOGY—The Principal, Medway College of Technology, Horsted, Maidstone Road, Chatham, Kent.

BIOCHEMIST, Basic grade (graduate in chemistry or Associate or Graduate Member of the Royal Institute of Chemistry), IN THE DEPARTMENT OF PATHOLOGY—The Group Secretary, Queen Elizabeth Hospital for Children, Hackney Road, London, E.2.

BIOCHEMIST (Senior grade), to take charge of the East Riding Group Laboratory—The Hospital Secretary, Westwood Hospital, Beverley, East Yorkshire.

BIOLOGIST or BIOCHEMIST, to work in the United Birmingham Hospitals, Department of Clinical Endocrinology, on the immunological properties of pituitary hormones; and a BIOCHEMIST (Basic grade), to work on the determination of steroid hormones—The Director, Department of Clinical Endocrinology, Birmingham and Midland Hospital for Women, Showell Green Lane, Birmingham 11.

CHEMIST/ASSAYER (man or woman, preferably under 40, with a good honours degree in chemistry or equivalent professional qualification, and preferably with experience in inorganic analytical chemistry and a good knowledge of instrumental methods and/or electronics) IN THE MINES AND GEOLOGY DEPARTMENT, Government of Kenya, for duties which will include assaying and quantitative analysis of rocks, minerals and ores, and advising on metallurgical and chemical treatment problems connected with mineral extractions—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.99/7/07/T.

GRADUATE ASSISTANT IN THE ENDOCRINE UNIT, to take part in biological, immunological and chemical techniques—The Chemical Pathologist, Hospital for Sick Children, Great Ormond Street, London, W.C.1.

GRADUATES IN CHEMISTRY OR METALLURGY, for fundamental studies of electro-deposition of metals and alloys—The Head of the Department of Metallurgy, Battersea College of Technology, London, S.W.11.

HEAD (preferably with a knowledge of the agricultural industry) OF THE DEPARTMENT CONCERNED WITH THE BIOCHEMISTRY OF ANIMAL NUTRITION—The Secretary, Rowett Research Institute, Bucksburn, Aberdeen.

LECTURER (with a good honours degree, and teaching experience, able to teach statistics to B.Sc. General Degree level, and preferably the ability to teach numerical analysis) TO TEACH PURE AND APPLIED MATHEMATICS AND STATISTICS to G.C.E. Advanced level and B.Sc. General Degree—The Clerk to the Governors, South-West Essex Technical College and School of Art, Forest Road, Walthamstow, London, E.17.

LECTURER (with an honours degree in electrical engineering and industrial experience) IN ELECTRICAL ENGINEERING with interests in Telecommunications—Northampton College of Advanced Technology, St. John Street, London, E.C.1.

RESEARCH WORKER (BIOCHEMIST or CHEMICAL PHARMACOLOGIST, with a Ph.D. or equivalent experience), to investigate the biochemical actions of drugs currently used in the treatment of mental illness—The Director of Clinical Research, Crichton Royal, Dumfries.

SENIOR LECTURERS or LECTURERS (with a first- or second-class honours degree, a thorough grounding in electrical engineering, experience in electrical power and machines, and/or electrical theory and measurements) IN ELECTRICAL ENGINEERING, at the Royal Military College of Science, Shrivenham, Berks—The Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting D.627/0A.

SENIOR TECHNICIAN (fully conversant with general workshop practice and with practical electrical experience) IN THE DEPARTMENT OF X-RAY TECHNOLOGY, for duties which will include routine maintenance of X-ray apparatus—The Administrative Assistant, Churchill Hospital, Oxford.

SOIL CHEMIST (with a good honours degree in chemistry or agricultural science with postgraduate training or experience in soil science) in Sarawak, to take charge of the Soils Laboratory and to undertake soil and plant analyses—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/24/08/T.

TECHNICAL ASSISTANT (preferably with some experience of standard histological techniques), for interesting and varied work in the Histology Department—The Administrative Officer, Nutritional Research Unit, Huntingdon.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

British Steel Castings Research Association. Seventh Annual Report, 1960. Pp ii+34. (Sheffield British Steel Castings Research Association, 1960.) [197

University of Birmingham: Institute of Education. Education in an Age of Technology. a Report on the Fifth Summer School held at Worcester 1959. Pp. 151. (Birmingham: University of Birmingham, Institute of Education, 1960.) [197

World Power Conference. Annual Report, 1959. Pp. 18. (London: World Power Conference, 1960.) [197

Notes and Records of the Royal Society of London, Vol. 15 (Tercentenary Number). Pp. ix+275+29 plates. (London The Royal Society, 1960.) 30*s*. [197

Institute of Physics. Fortieth Annual Report of the Board of the Institute of Physics for the year 1959. Pp. 19. (London. Institute of Physics, 1960.) [197

General Register Office. The Registrar General's quarterly return for England and Wales. No. 445 (1st Quarter 1960): Births, Deaths and Marriages; Infectious Diseases; Weather; Population Estimates, quarter ended 31st March 1960. Pp. 28. (London H.M. Stationery Office, 1960.) 2*s*. net. [197

Report by the Hydrographer of the Navy for 1959. Pp. 30+4 plates (London: Admiralty, 1960) [197

Other Countries

Annals of the New York Academy of Sciences. Vol. 83, Article 1: Molecular Organization in Solid High Polymers. By F. A. Bettelheim and 8 other authors. Pp. 1–76. 2.50 dollars. Vol. 83, Article 2: The Vagina. By Warren R. Lang and 43 other authors. Pp. 77–358. 4 dollars. Vol. 86, Article 1: Nonnarcotic Drugs for the Relief of Pain and their Mechanism of Action. By F. M. Berger and 50 other authors. Pp. 1–310. 3.50 dollars. (New York: New York Academy of Sciences, 1959 and 1960.) [197

Organization for European Economic Co-operation: European Nuclear Energy Agency. The Industrial Challenge of Energy, 3 Stresa Conference. Part 4 · The Market for Nuclear Equipment and Instrumentation. Pp. 272. (Paris: Organization for European Economic Co-operation, European Nuclear Energy Agency; London. H.M. Stationery Office, 1960.) 12 NF.; 18*s*. 6*d*.; 3 dollars; 12 Swiss francs, 10.20 D.M. [197

East Africa High Commission. East African Marine Fisheries Research Organization Annual Report, 1959. Pp. ii+18. (Nairobi: Government Printer, 1960.) Sh. 4. [197

XII Jornada Clinica de Verano, 1959. (Organizada por la Fundacion Lucas Sierra de Vina del Mar, y Sociedad Medica de Valparaiso.) Pp. xvi+379. (Vina del Mar, Chile: Fundacion Lucas Sierra, 1959.) [197

1st International Symposium on Fleming's Lysozyme, Milano, April 3rd, 4th, 5th, 1959—Abstracts of Relations and Communications. Pp. 151. (Milano: Museo della Scienza e della Tecnica, 1950.) [197

Smithsonian Institution: United States National Museum. Bulletin 216, Part 2: Ichneumon-Flies of America North of Mexico. 2: Subfamilies Ephialtinae, Xoridinae, Acaenitinae. By Henry and Marjorie Townes. Pp. vii+676 (378 figures). (Washington, D.C.: Government Printing Office, 1960.) 2.50 dollars. [197

United States Department of Agriculture. Index-Catalogue of Medical and Veterinary Zoology. Supplement 9, Authors: A–Z. By Mildred A. Doss, Judith M. Humphrey and Dorothy B. Segal. Pp. i+322. 1.25 dollars. Index-Catalogue of Medical and Veterinary Zoology. Supplement 10, Authors: A to Z By Mildred A. Doss, Judith M. Humphrey and Dorothy B. Segal. Pp. i+357. 1.25 dollars (Washington, D.C. · Government Printing Office, 1959 and 1960.) [197

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FREEDOM IN ACADEMIC RESEARCH

IN a recent address given in the University of Nottingham, Sir William Slater, secretary of the Agricultural Research Council, made a strong plea that universities should lead rather than follow contemporary thought, and in particular that they should be sufficiently independent financially to be able to allocate sufficient funds for research on lines of work entirely of their own choosing. Sir William was discussing the relative values of such research and of sponsored research, undertaken with the assistance of outside bodies, and he was firmly of the opinion that those carrying on research work in universities should have the freedom to decide whether they would pursue lines of work entirely of their own choosing, within the funds at their disposal, or whether they had problems to put to bodies, such as the Agricultural Research Council, for short-term assistance. The problem of course arises out of the extent to which the universities are now dependent on public funds, and how far, even with the University Grants Committee, it is possible for their independence from outside pressure to be fully maintained.

This was the subject of Prof. W. H. Linnell's address as chairman to the British Pharmaceutical Conference at Newcastle upon Tyne. Starting with the proposition that Britain's most valuable raw material is its young people, to whom education is of paramount importance if they are to develop the knowledge and powers of leadership which alone will ensure the country's survival as an important power, Dr. Linnell emphasized that the interdependence of education and research in science is fundamental. Further, whether or not Britain maintains her position in the world as a great power will depend, he said, largely on her research activities in the near future. These cannot exist unless we possess personnel capable of extending the boundaries of knowledge, and this, in its turn, depends on the education of the young and on some directive influence on their potential.

Against this background, and that of the economic threat developing behind the Iron Curtain, in consequence of the rapid expansion of scientific and technological education and research in the U.S.S.R., Dr. Linnell advanced his plea that academic freedom constitutes a fifth freedom to be set in importance along with President Roosevelt's four freedoms —freedom of speech and expression, freedom of worship, freedom from want, and freedom from fear. Moreover, powerful forces are working against academic freedom in many parts of the world, and these should be resisted at all costs. In particular, he referred to secrecy, especially in regard to publication of research. Secret work of any kind has no place in a university except during an emergency.

In establishing his thesis that our position in the world may well depend upon the fundamental research effort of the immediate future, Dr. Linnell followed in some respects Sir George Thomson's argument in his presidential address to the British Association, deprecating the evaluation of research solely by its contribution to modern living. He was, however, more concerned with the educational aspect—both with the need for greater expenditure on education and with the question of quality, particularly that of an adequate general education, though he recognized that it might be necessary also to encourage an increasing number of students into scientific and technological fields. The colleges of technology as well as the universities have their part to play in providing an adequate body of workers capable of original thought and possessed by a burning desire to extend the frontiers of knowledge.

Given, however, an adequate supply of research workers of the requisite quality, the question of the distribution of the research effort of Britain remains. Even the balance between fundamental and applied research is not easy to determine, and while Dr. Linnell urged that the larger industrial organizations should accept some responsibility for fundamental research in appropriate fields, he did not go into the question of the distribution of research effort as between the universities, independent research institutions, the research associations, Government research stations or departments and industry itself. This question of distribution, however, is quite as important as what Dr. Linnell describes as the basic problem of how to plan our research effort without detriment to intellectual freedom, and indeed its wise handling could go far to remove many dangers to academic freedom. Apart from this, the question of distribution is related to that of the effective utilization of the results of research.

In emphasizing that while it is impossible to plan discovery, it is quite possible to plan for it, Dr. Linnell suggested that more could be done within the universities to ensure that the existing potential for research is utilized in projects that are really worth while. Research within the universities, it is true, serves at least two different, but allied, functions, and this is equally true of research in the colleges of technology, where perhaps expert guidance is particularly needed if they are to make a serious contribution to the research effort. Moreover, the educational objective—both in respect of the teacher and the students he is training—is the more readily achieved if the research effort is itself directed at some objective really worth while.

Dr. Linnell clearly recognizes the difficulty of supplying any such guidance from outside without trespassing on academic freedom, and the Committee on Science and Freedom has evidence enough of how easily academic freedom is infringed even in countries like Canada and Australia. Dr. Linnell's own suggestion is for the universities themselves to set up separate science committees for each scientific discipline to advise on all matters concerning research.

He visualizes such committees acting as clearing houses for ideas, with contacts with research associations and other bodies, and arranging opportunities for people working on similar projects to meet; his suggestion is essentially an extension of what is already being done by the Council for Scientific and Industrial Research and the Medical Research Council, though all the arrangements would be in the hands of the universities.

Nevertheless, if we are to make the best use of the limited resources of scientific man-power in Britain, as Dr. Linnell intends, the Minister for Science must play some part. This is as essential if sufficient financial resources are to be available for research as it is in securing that such man-power is not wasted for lack of either equipment or supporting technicians or through excessive overlapping. Co-ordination is probably best effected by such informal arrangements as the Research Councils are already establishing and the University Grants Committee may also seek to foster; but if public support on the scale visualized by Dr. Linnell is to be secured, the full influence of the Minister for Science and the Advisory Council on Scientific Policy will be needed.

This will be no less essential in the campaign of public education for which Dr. Linnell calls. The scientist himself has indeed an essential part to play in educating public opinion so as to secure adequate support for research, and so also have bodies such as the Parliamentary and Scientific Committee. Finance, however, is only a part of the problem, and in securing the most effective use of scientific and technical man-power, as is indicated by Sir Lindor Brown in a Sir David Russell Memorial Lecture delivered before the University of St. Andrews on March 9, 1960, scientists must themselves exert an important influence.

Under the title "The Perils of Leadership in Science"*, Sir Lindor discussed some problems which bear closely on the quality and effectiveness of university research, and his unusual approach directs attention to factors determining the utilization of trained scientific man-power which are sometimes overlooked. In the main, he is concerned with teachers and research workers in the experimental sciences and those near to them in interest and activity, and at the start he points out that the use of the military analogy in describing the technique of promoting scientific advance can be misleading. Rarely is it possible in scientific strategy to define an objective within the reach of a life-time, and very rarely is such an objective attained.

Sir Lindor Brown's thought runs on the lines of the Barlow Report on scientific staff, now largely forgotten, and he thinks that too little is made of the needs of the scientist for inspiration, and of the quality of a work of art that good scientific work possesses. Sir Edward Appleton, of course, has emphasized this aspect, but Sir Lindor discusses its bearing on fundamental research work, in which he suggests there are three major decisions of strategy to take: what to start, when to stop and where to go, and in that order. Leadership, he suggests, consists essentially in the supply of inspiration, and he is convinced that the British Isles still have a unique supply of original minds and can offer unique opportunities for their cultivation and development.

It is in regard to the starting of a project that the young research worker, he suggests, nearly always needs guidance, and that the real qualities of leadership of his science are fully tested only when, after the younger man has started work on his problem, he has an idea of his own. The treatment of that idea may make all the difference to the younger man's future career, and Sir Lindor stresses the importance of taking every care to avoid damaging what should be the most profitable feature of a scientist's life, namely, the free interchange of ideas and argument. Sympathy and imagination, however, are equally required in helping the young worker to deal with the second difficulty, that of knowing where to stop and when to publish his results. In many fields research is more or less a continuous process, and even the experienced worker does not find it easy to take alone the decision when to publish.

Sir Lindor was concerned to emphasize the necessity of publication to complete the research process, and while this has an important bearing on the question of secrecy and academic freedom, his remarks about the continuous nature of such research and the difficulty of setting a clear objective direct attention to an aspect that has to be considered in determining the distribution of our research effort on the broadest scale. It indicates one reason why the maximum of choice must be left to the research worker himself, and recent reports from the Council of Scientific and Industrial Research show that it is a difficulty of which the Council is deeply conscious. If only for the personal effects and the bearing of such decisions on the whole atmosphere in which work is done, as much flexibility as possible is clearly desirable. Enthusiasm once really dampened is seldom easily re-kindled.

The third aspect, that of deciding where to go, is closely related to the second. The attractive vistas continually opened up as work proceeds on a problem set a series of difficult decisions in which even the most experienced scientist may make the wrong choice. The opportunity for wise and enlightened leadership is unmistakable, but even so the leader may take an incorrect decision and the effect on his team may be disastrous unless the right atmosphere already exists. Space, facilities, adequate finance, freedom from petty worries, either domestic or administrative, adequate recognition, someone to give a measure of encouragement at more serious moments of frustration or despondency, perhaps also, as Sir Lindor Brown suggests, some alternative activity, as a little teaching, to stimulateh is mind, all have a part to play; and if there is a leader whose wisdom and understanding have already won

* The Perils of Leadership in Science. By Prof. Sir Lindor Brown. (Sir David Russell Memorial Lecture No. 2, delivered before the University of St. Andrews at Queen's College, Dundee, 9 March, 1960.) Pp. 20. (London Oxford University Press, 1960) 3s. 6d. net.

the confidence of his colleagues, the essential conditions should be there to ensure that creative work is not thwarted by the inevitable mistakes in human judgment. Seldom, he recognizes, can the head of the laboratory claim sufficiently detailed knowledge to give more than general advice to his colleagues on their scientific problems; but if in good time he can detect the faltering of genius, or an alternative activity of promise, and secure its adoption without causing resistance and revulsion, a laboratory director has discharged one of his most important functions.

Nothing is more important, however, in Sir Lindor Brown's address, than the stress he lays, in conclusion, upon the human demands made on leadership in scientific activity It is a continuous process, intimately linked with that process of free discussion and criticism which is the essence of scientific advance, and Sir Lindor's own experience leads him to stress the importance of the research director himself working in the laboratory to maintain sympathy and close contact with his staff. He admits the desperate seriousness of the problem of time, but maintains unhesitatingly that to preserve our originality of approach, our capacity for unexpected discovery, and our unconventional freshness of ideas, in which we stand alone, we need leaders who will lead in the laboratory, leaders with sympathy and understanding for the man on the job and leaders with the humility of the true scientist.

That needed to be said, and should be marked in the universities and in Government departments and organizations as well as in industry. Unless those conditions are observed, we shall undoubtedly fail to make full use of whatever scientific and technological man-power is at our disposal, and above all in research. To ensure that such conditions are generally to be found is one of the most economic ways of expanding our existing research effort, but to achieve it may well demand some hard and constructive thinking about problems of administration. Sir Lindor is well aware of the increasing administrative burdens which are being placed on the heads of research units and departments in the universities, in the Government service and in industry, burdens which can scarcely be reduced to-day, however flexible our organization, except by sharing them more widely. That in turn requires a growing supply of scientists and technologists capable of assuming such responsibilities. From that point of view alone it is encouraging to note that in his presidential address to Section B (Chemistry) at the recent British Association meeting at Cardiff, Dr. James Taylor lent the weight of his own experience as a director of Imperial Chemical Industries, Ltd., to what Prof. T. L. Cottrell had said in his inaugural lecture at the University of Edinburgh last autumn as to the need for the universities to ensure that they gave their students not simply a good general education, with all that that implies as to an imaginative approach to human problems, but above all inculcated a critical and intellectual approach to whatever problems confronted them. The effective deployment of our limited resources for research and development demands indeed sound organization constantly kept under review by wise and imaginative administrators: it depends, in particular, on the quality of the man-power available, for the prosecution of research and for the handling of the myriad problems of co-ordination and co-operation, inspiration and guidance on which Sir Lindor Brown touched with vision and understanding.

THE STUDY OF SUB-ATOMIC PHENOMENA BY THE NUCLEAR EMULSION

The Study of Elementary Particles by the Photographic Method

An Account of the Principal Techniques and Discoveries illustrated by an Atlas of Photomicrographs. By C. F. Powell, P. H. Fowler and D. H. Perkins. Pp. xvi+669. (London and New York: Pergamon Press, 1959.) 250*s*. net.

THE study of sub-atomic phenomena, and in particular of the elementary particles, has been much aided by three techniques, the cloud chamber, the photographic emulsion, and the bubble chamber, by which the tracks of individual charged particles can be made visible. This volume is the third of a series designed to present carefully selected photographs of high technical quality to help students to acquire a better understanding of the physical principles involved in sub-atomic phenomena. In these volumes there are reproduced not only those photographs which have made history but also a sufficiently wide range of others to illustrate the power and limitation of the different techniques, and to serve as exercises in the recognition and interpretation of the nuclear phenomena produced by cosmic rays or artificially produced high-energy particles. The first volume, by the reviewer and J. G. Wilson, which appeared in 1952, and the second, by W. Gentner, H. Maier-Leibnitz and W. Bothe, published in 1954, were concerned with the application of the Wilson expansion chamber to cosmic rays and nuclear physics. The present volume covers the application of the photographic emulsion technique to the investigation of the elementary particles and cosmic rays. In common with the companion volumes, the photographs are central and the text is written around them, but unlike the previous volumes the text here is so extensive that the book has become a monumental work on the emulsion technique.

There are good reasons why the present time is opportune for such a work. The first reason is that with the advent of the bubble chamber and the production of beams of the new particles at the great accelerators, the period during which the emulsion technique has occupied a unique place in the study of the elementary particles is drawing to a close. The second reason is the growing confidence that, as the authors state in the preface, "most of the particles which play an important part at that level of penetration into the structure of matter which our present technical resources allow, have either been discovered, or their existence anticipated".

The nuclear emulsion makes possible the precise identification of most of the charged elementary

particles by virtue of its unusual power of discrimination and high stopping power. Its property of continuous sensitivity makes possible the accumulation of rare particles and 'events'. The emulsion is, however, not a very powerful technique for the study of the neutral unstable particles because of the lack of time correlation; and its chemical complexity can cause ambiguity in interpretation. The newly developed bubble chambers seem to combine most of the desirable features of both the nuclear emulsion and the Wilson chamber (apart from cost!), and, moreover, can operate at a speed appropriate to the rapid pulse-rate and high background of the great accelerators. Nevertheless, the nuclear emulsion technique still seems to be the technique most suited to the study of ultra-short-lived particles, in consequence of the extreme fineness of the photographic grain, and of certain aspects of the interaction of cosmic-ray particles of very great energies.

The book opens with a well-documented and illustrated history of the use of the photographic emulsion in nuclear physics and the steps which led to the production of the nuclear emulsion. There follow excellent sections on the basic technical features of emulsions, the range-energy relations, and the measurement of specific ionization and scattering, quantities of considerable importance in the emulsion technique. These sections are beautifully written and illustrated, and will be of great value in the training of research workers. Most of the rest of the book is concerned with the elementary particles, electrons and photons, μ-mesons, π-mesons, K-mesons, hyperons, protons and antiprotons; but there are also quite long sections devoted to hypernuclei, interactions in the energy-range 10^8–10^9 MeV., and heavy nuclei in the primary cosmic radiation. Fundamental discoveries made by use of the technique, for example, the π- and τ-mesons, heavy primaries and hypernuclei, are fully described, and with the original photographs serve as a reminder of the achievements of British physicists in the exciting early post-war years. In all there are 190 plates, superbly chosen and reproduced, and numerous excellent figures to illustrate the text. The text is a clear account of many of the technical aspects of the use of nuclear emulsion in the high-energy field and of modern high-energy nuclear physics. There are a few small errors, but on the whole the book is singularly free from error.

This magnificent volume can be most warmly recommended to anyone interested in nuclear physics, and is a worthy tribute to the part played by the nuclear emulsion technique in the study of the elementary particles. It is also a brilliant tribute to the research school of which the authors are distinguished members. G. D. ROCHESTER

ORIGIN AND DEVELOPMENT OF LIFE

You and the Universe

By Dr. N. J. Berrill. Pp. viii+215. (London: Dobson Books, Ltd., 1959.) 18*s*. net.

PROF. N. J. BERRILL has produced a tantalizing book. In it he sets out to show the origin of life, the way it has developed and the place it holds in an evolving universe.

The task is not beyond him and many readers would agree that, with impeccable prose, crystal-clear thinking and considerable scholarship, in this volume he leaves a stimulating picture of the one-ness of life and the whole-ness of the universe.

The theme is developed in an evolutionary sequence to show how scientific knowledge and thought eventually widen out to find common ground with spiritual insight and belief. Yet as soon as the author reaches a point where a philosophy which is spiritually satisfying might emerge, he breaks off as if at the end of his tether.

The result is a book which, because of the almost poetic style in which the biological and astronomical material is presented, could be hard going for the general reader whose learning is now adjusted to the superlative illustrative diagrams, photographs and models used by the B.B.C. in its current research series on television. The student with some knowledge of biology will be left somewhat frustrated because the end leads to unsatisfying whimpers rather than a statement of sustaining revelations and beliefs.

This is a disappointment, because, without question, Berrill has out-of-the-ordinary gifts in presenting ideas through the written word. He should use them to finish this book.

Whether "You and the Universe" is improved by the extracts from Walt Whitman which launch each chapter will depend on taste. Certainly, the physical presentation will not be to everyone's liking. T. H. HAWKINS

STRAIGHT-LINE DATA ANALYSIS

Analysis of Straight-Line Data

By Prof. Forman S. Acton. (Wiley Publication in Applied Statistics.) Pp. xiii+267. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1959.) 72*s*. net.

PROF. ACTON demonstrates that a book the object of which is utilitarian can also be attractive to the reader, perhaps mainly because of the freshness of his style and his insistence on keeping close to real experimental problems. He is interested in answering the questions that experimenters need to ask, and early makes plain his attitude by stating: "If we waited for all the epsilons and deltas to be supplied before we used techniques that statistical common sense suggests, we would be technical paupers". His second chapter is probably the best systematic account yet available of the classical problem of simple regression, with its many ramifications in respect of errors and limits for different estimates; it should be read by all who imagine that they have nothing more to learn about these techniques.

In another major chapter, the frequently evaded topic of regression with both variates subject to error is discussed, and the similarities and differences between various practical situations are considered. The methods proposed owe much to Tukey, but Acton's own contribution is evident. Acton's presentation is distinctive among statistical texts for the blunt common sense of his recognition that the duty of the practising statistician is not simply to construct models, to test hypotheses, or to make decisions in accordance with abstract principles; he must interpret numerical data in whatever manner may be most appropriate to their source and their intended

use, recognizing the imperfections of these data but seldom admitting total defeat in his efforts at rational analysis. The writing is interspersed with remarks of refreshing directness and practicality: ". . . if our purpose is to analyse data realistically, we must face the anomalous situations which all too frequently occur rather than pretend that they do not exist. If the information is not precise, it is usually necessary to make some subjective judgments, and the best place to make them is where they have the least influence on the information extracted. If the assumptions turn out to be wildly different from the physical facts, the conclusions will be bad too, but the fault will be with the person who made the assumptions—not with the method of analysis".

Chapters on analysis of variance and on orthogonal polynomials are more conventional in pattern, though still containing ideas that too many authors neglect. The account of multiple comparison procedures is much condensed; some may wish that the author had brought his admirable critical sense to bear on this complex of methods, instead of simply accepting one, even though that one is possibly among the most useful. Later chapters attempt little more than to direct attention to aspects of regression on which further research is needed. Although Prof. Acton disclaims all intention of writing a text for class use, neither students nor their teachers could fail to gain from his book; both the novelty of its content and a style of writing that is vivid, unafraid of the telling metaphor or colloquialism, yet never obscure or verbose, should commend it both for its own sake and as an example.

D. J. FINNEY

THE PARANORMAL: A FRENCH VIEW

Treatise on Parapsychology

Essay on the Scientific Interpretation of the Human Phenomena known as 'Supernatural'. By René Sudre. Translated by C. E. Green. Pp. 412. (London: George Allen and Unwin, Ltd., 1960.) 35*s*. net.

THIS book is an attempt to provide the general reader with a survey of the whole field of psychical research from early times until the present day. It was first published in Paris in 1956, and its plan was clearly to allow other than English-speaking people to know something of what has been done in this field both in Great Britain and the United States, where the general attitude towards parapsychology is not the same as in France, Italy and other countries on the European continent.

M. Sudre is well equipped for the task he has set himself, for he has long been one of the most distinguished exponents of that point of view common in France early in this century but now being superseded. Closely associated for many years with Prof. Richet, Dr. Geley and others connected with the Institut Métapsychique in Paris, he has seen much and his attitude is typical of this group of French inquirers, being keenly critical of any theories savouring of spiritism, while at the same time somewhat credulous as to the reality of the phenomena to be interpreted.

After a brief historical survey the author proceeds to a discussion of the phenomena, linking them with sudden changes in what he calls the 'psychological personality', an alteration he terms 'prosopopesis'. He then passes to a consideration of telepathy, clairvoyance ('metagnomy') and the relation of a supposed psychic fluid to mesmerism, radiations and telergy. From consideration of this supposed action at a distance he then goes on to discuss 'teleplasty', or the objectivization of forms, and concludes his study by dealing with spontaneous cases, haunts, mysterious behaviour in animals and phenomena claimed by spiritists to be striking indications of survival after death.

M. Sudre's own opinions are anchored to his faith in the reality of the so-called physical phenomena. He believes in materialization, even going so far as to credit the partial dematerialization of mediums' bodies in séances: he believes in psychic photography and has many good things to say about such dubious mediums as Guzik, Kluski, Florence Cook, Reese, Kahn and even Kraus, although he does not give Kraus's name nor let the reader know that this person confessed to his frauds in an unpublished memoir. He even maintains that the phenomena at Borley Rectory were 'incontestably genuine' and this in spite of incontrovertible evidence to the contrary.

Since the author is convinced that certain human beings are endowed with these astonishing faculties, he finds the spiritistic explanation of little value and the evidence for survival, so painfully collected by the British and the Americans, he brushes aside as simply examples of 'perceptive metagnomy' and 'collective psychism', while at the same time he defends the theory that the so-called telepathic apparitions are objective and that the hallucinatory nature of these experiences cannot be maintained.

The book is well produced and translated, although it lacks an index of subjects, and some of the mistakes and misprints in the French edition (for example 'Mac-Aba' for 'MacNab') have been carried over into the English version, where more care in the standardization of references would have improved the book.

E. J. DINGWALL

A CENTURY OF NAVAL ARCHITECTURE

The Institution of Naval Architects, 1860–1960

An Historical Survey of the Institution's Transactions and Activities over 100 Years. By K. C. Barnaby. Pp. 645+11 plates. (London: The Royal Institution of Naval Architects, 1960. Published in association with George Allen and Unwin, Ltd.). 105*s*. net.

IN 1791 a laudable attempt was made to found a 'Society for the Improvement of Naval Architecture', but the venture was premature and therefore short-lived. By 1860, however, sail and steam were in competition, iron was challenging timber as a shipbuilding material, the mercantile marine was expanding rapidly and an era of swift technical advancement had begun. In these circumstances, the Institution of Naval Architects was brought into being by a small group of founder-members. It has been stated that the history of the Institution is the history of naval architecture, and the Institution, now 100 years old, has been honoured by its new title of the 'Royal Institution of Naval Architects' and has celebrated its centenary by meetings in London and by the production of this excellent and fascinating volume.

The preparation of "The Institution of Naval Architects—an Historical Survey" was entrusted to Mr. K. C. Barnaby, himself a naval architect of high repute, and he has accomplished his task with extraordinary success. He writes with lucidity, perspicacity and with the saving grace of humour. His method is to review each volume of the Institution's *Transactions*, reminding the reader of the existing state of knowledge and summarizing each paper with admirable brevity. Such a course might well be hazardous in less-skilful hands, but Mr. Barnaby is a master of his subject and is never guilty of airing either hindsight or superior knowledge. He can be forthright without being rude, and he can be complimentary without being condescending. Occasionally he is devastating, as when he describes one early paper, by a gallant admiral pontificating on warship design, as "a farrago of nonsense".

A perusal of these pages gives a clear and connected account of the advances in naval architecture and marine engineering since 1860. One reflects ruefully that a final solution is rare in applied science, for the problems of resistance, strength, stability, rolling and steering discussed in the earliest volumes are still, although in modified forms, the subjects of continuing investigations. One point worthy of note is that in discussion our forefathers were frank to the point of rudeness. Our present-day discussions of technical papers are colourless and stilted by comparison.

A centenary is perhaps as suitable an occasion for taking stock as any other. The Institution has tried to improve the status and the training of naval architects and has always been active in furthering efforts to improve the design, construction and safety of ships. But merchant ships, although they may well continue to provide the cheapest form of transport, are now subject to forms of competition undreamt of by the founders of the Institution. With warships the changes are no less marked, as, for example, the aircraft carrier supplants the battleship.

Research in naval architecture has, until recent times, been left to private enterprise and not heavily supported by government bodies or trade associations. The volume records a hundred years of technical advance and the next centenary will, one hopes, see accelerated progress in technical developments, if Great Britain is to retain its position of eminence in shipbuilding.

J. F. C. CONN

GROWING UP

Growing up in Newcastle upon Tyne

A Continuing Study of Health and Illness in Young Children within their Families. By F. J. W. Miller, S. D. M. Court, W. S. Walton and E. G. Knox. Pp. xxi+369+9 plates. (London: Oxford University Press, 1960. Published for the Nuffield Foundation.) 25*s*. net.

THIS book is the second volume of an inquiry into the pattern and extent of illness during childhood in Newcastle upon Tyne. The first volume ("A Thousand Families in Newcastle-on-Tyne"), deals with the first year of life. The present volume is concerned with the age group of 1–5 years.

The investigation is continuing until 1962, when the children will be fifteen, and a third volume will cover the school years.

The study is based on observations during visits to the homes, by health visitors and doctors, on all infants born in Newcastle upon Tyne during May 1–June 30, 1947. The original 1,142 children have now shrunk by removals, withdrawals and deaths to 847.

The work, inspired by the late Sir James Spence, is an attempt to discover the occurrence and natural history of illness as they occur in families and to find out how the pattern and outcome of disease are influenced by the child's environment. Our knowledge of child ailments has hitherto been based on vital statistics, hospital attendances and the records of general practitioners. It shows how incomplete such knowledge can be, for in nearly half the illnesses the doctor was not called in.

The book follows the same pattern as the earlier one. A section is devoted to the environment of the child, under the headings: housing, family, and medical care. The housing, as one would expect in an industrialized city, left much to be desired, and many houses and flats were in a dilapidated condition and many families live in overcrowded conditions. About one quarter of the mothers were employed in whole- or part-time work.

After a preliminary discussion of the pattern of the illness in the first five years of life the authors go on to describe in detail the diseases group by group. It is shown that infective illness still causes 82 per cent of all morbidity in the first five years. Respiratory diseases ranging from heavy colds to pneumonias form nearly two-thirds of all infective illnesses. Fortunately, fatal illness is uncommon after the first year of life. The incidence of bronchitis was ten times higher in the families of labourers and unskilled workers than in professional families.

Tuberculous infection has steadily diminished in the period under review. In 1947, 85 deaths occurred in children under 15 years. By 1954 the total had fallen to four. As judged by tuberculin jelly tests, 7 per cent of the children had become infected by 5 years of age. This is a striking change as compared with the proportion of positive reactors twenty years ago.

One section of the book is devoted to conditions which are considered to be associated with the social environment. Alimentary infections occurred most frequently in families where there was deficient care of the child, or where the family was living in a small house with low rents and especially in tenamented and mouse-infected property in the older parts of the city.

Accidents, which are now one of the principal causes of death in childhood, comprise the other large group associated with the environment. Many of the home accidents such as burns, scalds and the swallowing of poisons are preventable. Accidents were found to be more prevalent in families where the quality of the mother's care was unsatisfactory.

In the final chapter the authors conclude that the health of the children and the outcome of diseases are closely related to family environment.

The statistical data are presented in a series of useful appendixes.

The book is a valuable addition to the knowledge of the pattern of childhood diseases in a community and of socio-economic factors which influence them. It should prove valuable to doctors working in family practice, preventive medicine and hospitals, as well as to health visitors and others who are responsible for the welfare of children.

G. H. NEWNS

Check-List of Birds of the World

Vol. 9. Edited by Ernst Mayr and James C. Greenway, Jr. (A Continuation of the Work of James L. Peters.) Pp. xii+506. (Cambridge, Mass.: Museum of Comparative Zoology; Copenhagen: Zoological Museum, 1960.) 7.50 dollars.

THIS is the basic modern work in systematic ornithology and was planned for fifteen volumes. Of these, Volumes 1–7 appeared in the period 1931–1951 and covered all the non-passerine birds and a few families of passerines. The death of Peters in 1952, with only a little more material ready in manuscript, made new arrangements necessary for completion. The editors appointed by the Museum of Comparative Zoology at Harvard are E. Mayr and J. C. Greenway, jun., and they have proceeded on the plan of apportioning the groups among selected specialists in America and Europe. This should speed up the issue of the remaining volumes, which will appear when ready and not in numerical sequence.

Volume 9 is thus the first to appear under the new arrangements. It covers a dozen passerine families of varying distribution—some cosmopolitan (for example, swallows), some purely Old World (bulbuls, etc.), some purely New World (for example, mocking-birds), and some very restricted (such as the vangas, peculiar to Madagascar). Each familial section has its own author, and other systematists who have read the manuscript in a consultative capacity are named in addition. The information given consists of the scientific names (with references) of each species and each sub-species thereof, and the distribution of each form.

The resumption of publication of this important work is most welcome, and on the new co-operative basis of authorship one may hope for early completion. One may then look forward to revised editions of some of the earlier volumes which are out of print as well as in parts out of date.

LANDSBOROUGH THOMSON

Institut National des Sciences et Techniques Nucléaires

Symposium de Métallurgie Spéciale organisé à Saclay les 27 et 28 Juin 1957 par le Département de Métallurgie et de Chimie Appliquée. Pp. iv+128. (Gif-sur-Yvette (S.-et-O.): Centre d'Études Nucléaires de Saclay; Paris: Presses Universitaires de France, 1958.) n.p.

AS the title suggests, this symposium concerned particular problems in nuclear metallurgy. Certain of the papers are transcriptions of previous published work. Naturally enough, the majority originate in France, but there are four outside contributions, from Holland, Sweden and Great Britain.

The main topic of the symposium is occupied with allotropic transformations, recrystallization and textures which result.

The transformations in uranium and zirconium and their various alloys are discussed from several aspects. One paper makes a comparison between uranium and iron.

The work on recrystallization and polygonization is treated from a variety of angles, and examples are illustrated from magnesium, aluminium, zirconium, cobalt and titanium, or alloys based on these metals.

As usual, some beautiful micrographs are reproduced, particularly those by Prof. P. Lacombe on polygonization in uranium, and the examination of alpha structures in uranium by Mme. Lehmann and H. Aubert. There is an interesting report on mechanical properties of magnesium-zirconium alloys which is relevant to British work soon to be reported by the Institute of Metals.

The discussion is included at the end of each paper, and the proceedings commence and terminate with the speeches of welcome and conclusion presented at the time.

C. R. TOTTLE

Sonderausschuss Radioaktivität

Bundesrepublik Deutschland, Zweiter Bericht, März 1959. Pp. 117. (Stuttgart: Georg Thieme Verlag, 1959.) 12.60 D.M.

AN impressive organization for measuring the contamination by radioactive materials has been set up in West Germany. The reported data for 1958 show a wealth of measurements of the concentration in the air near the surface, in water from different sources, in the soil, in plants, animals and bones of humans. Comparison of the data for 1958 with those of previous years shows no significant increase. An attempt to predict the increase in fall-out if testing of nuclear weapons is either discontinued or if it proceeds at the rate of the year under review indicates that substantial increases are to be expected. A survey of the results of the German film protection service shows that nearly 10 per cent of persons engaged in work connected with ionizing radiation receive doses of more than 0·4 r. per month. In future reports an estimate of the amounts of radiation received by patients in hospitals would complete an otherwise admirable survey. The data are set out in great detail in a large number of well-designed tables.

S. R. PELC

Linear and Stereoregular Addition Polymers

Polymerization with Controlled Propagation. By Norman G. Gaylord and Herman F. Mark. (Polymer Reviews, Vol. 2.) Pp. x+571. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1959.) 135*s*.

THE recent discovery of methods of synthesis of sterically regulated polymers is not only of fundamental scientific interest but also has opened up possibilities for far-reaching commercial application. Since Zeigler's spectacular discovery of the catalysts for the low-pressure polymerization of ethylene, and Natta's brilliant syntheses of stereoregular hydrocarbon polymers, an immense amount of research has been carried out during the past six years in scientific and industrial laboratories in Europe, the United States and Asia. This book summarizes systematically publications up to February, 1959, and also correlates the various characteristic features of the new processes. With the avalanche of new work being published it was a very noble task for the authors to attempt such a review. Much of the newer work is contained in an enormous number of patents, and since these still remain the most abundant source of information the chapter summarizing some 500 patent examples is one of the most valuable in the book.

While much more remains to be discovered about the mechanism of Zeigler catalysis and the nature of stereospecific polymerization, this book is the best source of information available. The authors have done a great service to polymer chemists in presenting a comprehensive and authoritative source of information on this new branch of polymer science.

C. E. H. BAWN

SCIENCE AND SOCIAL ORGANIZATION*

By SIR CHARLES GOODEVE, F.R.S.

THE scientific method has been as successful in helping in the operations of industry and civil government as it has in the military field; and there is also a growing amount of interest in a field which may be called 'social organization'. In this field, which is primarily a responsibility of government, the needs and the opportunities are great.

Scientists are repeatedly challenged by the accusation that they have been responsible for altering the lives of people and increasing their power to destroy one another, and yet have left most of the social problems so produced to others to solve. The advances of civilization arising from progress in science and technology have increased the extent of the interactions between what one person does and what another does or can do. These interactions require control, require social organization; but our knowledge of social interactions, and consequently our social organization, both lag behind.

Despite the encouragement of bodies such as the British and the American Associations for the Advancement of Science, scientists generally are, for a variety of reasons, reluctant to respond to this challenge. The objects and rules of social organization are substantially linked to moral issues, and science would not presume to replace faith or other human sources of principles in deciding these issues. Individual scientists, while confident that they can see moral issues as clearly as anyone, are often frightened of appearing unsophisticated or naïve if they intrude into the deep field of philosophy. They might even fear that they would have to relax the discipline of their scientific method; the controlled experiment, so fundamental to the scientific method, can rarely be relied upon in this field.

Similar fears were present when scientists began to enter the field of operations. However, confidence has grown through success, not only in solving particular problems, but also often simply by helping management to clarify their objectives and to define their terms (in the light of the objectives). Also scientists have taught management not just to measure but to subject their measurements, both in the taking and in the interpretation, to the rigorous methods developed by science. Operational research workers therefore have less excuse than other scientists for avoiding the study of social problems. They have not avoided them altogether, but they could do more.

The social sciences have made important advances in recent years, but these have been mostly of a qualitative nature. However, it is rapidly becoming possible to determine fairly accurately what people think and want and do. The science of 'attitude and behaviour surveys' has reached a stage such that governments now have a powerful tool to help them in their job of social organization. (By comparison, the referendum or town poll is very inaccurate and will become obsolete as soon as people learn this.)

Almost every operational research study has the difficult initial task of finding and stating the objective or the objectives; the solution of this is often in itself of great value to management. What is the objective of social policy, of social organization? The answer is, of course, more than just to control the interactions between people, more than just to raise the standard of living. Social policy has been a subject of infinite discussion since civilization began. Jeremy Bentham, the great English philosopher, was one of the first to attempt a precise definition with his proposed social policy: "what serves the greatest happiness of the greatest number".

It should help to clarify the objective if we could define some terms in a manner in which they can be measured and, with considerable hesitation, such an attempt is made here. People have wants or desires known to themselves which can be defined as the basis of motivation; their decisions will be generally in the direction of satisfying these wants. The extent to which material wants are satisfied is, of course, the 'standard of living', but this quantity is measurable only in respect of people living near the subsistence-level, and then only in a rather arbitrary way. For an increasing number of more affluent people, a much more comprehensive meaning of the word 'wants' is required—one to include those arising from psychological, spiritual and any other human source. It must also include a promise for the future and a reasonable insurance against sorrows and fears. Sometimes the expression 'standard of life' is used to indicate the extent to which all types of wants are satisfied. These comprehensive wants are, of course, impossible to measure directly, but their total is the basis of one important type of human action—migration.

Let us consider first two clearly specified groups of people, between which there is complete freedom to migrate. These groups may be specified geographically or by profession or in other ways. If there is a net migration towards, say, the second group, then the conditions under which that group lives, including its social organization, has a greater attraction, a greater drawing power than has the first. Let us associate with each group a quantity to represent the attraction and designate this quantity by the Greek word 'eudemony' (eudæ-mony).

To a scientist, quantities or properties are either 'intensive', such as temperature and pressure, or 'extensive', such as volume or length (the total being the sum of the parts). Eudemony, as here used, is

* Closing address at the Second International Conference on Operational Research, Aix-en-Provence, September 5–9.

clearly an intensive property, and furthermore it has all the characteristics of a potential, a sub-group of intensive properties. This means that it should be measurable in the same manner as other potentials, that is, by the spontaneous movement of the associated extensive quantity. Just as the comparative temperature of two bodies is determined by the direction of movement of heat, when restrictions or influences on its flow are absent, so the comparative eudemony of two groups of people can be determined by the direction of migration; this will tend to be from the region of lower eudemony to the one of higher.

Most actual migrations are not altogether free, and in addition are influenced by lack of knowledge or are biased by inertia or physical obstacles such as cost. For accuracy, one should carry out a controlled test in which representative samples of each group were exchanged and later the return migration studied. Where this is impracticable, perhaps the simulation techniques of operational research could be used. At all events, the influences due to ignorance or the special obstacles which cause actual migration to deviate from that of free conditions can usually be identified and allowed for.

These restrictions and influences should not weaken our confidence in the relationship between eudemony and migration; the impossibility of carrying out the frictionless Carnot cycle does not alter our confidence in defining and measuring temperature. Indeed, this parallel situation may encourage us to go further and to define the difference in the eudemony of two regions quantitatively as the influence or bias that would deliberately have to be put in to equalize the two return migrations in a controlled test. This influence could be put in by, for example, giving a monetary compensation to the sample that would go to the region of lower eudemony.

Essentially, what we have done is to define a property, the 'eudemony', of a group of people in a social system in terms of a measurable quantity, net migration. This concept of eudemony will require further analysis, but it will be generally agreed that it is related to the satisfaction or fulfilment of wants. Indeed, one can get a somewhat satisfactory physical picture of eudemony by considering it as the ratio of the satisfied to the unsatisfied wants. The acceptance of this latter picture is, however, not essential to the main conclusion, namely, that it is possible to measure the size of this property, because it is a potential, even though its components cannot be measured.

By the choice of the word 'eudemony' we are touching on the field of philosophy: Aristotle used this word to mean happiness through the satisfaction of all types of wants, with special emphasis on the non-material wants. However, it is to be emphasized that we are concerned here only with studying human behaviour and not with moral issues, not with whether the wants people feel are the right ones or not.

This hypothesis can be tested immediately against one's own intuitive ideas arising from the consideration of particular cases. Some cases will fit, some may not. Those scientists who have been brought up in the approach of thermodynamics and kinetics, of forces, equilibria and rates of change, may be more readily able to accept this than others. Most, however, will agree that the argument underlines the importance of freedom to migrate if one is ever to achieve an objective meaning to 'standard of life' or its associated quantity, eudemony.

In attempting to pull out a basic hypothesis from such a complex thing as life, one can scarcely expect to avoid some limitations or qualifications. A full analysis of these cannot be made here; but some important ones should be dealt with. I have defined eudemony as a property of a 'clearly specified group of people', but obviously it is necessary that there be a reasonable degree of similarity between the composition of the groups; if not, migration would need to be analysed in terms of sub-groups. We could not easily compare the eudemony of a group of Jamaicans in Kingston with a group of Englishmen in Birmingham, but we could with another group of Jamaicans in Birmingham. It would become practically meaningless to try to compare the eudemony of two individuals; but of course, it is part of the hypothesis that any one individual in a group can examine the eudemony of his present circumstances in relation to that of any other possible set of circumstances.

So far, the definition has been related to groups existing at one period of time, so that two-way migration is possible. However, we have already at hand a reasonable way of overcoming this limitation. For example, should a government wish to know whether a proposed change in the social organization will increase or decrease the eudemony of a particular group, then the attitude and behaviour survey techniques referred to above can provide a reliable answer in most cases, because these techniques can predict the effect of the change on migration.

An increase in eudemony could by itself be used as a basis for social policy; but, if used alone, progress would be very slow. In history it is the 'reformer', the man with vision for the future of mankind, who is the initiator of most social progress. However, each man of vision has strong, highly individual and often conflicting views as to what people should want, as to what should constitute a high standard of life. The attitude of the group, while objective, suffers from relative conservatism and ignorance.

Social progress requires the existence of the reformer, but if he is to succeed he must do two things: get the support of the knowledge of the specialists responsible for studying particular problems, and get his ideas of wants accepted by the people of the group. This means that he should continuously measure his ideas for any change in social policy against the effects of such a change on migration. By thus narrowing the gap of controversy, social progress may be facilitated.

The above analysis of an objective of social policy has been chosen in the hope that, among scientists, interest may be stimulated in the field of social organization. The need for such interest is very great. Could we help by analysing the systems used in choosing our leaders, by analysing further the methods of decision-taking in groups of people? Could we measure the 'democratic' content of a particular system of government, perhaps by determining the extent to which considerations of eudemony influence the policy of that government? If so, we might bring the word 'democratic' out of the realms of emotional politics into clearer focus. These are bold targets, but boldness and courage are needed if we are to bring social organization up to the standard required to-day.

AEROBIOLOGY AND MEDICINE

THE pioneer of aerobiology in the service of medicine was C. H. Blackley, a medical practitioner living in Manchester and a sufferer from hayfever, whose book, published in 1873[1], was a model of scientific method and is now indeed a classic. Blackley's countrymen were ultimately converted to his view that hayfever could beyond doubt be produced by inhaling pollen, but it was in the United States that the need for botanical collaboration in solving the medical problems arising from the inhalation of plant spores was first realized: and by 1940 the Americans had established an undoubted lead in this field. The extent to which knowledge of the botanical aspects of allergy has been advanced in Britain since that date was illustrated in the symposium held by Section K (Botany) of the British Association meeting at Cardiff entitled "Botanical Aspects of Allergy".

Dr. D. A. Williams, physician to the Asthma and Allergy Research Unit at Cardiff, set the stage for subsequent speakers. He recalled that the word allergy, meaning a different or altered reaction, was first coined in 1906, and that the two allergic diseases in which pollen and fungus spores play an important part are hayfever and asthma. Hayfever affects some 0·5 per cent of the population. It is entirely an allergic disease, due to pollen, in the main to grass pollen, and some 30–40 per cent of grass-pollen hayfever patients also have pollen asthma. Tree pollen, in particular birch, ash, elm and in some districts, plane, can cause quite severe hayfever and asthma, but it accounts for only a small percentage of hayfever patients; and the pollen grains of herbs other than grasses appear to be relatively unimportant. Asthma affects some 1·0 per cent of the population, and frequent incapacity occurs in some 15 per cent of asthmatics: its causes are only partially understood. The main causes are infections (colds) in the upper air passages, psychological factors and extrinsic allergens (inhalants or organic dusts, and also, but less frequently, foods).

Recent advances in our knowledge of the ætiology of inhalant allergy are almost all linked up with research on plant spores. Thus the clinical investigation of certain types of fungus spore as allergens has followed the lines suggested by the census (centred on Cardiff and referred to here) of culturable moulds in the air over Great Britain: some 5 per cent of asthmatics have been found to have asthma caused by such spores; the most abundant single type, *Cladosporium*, is also (among fungus spores) the commonest cause of asthma, which in this instance is often severe and persistent in summer. Less common, but accepted causes of summer asthma, are *Botrytis* and *Alternaria*. Apart from these common constituents of the aerospora, *Cladosporium fulvum* has long been known to cause allergic symptoms in those who work in greenhouses; and *Aspergillus fumigatus* has recently been shown in London to cause, not infrequently, quite severe asthma. Many other fungal spores are capable of producing asthma, but their exact medical importance awaits investigation.

Mr. H. A. Hyde (National Museum of Wales, Cardiff; honorary director of botanical research at the Asthma and Allergy Research Unit) reviewed the results of aerobiological research in the interest of medicine. When the investigation of plant spores in the air over Great Britain was first contemplated in 1941, no exact information existed on the kinds of pollen (or other spores) occurring in the air, or even of their dates of liberation, still less their relative abundance. Systematic trapping by the so-called gravity slide method began at Cardiff (where it has continued without a break since January 1942) and has since been extended in most instances for a period of a year or more to 15 other stations from the Scillies to Aberdeen and situated in urban, rural, coastal, mountain and maritime situations.

The order in which the various types of pollen appear in significant numbers in the air of Great Britain varies little from year to year; though it may be telescoped or drawn out according to weather. The most abundant types on the average probably throughout the country are four kinds of tree (elm, ash, birch and oak), three kinds of 'weed' (non-gramineous herbaceous plants), namely, plantain, *Rumex* (sorrel and dock), and nettle, and above all grasses. Of these, grass pollen is the least variable in its period of prevalence: its concentration, as measured by the Hirst trap, is almost negligible (a few grains per cubic metre) until late May, after which it soars rapidly to mean 24 hr. values of 500/m.^{3} or more by or before mid-June, and then falls more or less rapidly (except locally in the neighbourhood of late-flowering grasses) to a low figure by August. On sunny days during the peak period the 'spot' count rises late every afternoon in central Cardiff to between 1,000 and 1,750 grains/m.^{3}; though in sunless weather it may scarcely rise above zero. The grass pollen 'season' is probably more or less equally severe over the whole of the lowlands of England and Wales, but less in the mountains and of course increasingly less as one goes out to sea. Strictly indoor air (with doors and windows tightly closed) even on a sunny day in the lowlands at the height of the season contains little pollen. The inhalation of grass pollen in quantity can largely be avoided by following simple rules based on the present knowledge of its variation according to time, place and weather.

Tree pollens vary in their abundance very widely from year to year, so reducing the probability of sensitization to them. Nettle pollen is on the average numerically more abundant than any other kind except that of grasses, and, like its near relative pellitory-of-the-wall in southern Europe, it may prove to be an important allergen.

Study of the fungus aerospora in Britain began with a (gravity slide) census of *Alternaria* spores at Cardiff 1942–43: they were found to be present in numbers which suggested that *Alternaria* allergy might well occur in the human population. Further observations (by means of culture plates) followed from 1947 onwards.

Examination of the complete fungus aerospora by means of the Hirst trap, from 1957 onwards, has confirmed the findings of Drs. Gregory and Hirst at Rothamsted on its composition and has shown that

on average the fungus spores are 60–70 times as numerous as pollen grains. But this figure does not indicate their relative importance as allergens: the volumes of the various types of grain or spore must also be taken into account. When this is done and the various kinds are arranged in order of bulk abundance, that is, the volume of the spore (in μ^3) per unit volume of air, it is found that present views on the importance of grass pollen (which comes at the top of the list) and *Cladosporium* spores (which come second) are confirmed, and several kinds of pollen and fungus spores, all of them known or strongly suspected to act as allergens in Great Britain, come fairly high. Ascospores and basidiospores (both as yet mainly undifferentiated) come respectively third and fourth. It may well be that the latter will prove, as Gregory and Hirst have suggested, to merit serious consideration as allergens.

Principles are emerging from the work on inhalant allergens. Some types of plant spore are inherently more likely to evoke symptoms than others: among flowering plants high allergenicity is confined to a small number of families; we cannot yet say how it is distributed among the fungi. Other things being equal, the most abundant types of spore are the most likely to be important as allergens. Some kinds of spore are present in the air in effective concentration year after year; these are much more likely to produce sensitization than those the concentrations of which become high at longer and less regular intervals. When the concentrations of different kinds of spore are being compared, numbers should be weighted for size.

Dr. Merfyn Richards (Beecham Laboratories, Ltd.) discussed the mould spore population of the air. He said that work, by means of culture plate techniques, on the mould spores present in the air has enabled a picture to be drawn of the relative quantitative importance of the various kinds, and of when and where they occur. Surprisingly, perhaps, but fortunately for the allergist and the allergic individual, there are relatively few genera of moulds of great numerical importance in the air. At Cardiff more than 80 per cent of the colonies grown from trapped spores are identifiable. Of these 95 per cent or more are assigned to only a dozen genera; during three years, 1951–53, *Cladosporium* alone made up nearly half, and with *Penicillium* and *Pullularia* nearly three-quarters of the identified catch.

Several of these moulds have a 'season' of higher incidence. *Cladosporium*, *Epicoccum*, *Alternaria* and *Botrytis* occur in much higher numbers in the summer months than at other times. *Penicillium*, on the other hand, seems to be present in the same sort of quantities the year round.

The same kinds of mould spores occur in quantity at seven other centres up and down Great Britain, but *Cladosporium* shows a much greater incidence in rural areas, while higher counts of *Penicillium* are associated with the big cities.

The same mould genera which are most important numerically in the air over Britain are also the most important elsewhere in Europe, North and South America and New Zealand. In warmer climates than Britain, *Alternaria* assumes greater importance, and in places, for example the central United States, vies with *Cladosporium* for predominance.

The spores produced and released from the moulds growing in damp houses, cellars, barns, haylofts, granaries and workshops may in these places predominate over spores coming in with the ordinary outdoor air: such local modification of the spore load may be significant from the point of view of allergy.

Dr. Elizabeth Hamilton (Wright-Fleming Institute) described her current research with the Hirst automatic volumetric spore trap, in which airborne particles are impacted on to the sticky surface of a slowly moving microscope slide. The number of spores counted under the microscope on a traverse of known area can be converted into an estimated number per cubic metre of air, and it is possible also to tell, to within an hour, the time of day when any particle was deposited.

The 'spore-season' in London stretches from mid-May to November. Individual spore types have their particular seasonal incidence and there is within the season a day-to-day fluctuation in the counts, depending mainly on meteorological factors: there are 'associations' of spores which are predominant in dry weather and others which are predominant in wet weather.

Besides the annual and seasonal variations many airborne spores also have a distinct pattern of diurnal periodicity. This is dependent on the individual spore-type and also on the occurrence of those conditions of humidity, temperature and local air turbulence required for the liberation and dispersion of the spores. It is therefore apparent that if spore trapping is not continuous, the time of day when samples are taken will bias the findings.

This information on the season, the abundance, the time of day and the type of weather favouring different spores is all likely to aid the clinician in his diagnosis of spore allergy.

A note of the daily count is given to the Allergy Clinics at St. Mary's Hospital and data sheets summarizing the counts are sent each week to doctors who are interested in allergy.

Mr. R. Harvey (University College, Cardiff) described his investigations into the ecology of the genus *Cladosporium*, at least six species of which are in the aerospora, their proportions ranging at Cardiff from 0·2 to 45 per cent of the total. Under identical conditions growth-rates of individual species vary significantly, and in each species the process of spore production is much more sensitive to adverse environmental conditions than is vegetative development. Conidiophore development at humidities less than 65 per cent is often abnormal, and few spores are produced. Temperatures above or below the optimum range of 15–20° C. restrict sporulation, and at extremes above 27° C. or below 10° C. lead to abnormal conidiophore development. The presence of water droplets in the air markedly accelerates spore liberation.

The 'peak development' of each of the various species is reached at the time of maximum sporulation. Following their release, the further development of the fungus continues to be limited because of the effect of environmental factors (especially humidity) on the spores during their dispersal.

More than 10 per cent of the spores are released in clusters of 30 or more spores, but during dispersion these break up to form smaller clusters and, eventually, single spores. Both large clusters and single spores are essentially dispersal *units*—each of which effectively produces only one fresh growth on deposition.

Airborne spores are able to colonize a wide variety of ubiquitous organic materials. During spore

germination and subsequent colonization the environment continues to exert a restrictive influence, especially through the competition of other components of the mixed microflora.

The capacity for spore production is so great in each life-cycle that even in the winter months they are always present in the air in appreciable quantities.

The symposium showed that the aerospora has come to be recognized as a factor, or rather a complex of factors, comparable with those of weather, in the human environment. Observation on these factors is becoming increasingly detailed and precise: it is vitally important to the study of allergy.

H. A. HYDE

[1] Blackley, C. H., "Experimental Researches on the Nature and Causes of Catarrhus Aestivus (Hayfever)" (1873).

POLYMER CHEMISTRY

HIGH polymers were the predominant theme of the proceedings of Section B (Chemistry) of the British Association's meeting in Cardiff. Addresses were given on the technical and commercial developments of new products and their applications, the topics selected being polythene, epoxide resins and silicones. A full session was devoted to a discussion of current work on polymer chemistry, and although it was possible to cover only a small part of their enormous and expanding subject, the four papers presented gave a fair perspective of some of the important problems now engaging polymer chemists.

The recent discovery and commercial development of stereospecific polymers was the obvious starting point, and in the opening address Dr. P. R. Thomas referred to the significant discoveries of Ziegler on the synthesis of linear highly crystalline polythene, and of Natta on the polymerization of propylene and other α-olefins to high molecular weight crystalline products. He then described the investigations carried out by the British Nylon Spinners on the synthesis of stereoregular addition polymers containing amide groups, and in particular the N_1N disubstituted acrylamides:

$$\left(\begin{matrix}R_1\\R_2\end{matrix}\right)\!\!>\!N - CO - CH = CH_2\Big)$$

Using hexane or toluene solutions of lithium ethyl as catalyst, highly crystalline polymers were formed in contrast to free-radical or electron-transfer initiators, such as peroxides or sodium naphthalene, which gave polymers of low tacticity. Significant differences between the physical properties, infra-red absorption spectra and rate of hydrolysis of the isotactic and atactic forms were reported.

When polyethylene is irradiated *in vacuo* with X-rays the main effects observed are the production of hydrogen, cross-linking of the polymer and the formation of unsaturation at points along the chain. The cross-linking results from the union of free-radical centres formed on different chains. Not all the radical centres produced in the irradiation process are used in this way. Some are trapped and are potential centres for further reactions. Dr. T. T. Jones described their use in the grafting of polystyrene chains on to the polyethylene backbone. He showed that the rigidity of the swollen gel, in which polymerization takes place, greatly influenced the grafting reaction. Kinetic measurements indicated that, due to the immobilization of free radicals, the termination coefficient of the styrene polymerization reaction was considerably reduced compared with reaction in free styrene. The observed changes in the dynamic mechanical damping properties of the grafted structure were attributed to the interference of the graft polymer and the intimately mixed polystyrene in the crystallization of the polyethylene.

In the third paper, Mr. J. L. B. Benton reviewed the modern aspects of polymer structure and its relation to properties. He discussed the factors which determine the configuration taken up by the long-chain molecules in the crystalline regions of a high polymer, and showed how these depend on forces within the molecule—which determine the minimum energy configuration of the isolated molecule—and the interaction between molecular chains. Since the configuration taken up is the one of lowest energy, the plane all-*trans* plane zig-zag corresponded to the minimum energy configuration in polyethylene. In polytetra-fluoro-ethylene, the van der Waals's diameter of 2·7 Å (cf. hydrogen 2·2 Å.) caused an overcrowding in the all-*trans* configuration, and this was relieved by twisting each successive carbon–carbon bond 20° away from the precise *trans* form and opening up the tetrahedral bond-angle to 110°. This puts the fluorine atoms 2·8 Å. apart and leads to a spiral chain with thirteen CF_2 groups for each repeated distance. For the same reason he showed that isotactic vinyl polymers $(CH_2—CHR)_n$ with the R groups in corresponding positions—either all left-hand or all right-hand—formed a helical structure. In syndiotactic polyvinyl chloride no overcrowding occurs and the polymer assumes the all-*trans* form.

The crystalline melting point of a polymer is closely related to the flexibility of the chain—the more flexible the chain the lower the melting point, or the higher the potential energy barrier for rotation the higher the melting point. Dr. Benton showed that the same properties have a determining influence on the mechanical properties of the polymer. The transition in an amorphoris polymer does not involve bodily movement of whole molecules past each other, but only deformation of chain segments and these are determined by bond rotations. Rubbery properties will thus disappear in some critical temperature range where the thermal energy available to the bonds becomes so low that the co-operative rate of passage of the rotational barriers is reduced to negligible dimensions. This explains the high increase in modulus in the region of the glass temperature.

In the final paper, Prof. A. G. Evans surveyed his recent work on the ionic polymerization of 1 : 1-diphenyl ethylene. This monomer polymerizes only to the linear dimer 1,1,3,3-tetra phenyl but-1-ene because of the presence of the bulky phenyl groups. The reaction was initiated by cationic catalysts of the Friedel–Crafts type, and reproducible kinetic data were obtained only by working under conditions of extreme purification. No dimerization occurred with stannic chloride as catalyst unless water or hydrogen chloride was present as co-catalyst. There was no optimum ratio stannic chloride : hydrogen chloride, but with water a maximum rate occurred at the ratio 1 stannic chloride : 2 water. Similarly, titanium

chloride requires hydrogen chloride as co-catalyst and this and the above reaction were interpreted in terms of the rate-controlling reaction :

$$M + HM^{+}(SnCl_5^{-}) \rightleftharpoons HD^{+}SnCl_5^{-}$$

where M is a monomer, D is a dimer and $HM^{+}(SnCl_5^{-})$ is a complex formed in the initiating step. Prof. Evans said that although lithium butyl formed a complex with the monomer in benzene solution, no dimerization occurred, and this he ascribed to steric influences. In the presence of $TiCl_4 + HCl$ the lithium butyl was, however, a powerful dimerization catalyst. The reaction was heterogeneous and occurred under conditions in which $TiCl_4 + HCl$ alone did not induce reaction. C. E. H. BAWN

CARBON-14 MEASUREMENTS OF KNOWN AGE SAMPLES

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THE reliability of the carbon-14 method of dating was admirably demonstrated initially by W. F. Libby[1] with a series of measurements of samples of known age. These afforded confirmation of the basic assumptions of the method with an accuracy of approximately 10 per cent. Now, eleven years later, greater precision can be achieved with the improved techniques, and measurements of samples of known age are being conducted by several laboratories. These measurements are important because, with counting accuracies of the order of 1 per cent, the basic factors involved in carbon-14 dating must also be tested with equal precision. The basic factors are subject to the following questions : (1) Has the cosmic ray intensity been constant as assumed ? (2) Has the equilibrium condition between atmospheric $^{14}CO_2$ and the reservoirs, primarily the oceans, been stable ? (3) Is the distribution of atmospheric $^{14}CO_2$ uniform throughout the world ? (4) Is the accepted half-life value (5568 ± 30 years) correct ? (5) Are the isotopic ratios of the atmospheric carbon unaltered in the process of carbon intake by plants ?

These questions cannot be answered individually by measurements of single or small groups of samples of known age ; but, when a sufficient number have been dated, the specific answers will become apparent In the meantime, the contributions of the various laboratories furnish information about the over-all accuracy of the method.

Samples of known age which have been measured in the laboratory at the University of Pennsylvania from 1958 until May 1960 are described here and the carbon-14 determinations are illustrated in Fig. 1 and listed in Table 1. In Fig. 1 the known ages are plotted versus the percentage deviations of carbon-14 counting-rates. These deviations are the percentage departures of each sample (after correction of the counting-rate for the age of the sample) from the average counting-rate value of 39 measurements of oak samples ranging in age from 110 to 203 years before present[2]. A statistical analysis of the data from these oak measurements (see Satterthwaite and Ralph[3]) demonstrates that within this small range of years, the carbon-14 oak values did not differ significantly from those determined by tree-ring counts of the samples, and that the efficiency of the counter remained stable during the period in which these measurements were made.

Moreover, the average counting-rate value, corrected to 'zero age', is 95 per cent of the value of the oxalic acid standard (National Bureau of Standards No. 4990). This percentage value agrees with that determined by other laboratories, and with the value decided on at the Groningen Radiocarbon Conference[4] for interlaboratory standardization. With this basis of calibration, the measurements of samples of known age may be compared with those of other laboratories using the oxalic acid standard. The oak measurements demonstrate, in addition, that this 95 per cent value is in agreement, at least within 1 per cent in counting-rate, with true ages in the time span of A.D. 1849 to A.D. 1756 (the range covered by the oak samples). It is, therefore, the best available basis for calibration for use in carbon-14 dating until the complete time span of known ages has been measured.

In Fig. 1 there appear to be three possible deviations from the average oak value. The deviations occur at 272 (A.D. 1687), 3256 (1297 B.C.), and at 3884 (1925 B.C.) years before present. The first of these, at approximately A.D. 1700, is confirmed by known age measurements of several laboratories[5–7]. The second deviation (1297 B.C.) may be indicative of a similar fluctuation in that era, or in combination with P-11, of an upward trend. Carbon-14 measurements of tree-ring dated *Sequoia* sections by Hans E. Suess[8] lend support to the latter. The third occurs close to the 2000–4000 B.C. time-interval, where other nonconformities between carbon-14 dates and archæologically estimated chronologies, notably Egyptian, have been found. These older samples have not

Table 1. LIST OF PERCENTAGE DEVIATIONS OF SAMPLES OF KNOWN AGE FROM OAK STANDARDS

Sample No.	Known age Years A.D. or B.C.	Years B.P.*	Percentage deviation from oak standards
P-263 (oxalic acid standard)			+ 4·99 ± 1·06
P-259	A.D. 1779 ± 5	180 ± 5	+ 0 591 ± 0 551
P-168	A.D. 1773 ± 15	186 ± 15	+ 0·040 ± 0·940
P-226	A.D. 1703 ± 3	256 ± 3	+ 1·039 ± 0·457
P-167	A.D. 1686 ± 16	273 ± 16	+ 2 654 ± 0·554
P-274	A.D. 907 ± 10	1052 ± 10	− 0 134 ± 1 216
P-283	A.D. 753 ± 28	1206 ± 28	− 0·591 ± 0 516
Tikal IV	A.D. 746 ± 5	1218 ± 5	0·00 ± 0 156
Tikal I	A.D. 704 ± 9	1255 ± 9	− 0 240 ± 0·215
P-268	A.D. 617 ± 7	1342 ± 7	+ 1·139 ± 0·538
P-272	A.D. 575 ± 10	1384 ± 10	− 0 501 ± 0·408
P-30	525 ± 25 B.C.	2484 ± 25	+ 0·688 ± 0·380
P-222	550 ± 25 B.C.	2509 ± 25	− 0·003 ± 0 445
P-134, P-275	714 ± 9 B.C.	2673 ± 9	+ 1 058 ± 0·342
P-227	1297 ± 7 B.C.	3256 ± 7	+ 2·234 ± 0·457
P-11	1925 ± 75 B.C.	3884 ± 75	+ 2·340 ± 0·246

Average counting-rate of 39 oak measurements = 32·143 ± 0 033 c./m.
* B.P., before present.

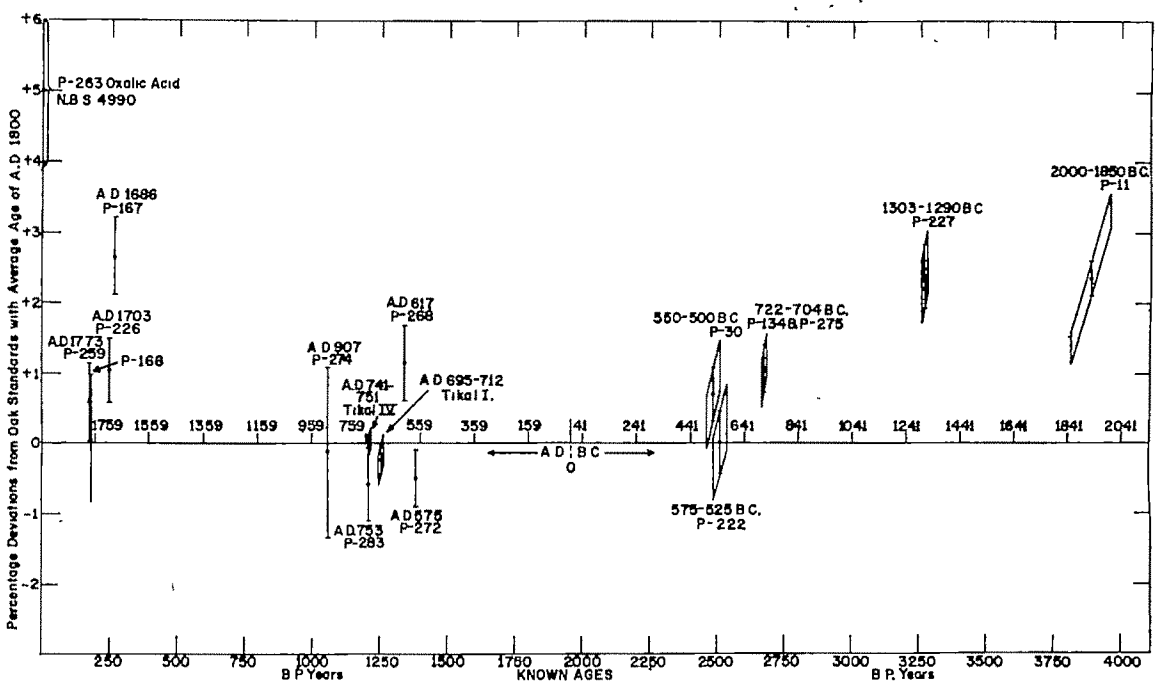

Fig. 1. Percentage deviations of samples of known age from oak standards. The 'zero age' counting-rate of 39 oak measurements is represented by the horizontal line through 0 per cent. Standard statistical deviations (one sigma) of the average of the carbon-14 known age determinations for each sample are represented by vertical lines drawn through the midpoints of the known age ranges. For tree-ring dated samples, the midpoints of the known age ranges are assumed to be the average ages of the portions selected for carbon-14 dating. The uncertainties in known ages of the archæologically dated samples are represented by parallelograms to allow for the possibility that the true age of the sample may lie at either extremity of the given range, thus presenting a greater uncertainty in the known date than if the true date were at the midpoint of the range

been included in this summary because of the greater uncertainties in the archæological dating.

If we accept these three fluctuations as significant, the nonconformities in terms of years are as follows :

P-167 (A.D. 1687) 211 ± 45 years too young
P-227 (1297 B.C.) 176 ± 53 years too young
P-11 (1925 B.C.) 186 ± 31 years too young.

It is obvious that these few measurements do not cover completely the time-interval of the past 4,000 years, nor do they answer the specific questions. However, they do indicate that the maximum error in carbon-14 dates due to methodological uncertainties could be of the order of approximately 200 years. In some time-intervals, A.D. 1849–1756, A.D. 900–600, and 500–700 B.C., this maximum error is very much smaller, and perhaps negligible (see Fig. 1). Further conclusions must await the completion of measurements covering the whole known age time span and more regions of the world.

Descriptions of Known Age Samples

A. Dendrochronologically Dated Samples

Oak Samples. *Quercus* sp., probably *alba*. Laboratory standard samples. Thirty-nine measurements of nine different oak samples from Round Top Hill (40° 20′ 30″ N., 74° 50′ 0″ W.), Mercer County, New Jersey, U.S.A., elevation 400 ft., which range in age from 110 to 203 years before present. Average age of the nine samples is A.D. 1800.

P-259. *Pseudotsuga taxifolia*. From 'Hitchcock Tree' from Santa Catalina Mountains (32° 25′ N., 110° 40′ W.), 25 miles north of Tucson, Arizona, U.S.A., elevation 6,500 ft., blown down in 1951. Rings marked A.D. 1774–1784 processed. Expected date : A.D. 1779 (180 before present). Two counting runs.

P-168. *Pseudotsuga taxifolia*[9]. From Mesa Verde (37° 12′ N., 108° 30′ W.), Colorado, U.S.A., elevation 6,900 ft., cut in May 1950. Laboratory of Tree-Ring Research No. *MVR* 3041-6*D*. Rings marked A.D. 1758–1788 processed. Expected date : A.D. 1773 (186 before present). One counting run.

P-226. *Pseudotsuga taxifolia*. From same section as *P*-259. Rings marked A.D. 1700–1706 processed. Expected date : A.D. 1703 (256 before present). Three counting runs.

P-167. *Pseudotsuga taxifolia*. From same section as *P*-168. Rings marked A.D. 1676–1702 processed. Expected date : A.D. 1686 (273 before present). One counting run.

P-274. Pine. From Chetro Ketl, Chaco Canyon (36° 05′ N., 107° 55′ W.), New Mexico, U.S.A. Laboratory of Tree-Ring Research No. *CK*-852. The pith year (start of growth) of this tree is A.D. 883. Rings marked A.D. 897–916 processed. Expected date : A.D. 907 (1052 before present). Two counting runs.

P-283. *Pseudotsuga taxifolia*. From Nine Mile Canyon (39° 48′ N., 110° 20′ W.), Utah, U.S.A., elevation 6,500 ft. Collected by John Gillin in 1930 (University of Utah, Museum of Anthropology No. 21754 ; 13–3)[10]. The pith year of this tree is A.D. 725. Rings marked A.D. 725–781 processed. Expected date : A.D. 753 (1206 before present). One counting run.

P-268. *Pseudotsuga taxifolia*. From Broken Flute Cave (36° 45′ N., 108° 50′ W.), 40 miles north of Chinle, Arizona. Sample from Room 6, north-east post, Laboratory of Tree-Ring Research No. *MLK*-127. Rings marked A.D. 610–624 processed. Expected

date: A.D. 617 (1342 before present). Two counting runs.

P-272. *Pseudotsuga taxifolia*. From same section as *P*-268. Rings marked A.D. 570–580 processed. Expected date: A.D. 575 (1384 before present). Three counting runs.

The dendrochronological analyses of samples *P*-259, *P*-226, *P*-274, *P*-283, *P*-268, and *P*-272 were made by the Laboratory of Tree-Ring Research, University of Arizona, Tucson, Arizona, and those of samples *P*-168 and *P*-167, by J. L. Giddings, Brown University, Providence, R.I. Sample *P*-283 was obtained from the University of Utah, Salt Lake City, Utah; the others, from the Laboratory of Tree-Ring Research. We wish to express our appreciation to T. L. Smiley (University of Arizona), to J. D. Jennings (University of Utah), and to J. L. Giddings (Brown University) for these important contributions to the known age dating project.

B. Archæologically Dated Samples

Samples obtained from the University Museum of Philadelphia.

Tikal IV and Tikal I. *Achras zapota*. Samples from vault and lintel beams from Temple IV (*P*-235, *P*-236, *P*-237, *P*-238, *P*-242, *P*-243, *P*-244, *P*-245, *P*-248, and *P*-249) and Temple I (*P*-230, *P*-232, *P*-234, *P*-247, and *P*-251), Tikal (17° 13′ 18″ N., 89° 38′ 30″ W.), Peten, Guatemala For Temple IV, thirty-three counting runs of ten different beams and for Temple 1, seventeen runs of six different beams were made. According to the "11–16" Maya-Christian correlation, the dates of the Temple IV beams are within the range of A.D. 741–751 (1218–1208 before present) and those of Temple I, A.D. 695–712 (1264–1247 before present). Reasons for acceptance of this correlation and details of samples selected are given by Satterthwaite and Ralph[3].

P-30, *P*-222, *P*-134 and *P*-275. Gordion Samples. Gordion (39° 45′ N., 31° 55′ E.), Turkey is the capital of a Phrygian Kingdom which fell before an invasion of Cimmerian barbarians early in the seventh century B.C. The town (the City Mound) was rebuilt in the time of the Persian Empire and continued to be occupied to about the third century B.C., but most of the numerous tomb mounds were undisturbed until excavations were begun in 1950 by the University Museum of Philadelphia under the direction of R. S. Young.

P-30. Tumulus *F*, Gordion. Charcoal from an undisturbed cremation-burial. Among the finds was jewellery of the Persian period (post-546 B.C. at Gordion) parallel to that from Tumulus *A*. Tumulus *A* was a similar cremation dated by the presence of a terracotta 'kore-unguentarium' with the same front- and back-moulds as those used in Samos in strata dated to the tyrant Polycrates (532–522 B.C.)[11]. Allowance of a short period for travel to Gordion, and for its worn condition, makes 550–500 B.C. (2509–2459 before present) a reasonable date for the Tumulus *A* cremation, and, therefore, for Tumulus *F*. Three counting runs.

P-222. Tumulus *H*, Gordion. Charcoal from Tumulus *H* cemetery, Burial *A*-161, an undisturbed grave of the Lydian period which contained a 'lydion' or ointment-jar painted in the 'marbled' technique. Such lydions have been found associated with the burnt fortification on the 'smaller mound' (*KH*) at Gordion. Estimated date: 575–525 B.C. (2534–2484 before present). Two counting runs.

P-134 and *P*-275. Tumulus *MM*, Gordion. The largest of these mounds (Tumulus *MM*) contained the 'Gordius' tomb. Young[12] has determined the date of completion of this tomb by parallels with Assyrian objects from the time of Sargon II, who reigned from 722 until 705 B.C. (2681–2664 before present). Samples *P*-134 (reported previously[12]) and *P*-275 were found in this tomb and are probably contemporaneous with its completion. *P*-134 consisted of fragments of organic matter, possibly food, from bowl No. 148, and *P*-275, of maple (*Acer pseudoplatinus*), part of a table-top, which is believed to have been made for the entombment. There was no necessity for re-use of wood, as the rolling hills on the plateau around Gordion are known to have been forested, on evidence of abundant deer bones found in habitation-levels. These two samples (*P*-134 and *P*-275) exhibited no significant differences in carbon-14 counting rates. One counting run of *P*-134 and three of *P*-275.

P-227. Seti I Beam. Wooden beam from Egypt with a cartouche containing the name of Seti I who reigned from 1303 until 1290 B.C.[14] (3262–3249 before present). The reign of Seti I has been firmly dated by its relationship to the recorded Sothic cycles. The collection date and original location of this sample in Egypt are not known. The beam is small, approximately 9 × 6 cm. in cross-section. The tree-ring patterns indicate that it was part of a small tree or branch. In other words, the portion used for dating was probably representative of the date of the cutting of the tree and of inscribing the cartouche unless it was an older re-used beam. Two counting runs.

P-11. Aha-nakht Sarcophagus. Wood, probably cedar, from the outer sarcophagus of Aha-nakht, El Bersheh (27° 45′ N., 30° 45′ E.), Egypt. Found in a tomb which was covered with earth. Aha-nakht lived sometime between 2000 and 1850 B.C. (3959 and 3809 before present), based on the early Kings' lists and archæological evidence[15]. As can be seen in Fig. 1, this sample is not so firmly dated as the others in this list. In addition, there may be a post-sample-growth error (not shown in Fig. 1), that is, the sample dated may be from the inner rings and, therefore, possibly 100 years older than the time of death of the tree. The portion for dating was taken from a beam approximately 45 cm. wide which had been squared and reduced in thickness to approximately 10 cm. Eight counting runs. (Preliminary carbon-14 dates for both *P*-227 and *P*-11 were reported previously[12].)

We wish to acknowledge with gratitude the financial support of the National Science Foundation for these measurements.

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OBITUARIES

Prof. N. E. Svedelius, For.Mem.R.S.

PROF. NILS EVERHARD SVEDELIUS, the eminent Swedish botanist, died at Uppsala on August 2. He was born at Stockholm on August 5, 1873, of an old family noted for its scholarship and public service, which took its name from the small town of Sveden, in Dalecaria. Going to the University of Uppsala in 1895, he was later elected curator of the Stockholm nation. This student office gave him an early acquaintance with the business side of university affairs and led to his abiding interest in administration in which he played a prominent part at Uppsala.

Uppsala has always played a very prominent part in cryptogamic botany, for a long line of eminent botanists have made the different groups their special study. Svedelius, under the guidance of F. R. Kjellmann, who was noted for his researches on Arctic algae, took up the study of those of the Baltic, which provided the subject of his doctorate thesis in 1901. After studying at Munich that year, he journeyed to Ceylon, the East Indies and Java, 1902–3, where he gained a knowledge of tropical algae which ever afterwards stood him in good stead; a paper on the algae of the coral reefs of Ceylon, 1906, was one result of these travels, but their influence is seen in his discussion of the discontinuous geographical distribution of some tropical and subtropical marine algae, 1924. He was a prolific writer on algology, treating practically every aspect of this wide field, but his most important contributions were on the anatomical structure and development, and on reduction divisions and alternation of generations in the Florideae. It may be said that Svedelius and his pupil J. H. Kylin, later of Lund, initiated the study of algal cytology at Uppsala.

In 1908, he found that, in the tetrasporangium of *Martensia*, the tetrad is formed by only one of the numerous cell nuclei. Working with *Delesseria sanguinea* in 1912–14 he confirmed Yamanouchi's discovery of alternation of generations with changes of nuclear phase in the red algae.

In 1915 he discovered that in *Scianaia furcellata*, which lacks tetraspores, meiosis sets in immediately after the fertilization of the female nucleus which had invaded an auxiliary cell; one of the four nuclei gives rise to the gonimoblast which has haploid nuclei. Then, in 1933, he showed that meiosis begins immediately after fertilization in *Asparagopsis* and *Bonnemaisonia*. In monospore cultures, 1937, he proved that in *Lomentaria rosea*, where there are no sexual individuals, tetraspores are formed without meiosis, unlike *L. clavellata*, which is typically diplobiontic, having separate tetrasporous and sexual individuals. In 1942 he found that *Galaxaura*, closely related to *Scianaia*, has separate tetrasporous individuals. He finally reached the conclusion, therefore, that the sole criterion of a haplobiontic or diplobiontic development can no longer be regarded as of any great systematic importance.

Svedelius was soon regarded as among the foremost algological systematists; indeed, so early as 1911 he wrote the section on Bangiales in Engler and Prantl's "Pflanzenfamilien".

It would probably be true to say that Svedelius used his extraordinarily wide knowledge of algology to note problems which needed to be solved if theories based on insufficient facts were not to hold continued sway. By selecting these for the most part, though in no wise neglecting other opportunities which came to hand, he deservedly gained his great reputation.

In 1914 he succeeded H. O. Juel as professor of botany at Uppsala, and prælector of the University Garden. Juel had written a full account of Burser's herbarium and Svedelius saw it through the press. Burser, who died in 1639, left a *hortus siccus* of twenty-five volumes, the result of extensive continental journeys. This, one of the treasures of Uppsala Museum, had many vicissitudes before, surprisingly, reaching Uppsala—and then suffered the loss of two volumes in the great fire of 1702. It contains many specimens of C. Bauhin which enabled Linnæus to recognize his types. It is of fundamental importance in botanical nomenclature which, however, does not do away with its intrinsic historical value.

Svedelius was an authority on the lives and works of his great predecessors and, not unexpectedly, of Linnæus. The old University Botanic Garden, which Linnæus had reorganized and made famous, was left to become scientifically derelict after Gustav III had presented the gardens of the Royal Palace to the University on the urgent representation to him by C. P. Thunberg that the old garden was in a marshy district and otherwise unsuitable. Svedelius was one of the foremost of those who forced through a scheme in the early '20's for rearranging the Garden as it was in Linnæus's time and to ensure its future care.

Like most Swedish botanists, Svedelius did a good deal to popularize the subject in articles, and also wrote a popular book.

Prof. Svedelius represented Sweden at many botanical congresses and was also personally well known from his visits to foreign institutions. His quiet demeanour, with apt comments when such were in place, together with his evident enjoyment of the humorous gained him general affection.

He held many foreign distinctions. In Britain he was foreign member of the Linnean Society (1917), and the Royal Society (1944), and honorary member of the Botanical Society of Edinburgh (1938).

JOHN RAMSBOTTOM

Sir Arthur Fleming, C.B.E.

THE death of Sir Arthur Fleming on September 14 will have saddened all who are concerned with the improvement of our national facilities for engineering education and training, and most of all those many thousands of men who were privileged to benefit from the schemes of apprenticeship which he pioneered within the Metropolitan-Vickers Electrical Co., Ltd. (now, Associated Electrical Industries (Manchester), Ltd.) more than fifty years ago.

He was born at Newport, Isle of Wight, in 1881, and was educated at the Portland House Academy there and at the Finsbury Technical College in London. After occupying positions with the London Electric Supply Corporation and a firm of instrument makers, he was selected by the British Westinghouse Co., later Metropolitan-Vickers, Manchester, as one of the 'holy forty', to undergo a course of training

with the Westinghouse Electric and Manufacturing Co. at its East Pittsburg works. On joining the Manchester company, he was engaged as a specialist in electrical insulation and soon became chief designer, and then superintendent and chief engineer, of the Transformer Department.

It was not long before Fleming introduced arrangements for the systematic training and further education of the young men in this Department, and from this beginning grew the Education Department of the Company, of which he became director. He used often to say that the most important raw material of industry was its young people, and he devoted himself to ensuring that his own young people, from the embryo craftsman to the university graduate, were recognized and treated as such. They came not only from schools and universities in Britain, but also from all over the world, for in the sphere of industrial training the names of Fleming and Metro-Vickers became international bywords; and there can scarcely be a country in which there are not several, indeed many, men who hold 'A. P. M.' in honour and who would welcome the opportunity to express their deep gratitude for his efforts on their behalf. His influence and inspiration in this sphere were not, of course, confined to his own Company; they penetrated widely within the electrical industry as a whole, and the benefits they have brought to the progress of this industry have been profound.

All this, however, was only part of his achievement. His far-sighted views on engineering education and training were matched by his realization of the need for research within industry, and especially for research which was not bounded by the problems of existing products. In parallel, therefore, with his establishment of schemes of apprentice training, he began to create a research department within the Company, to which he attracted a succession of men of outstanding ability and who responded to his inspiration by making many notable contributions in pure as well as applied science. A particular example of his remarkable foresight was his forceful contribution to the establishment of radio broadcasting in Britain. He retired from his directorship of research and education in Manchester in 1952.

Fleming's outside interests and activities were manifold. He was a member of the Council of the University of Manchester, of the Governing Body of the Imperial College of Science and Technology in London, of the Delegacy of the City and Guilds of London Institute, of the Ministry of Education Committee on the Training of Teachers and Youth Leaders, and of the War Cabinet Engineering Advisory Committee; chairman of the Electrical Engineering Committee of the Central Register of the Ministry of Labour, of the Athlone Fellowship Committee of the Board of Trade, and of the Federation of British Industries Overseas Scholarships Committee; and president of both Sections G (Engineering) and L (Education) of the British Association, and of the British Association for Commercial and Industrial Education. He also played an important part in the establishment of the Department of Scientific and Industrial Research and of the Electrical Research Association.

Within all these interests, the Institution of Electrical Engineers occupied a place of special importance; he became a member of its Council in 1932, was elected a vice-president in 1935 and president in 1938; and for his outstanding services to the profession was awarded the Faraday Medal in 1941 and elected to honorary membership of the Institution in 1952.

The Universities of Manchester and Liverpool conferred honorary doctorates upon him; he was made C.B.E. in 1920 for his contribution to submarine detection; and knighted in 1945 for his services to education.

Those who knew him well will remember him with admiration for his exceptional foresight, his unlimited enthusiasm and vitality, his unrestrained willingness to make his knowledge and experience widely available, and his devotion to the needs of the younger generation. Many more who did not know him have cause to be grateful for the benefits that have come from his life of public service. WILLIS JACKSON

NEWS and VIEWS

Chemical Technology at the Imperial College of Science and Technology, London: J. S. Rowlinson

THE chair of chemical technology in the Imperial College of Science and Technology was held for many years by the late Sir Alfred Egerton, but it was not filled after his retirement in 1952. It has recently been announced that Dr. J. S. Rowlinson, senior lecturer in the Department of Chemistry, University of Manchester, has now been appointed to the chair. Dr. Rowlinson had a distinguished career at Oxford, where he was Millard Scholar at Trinity College. He obtained first class Honours in chemistry in 1948 and the degree of D.Phil. in 1950. Leaving Oxford, he went as a Research Associate to the University of Wisconsin for a year, before going to the University of Manchester, where he was first an I.C.I. Fellow and afterwards lecturer, and more recently senior lecturer. Dr. Rowlinson received a Meldola Medal of the Royal Institute of Chemistry in 1954 and the Marlow Medal of the Faraday Society in 1957. Among his outside contacts it may be mentioned that he was formerly a member of the Thermodynamics Committee, National Engineering Laboratory, and he is at present a member of the Joint Sub-Committee of the National Physical Laboratory and the National Chemical Laboratory on Fundamental Properties of Pure Materials. He has carried out research on experimental and theoretical aspects of compressed gases, liquids and solutions, and he is the author of a book entitled "Liquids and Liquid Mixtures" published last year. Dr. Rowlinson goes to the Imperial College at a time when it is expanding rapidly.

Physiology at the Royal Free Hospital School of Medicine, London: Prof. C. B. B. Downman

DR. C. B. B. DOWNMAN has been recently appointed to the Sophia Jex-Blake chair of physiology at the Royal Free Hospital School of Medicine, London, in succession to the late Prof. Esther Killick. Dr. Downman was educated at the City of London School and St. Thomas's Hospital Medical School.

In 1937, after preclinical studies, he graduated B.Sc. (Lond.) with first-class honours in physiology and in 1953 he obtained his Ph.D. (Lond.). In 1938, a junior appointment in the Department of Physiology marked the beginning of his research association with the late B. A. McSwiney. In 1941, he was promoted to lecturer and later senior lecturer, until 1954, when he moved to the Royal Free Hospital as reader in physiology. Dr. Downman is well known internationally for his investigations in neurophysiology. His main work lies in the field of visceral afferent reflexology, early papers being concerned with vascular reflexes of skin and with the distribution of afferent fibres of the intestine; the spinal cord and cerebral distribution of splanchic afferent impulses has been mapped and the properties of the reflexes set up by such impulses has been analysed. More recent work has been concerned with the controls of these arcs in the brain stem. During the Second World War Downman was for a time a member of a team investigating oxygen poisoning at the National Institute for Medical Research under the leadership of Sir Lindor (then Dr. G. L.) Brown. In 1948 he went to Dunedin, New Zealand, for one year, where in collaboration with J. C. Eccles he studied spinal motoneurone physiology. In 1953 he went to the United States and together with C. N. Woolsey studied the interdependence of the subdivisions of the auditory cortex.

The British Biophysical Society

It is proposed to form a new society, to be known as the British Biophysical Society, the object of which will be to provide a common meeting ground for those interested in the functioning and structure of living organisms viewed from a physical point of view and in the application of physical and physico-chemical techniques to biological problems. The first meeting of the new society will be held at King's College, London, during December 19–20. It will consist in part of symposia, with invited speakers, on comparative work on muscular contraction and on the structure of ribonucleic acid, and in part of short contributed papers on the subjects of the symposia or on other subjects. Those interested in joining the Society or in attending (or contributing papers to) the meeting should apply to the honorary treasurer, Dr. P. M. B. Walker, Department of Zoology, West Mains Road, Edinburgh 9. All other correspondence should be addressed to the honorary secretary, Dr. J. C. Kendrew, Peterhouse, Cambridge.

Radioactive Contamination of Materials and Reagents

The Committee of the International Commission on Radiological Units which is concerned with Standards and Measurement of Radioactivity has appointed a sub-committee to report on problems arising from low-level radioactive contamination of raw materials used in various types of scientific work. Particular attention is being given to: contamination in shielding materials; contamination in the materials used in the construction of detectors and in the mounting of sources; contamination of reagent chemicals used in the separation for analysis of small quantities of radioactive material. The aims of the Sub-Committee are four-fold: to collect general information on the occurrence of contamination, in raw materials, for the information of possible users; to trace the origin of the contamination found in particular materials; to consider whether tests might be made at certain points in a manufacturing process or in distribution, to ensure that the level of any possible contamination was less than a defined amount; to consider special operations in tracer work or in the preparation and use of standards of radioactivity, where unsuspected radioactive contamination of reagent could lead to significant errors in measurements. The chairman of the Sub-Committee is Dr. N. G. Trott (Institute of Cancer Research), and the members are as follows: Mr. C. O. Peabody (Atomic Energy Research Establishment); Dr. B. Grinberg (Centre d'Etudes Nucléaire de Saclay); Dr. W. W. Meinke (University of Michigan); Dr. R. Brown (Atomic Energy of Canada, Limited, Chalk River). Dr. J. Rundo of the Health Physics Division, Atomic Energy Research Establishment, Harwell, is to act as consultant.

Russian Intelligentsia

The summer issue of *Daedalus* deals with the condition and prospects of a body of intellectuals known in Russia, pre-Revolutionary and Soviet, as the 'intelligentsia'. In Russia the question of the social function and historic mission of the intellectuals has a particular urgency, first because the early and rapid Westernization of the country produced an extraordinarily large, virile and self-conscious body of intellectuals, and secondly, because there modernization has been carried out with greater intensity and single-mindedness than anywhere else in the world.

What is the 'Russian intelligentsia', or an 'intellectual' or 'intelligent' anywhere? As the passage quoted by Leopold Labedz at the beginning of his essay suggests, these terms can mean all sorts of things to all sorts of people. Some use the term intelligentsia to refer to anyone engaged in non-physical labour, whether he is a lyric poet or a veterinarian (such, for example, is the official Soviet definition); others apply it to a person with a liberal education regardless of the nature of his employment; yet others confine it to persons critically disposed to the existing economic and political order, and ready to sacrifice themselves in order to change it fundamentally in accord with some higher (but secular) ideal. Ultimately, the criterion turns out to be a subjective one, and, to define the term 'intelligentsia' with any degree of accuracy, it would be necessary to have free access to all the groups which could possibly come within the meaning of the term. But this is not possible. The lack of direct access to the Russian intelligentsia of to-day posed difficulties for the writers in *Daedalus*. Rather than seek a comprehensive treatment of the intelligentsia of Russia, it seemed preferable to the authors to concentrate on several crucial aspects of the problem. To begin with, there is the question of the character of the pre-Revolutionary intelligentsia; in particular, its attitude toward civic responsibility. The first of these topics is treated by Martin Malia, the second, from different standpoints, by Leonard Schapiro and Boris Elkin.

"Science, the Endless Frontier"

As part of the observance of its tenth anniversary, the National Science Foundation has re-issued the report, "Science, the Endless Frontier", which Dr. Vannevar Bush, director of the Office of Scientific Research and Development, presented during July 1945 to the President of the United States on a pro-

gramme for post-war scientific research. The report is reprinted as a handsome brochure together with the reports of the four specialist committees—the Medical Advisory Committee, the Committee on Science and the Public Welfare, the Committee on Discovery and Development of Scientific Talent, and the Committee on Publication of Scientific Information. Dr. Bush himself contributes a foreword, and the whole is now provided with an index, which enhances its value to all concerned with the relations between science and government and education. An admirable introduction by Dr. A. T. Waterman, director of the National Science Foundation, summarizes the extent to which the recommendations of the report have been implemented during the past fifteen years and points to some of the problems which still await solution. The reprint is to be welcomed as making readily available to a further generation of those responsible for the ordering of the national effort in scientific research and development in Britain, no less than in the United States, the clear and creative thinking of a distinguished group of experienced and responsible scientists. The report is obtainable from the National Science Foundation, Washington, D.C.

IGY Bulletin

WITH the July issue (Number 37, 1960) the *IGY Bulletin* entered its fourth year of publication. The original aim of the *Bulletin* was primarily to keep participating scientists informed of progress in the United States programme, and to a limited extent, in programmes of other countries, but a large number of students, teachers and other interested persons expressed interest in the work and near the end of its first year of publication the *Bulletin* was made available on a subscription basis. The observational phase of the International Geophysical Year ended on December 31, 1958, but the programmes were continued during 1959 and have been succeeded by world-wide geophysics and space-science programmes. The great body of accumulated data still requires analysis, and the *IGY Bulletin* is being continued in order to complete the record of reports of the International Geophysical Year and the related studies, and of investigations in geophysics and space research as they become available. The *Bulletin* is also re-printed in the *Transactions of the American Geophysical Union*.

The Weizmann Institute of Science

THE annual report for 1958–59 of the Weizmann Institute of Science records a steady increase in support, and the president, Abba Eban, records the intention in 1960 to explore the potentialities of science and technology in the development of new independent States, especially in Asia and Africa (Pp. 108. Rehovoth, Israel: Weizmann Institute of Science, 1960). Of the scientific activities, Prof. A. M. J. Schmidt, chairman of the scientific committee, refers to the expansion of the two-year-old programme of virological research in the Department of Experimental Biology; the exploitation by nuclear physicists of the possibilities offered by the Van de Graaff accelerator for designing experiments along new lines; the growing demands on the electronic computer *Weizac*, to growing international interest in the work of the Biophysics Department; and to the pooling of resources by scientists in the Departments of Biochemistry, Biophysics, Experimental Biology and X-Ray Crystallography for a major collaborative effort in molecular biology. Much thought has been given to the founding and work of Yeda, a research and development corporation, to foster the commercial exploitation of discoveries made in the Institute's laboratories and to provide stimulus by closer contact with the scientific problems of industry. At the Graduate School in the Natural Sciences there are now seventy-five research students, and eighteen obtained their Ph.D. degree during the year. Besides brief accounts of some of the investigations in progress in the various Departments, the report includes a list of scientific, administrative and technical staff. A list of papers published by members of the scientific staff, 1958–59, has been issued simultaneously with this annual report, but independently, and the library has also issued a definitive edition of "Serial Holdings of the Weizmann Institute of Science, 1959".

An Investigation on Mounting Boards

RECENTLY a report concerning mounting boards has been made by the Fibre Research Institute of the Central Netherlands Organization for Applied Scientific Research at Delft at the request of the Dutch Museums Association. The *Museums Journal* for August, 1960, contains extensive notes from this report. In the past little has been known about the precise properties required in this type of board and it was considered useful to investigate various widely differing boards and so provide a basis for a set of standards. The properties which mounting boards should possess were considered under various headings and include flatness, colour, opacity, resistance to light, polluted air and micro-organisms, durability, strength, bulk and stiffness. The report makes some definite recommendations concerning the factors on which information was sought and the paper quoted gives these in some detail. It is interesting to note, for example, that the board should be free of ground wood and be manufactured from good-quality bleached pulp. For this, unused rags and soft-wood sulphate pulp bleached by the chlorine dioxide process are acceptable.

Bibliography of British Archæology

THE Council for British Archæology has produced "A Booklist", slim and paper backed, with 41 pages of book titles and with very occasional explanatory notes as to their contents (Pp. 43. (London: Council for British Archæology, 10 Bolton Gardens, S.W.5, 1960.) 5*s*. 6*d*.). These are divided into sections dealing with: (1) Periods—from the Palæolithic to the Industrial Revolution; (2) Regional books, covering England, Scotland and Wales; (3) Books for children, and a short section of regional studies of a more elementary nature. The list is intended to help those of all ages who wish to take an intelligent interest in the past of Great Britain whether it be the Stone Ages, the Roman Period, the Gothic architecture, the domestic building or the furniture, clothes, crafts, silver or ceramics which interest them most. It is not stated who is responsible for the selection of titles.

Sinhalese Sports and Pastimes

ATHLETICS have always been popular, but there has often been held an erroneous idea that activities such as wrestling and the like were mainly sports indulged in by peoples living in the more western and northerly parts of Europe. Dr. P. E. P. Deraniyagala, director of the National Museums in Ceylon, has now shown in his fascinating volume "Some

Sinhala Combative, Field and Aquatic Sports and Games", published by the National Museums, that all these activities flourished in Ceylon even many centuries ago (Pp. 51+5 plates. Colombo: Department of National Museums, 1959. Rs. 2.00). The illustrations are delightful, and it is perhaps surprising to see that when wrestling the pulling of one's opponent's long hair was permissible. In one illustration this is being done by the hands, in another by the feet. Besides wrestling there are accounts of combats between men and animals, and also bull-fighting and cocking. Hunting, falconry, horse racing and bull racing are mentioned, as well as a number of field and water games. Those keen on sports generally will be very interested to peruse this revised edition of Dr. Deraniyagala's important work.

Gyromagnetic Ratio of the Proton

In order that all measurements of the intensity of the geomagnetic field, made by investigators and observers throughout the world, might be referred to the same fundamental physical constant, the following recommendations were made by the Association of Geomagnetism and Aeronomy, International Union of Geodesy and Geophysics, at the twelfth general assembly of the Union in Helsinki, Finland, during July 25–August 6: "The International Association of Geomagnetism and Aeronomy, considering the need for a universal agreement regarding the value of the gyromagnetic ratio of the proton for measurements of the geomagnetic field, strongly recommends that, pending the agreement and specification by an appropriate international scientific organization of a final value, all measurements of the geomagnetic field with a proton free-precession magnetometer, using pure water as a proton sample, shall be based on the following value of the gyromagnetic ratio: $2{\cdot}67513 \times 10^4$ radians/gauss sec.".

Classification of Mental Disorders

Psychiatrists disagree about the concepts on which a classification of mental disorders should be based; hence the many classifications, and the frequent description of the same or similar conditions under a confusing variety of names. The effect of this diversity of classifications has been to defeat attempts at comparing psychiatric observations and the results of treatment in different countries, or even in different centres of the same country. In recent years the epidemiological approach to mental disorders has been more and more employed. To be used successfully and on a wide scale such an approach requires a common basic terminology and classification. As a first step towards this, Prof. E. Stengel, of the University of Sheffield, has examined the classifications in current use ("Classification of Mental Disorders", by E. Stengel. Offprint from *Bull. World Health Org.*, 21; 1960. 3*s*. 6*d*. 0.60 dollars. Sw. Fr. 2). He shows that some of the difficulties created by present-day lack of knowledge are surmountable by the use of "operational definitions", and outlines the basic principles on which a generally acceptable international classification could be constructed.

Tissue Injury by High-frequency Electric Current

Ian K. Buckley, of the Department of Pathology, University of Melbourne, has employed high-frequency current to produce minute injuries to selected blood vessels within Sandison-Clark rabbit ear-chambers. There are two principal findings, which he outlines in the June edition of the *Australian Journal of Experimental Biology and Medical Science*. First, at the surface of injured endothelial cells, transparent blister-like structures appear which, after increasing in size, separate from the cell as transparent globular bodies, floating freely in the plasma. He concluded that these structures are produced by the damaged endothelial cells. Secondly, the area of vascular damage apparent within 1 hr. of injury is increased five-fold by 24 hr. It is suggested that the initially injured cells may release diffusible chemical factors which secondarily injure the surrounding endothelial cells. Alternatively, or perhaps additionally, this phenomenon may be due to initial latent cell injury which only gradually becomes visible with the passage of time. Further consequences of cellular injury were the very rapid formation of cytoplasmic vacuoles by some cells and the active migration of granular leucocytes to the site of the injury. Leucocyte accumulation under these conditions strongly suggests a chemotactic effect by products of injured cells.

Blast Disease of Oil Palm

In Central and West African oil palm (*Elaeis guineensis*) growing regions, a severe nursery root disease, occurring at the end of the rainy season and known as 'blast', has caused serious losses and dislocation of field planting schedules during recent years. The diagnosis of the disease has proved to be difficult and troublesome. J. S. Robertson, of the West African Institute for Oil Palm Research, Nigeria, has now attributed the disease to the co-infection of roots by a species of *Pythium* and *Rhizoctonia lamellifera* (*Trans. Brit. Myc. Soc.*, 42, 401; 1959). The leaf and root symptoms of blast disease are described. Isolations from roots in an advanced state of decay yielded *Rhizoctonia lamellifera*, whereas isolations from primary infections yielded a *Pythium* species. Inoculation experiments are reported which demonstrate that typical blast symptoms develop only when a mixed inoculum of *R. lamellifera* and *Pythium* sp. is employed. A laboratory experiment showed that *R. lamellifera* is capable of parasitizing the *Pythium* species.

National Certificates in Biology

In view of the increasing measure of support for courses leading to the award of endorsed certificates in biology, and of the growing importance of this subject in industry and public services, the Secretary of State for Scotland and the Institute of Biology have agreed that the stage has been reached at which a national scheme in Scotland should be introduced. They have accordingly decided to appoint a joint committee, representative of the Institute and the Scottish Education Department, to receive and approve schemes for Ordinary and Higher National Certificates in biology. This is discussed in a recent issue of the *Journal of the Institute of Biology* (7, No. 3; July 1960). The Joint Committee is preparing instructions supplementary to those already provided for other National Certificates for the guidance of colleges wishing to submit schemes. Copies of these instructions may be obtained on application to the Joint Secretary, Joint Committee for Biology, Room 365, St. Andrew's House, Edinburgh 1.

The Tarlton Rayment Collection of Australian Insects

Mr. Tarlton Rayment recently donated his collection of Australian bees, wasps, thrips and mites to

the Commonwealth Scientific and Industrial Research Organization. These will be added to the comprehensive collection of the Organization's Division of Entomology and will become part of the Australian National Insect Collection. Mr. Rayment has earned world-wide recognition as an authority in the Hymenoptera, especially the Aphidae, both for his work in classifying the Australian species of the latter, and for his interesting studies on their biology. The collection is regarded as a very important addition to the National Collection as it contains many type specimens and hence will be widely used for reference work.

Harkness Fellowships of the Commonwealth Fund

THIRTY Harkness Fellowships of the Commonwealth Fund are tenable for 1961 in Continental United States and are offered, in separate series, to candidates from the United Kingdom, Australia and New Zealand, and Western Europe. The Fellowships are offered to candidates from the United Kingdom who are British subjects and either are graduates or have experience in government service, the professions, the creative arts, journalism, branches of business or industry, or other comparable careers and vocations, and have the equivalent of a degree in qualifications conferred by professional bodies or an attested level of professional accomplishment. Forms of application, which must be returned before December 1, can be obtained from the Warden, Harkness House, 38 Upper Brook Street, London, W.1, from whom further details can be obtained.

The Association of Consulting Scientists

THE following have been elected honorary officers and members of the Council of the Association of Consulting Scientists for 1960–61: *Chairman*, Dr. J. G. Davis; *Honorary Treasurer*, Dr. G. W. Ferguson; *Honorary Secretary*, Mr. W. H. Stevens; *Members*, Dr. M. Barent, Dr. H. H. Chambers, Dr. J. Grant, Dr. J. H. Oliver, Mr. O. W. Roskill, Mr. F. G. Sarel Whitfield.

Medical Research Council: Tropical Medicine Research Board

THE Medical Research Council recently established a Tropical Medicine Research Board to advise them on the promotion and co-ordination of all research in this field. The membership of the Board includes the following: Sir Harold Himsworth (chairman); Prof. A. C. Frazer (vice-chairman); Brigadier Sir John Boyd; Prof. P. C. C. Garnham; Prof. W. E. Kershaw; Dr. R. Lewthwaite; Prof. G. Macdonald; Prof. B. G. Maegraith; Prof. B. S. Platt; Prof. M. L. Rosenheim; Mr. H. J. Seddon; Prof. E. T. C. Spooner; Prof. A. W. Woodruff; Dr. B. S. Lush (secretary). The Chief Medical Officer and the Head of the Research Department of the Colonial Office have been appointed assessors on the Board, and two assessors have been nominated by the Secretary of State for Commonwealth Relations.

Medical Research Council: New Members

THE Committee of Privy Council for Medical Research has re-appointed the Right Hon. the Earl of Limerick and, in succession to Sir Geoffrey Vickers, have appointed Dr. E. F. Collingwood to membership of the Medical Research Council. Lord Limerick will continue as chairman of the Council and Dr. Collingwood will serve as treasurer. Prof. T. Crawford and Prof. W. M. Millar have been appointed members of the Council in succession to Prof. G. Payling Wright and J. D. N. Hill, who are retiring after their normal four-year term of service. All these appointments dated from October 1, 1960.

Announcements

PROF. B. BLEANEY and Dr. James Cook have been appointed members of the Council for Scientific and Industrial Research. Together with a third member yet to be appointed, they succeed Prof. P. M. S. Blackett, Sir Eric Ashby and Mr. H. Douglass, who have retired on completion of their period of service.

DR. J. M. WINTERBOTTOM has been appointed director of the Percy Fitzpatrick Institute of African Ornithology, University of Cape Town, and took up his office there on September 1.

DR. W. S. STILES has been elected president of the Illuminating Engineering Society for 1960–61. Dr. Stiles is a deputy chief scientific officer at the National Physical Laboratory, which he joined in 1925. His work in the past has included problems of vision, photometry, illuminating engineering, and visual response by psychophysical methods; his discovery with Dr. B. H. Crawford of the directional sensitivity of the retina being his best-known contribution. He was elected to fellowship of the Royal Society in 1957 for his work on vision.

THE first major exhibition on atomic energy to be held in Edinburgh opened at the Royal Scottish Museum on October 15. The exhibition, which has been mounted by the Atomic Energy Authority, will continue until October 29; it will provide a comprehensive review of Britain's nuclear power programme and of Scotland's contribution to this major scientific and industrial effort. The exhibition will illustrate the way in which Britain's research and development resources are being deployed to meet the future power needs. These are likely to be well over double the present level, expressed in terms of coal equivalent, by 1975.

THE ninth International Colloquium on Spectroscopy will be held at Lyon during June 5–10, 1961, under the auspices of the 'Groupement pour l'Avancement des Méthodes Spectrographiques'. Further information is available from Groupement pour l'Avancement des Méthodes Spectrographiques L.N.E., 1, rue Gaston-Boissier, Paris 15e.

THE twenty-first International Conference of Pure and Applied Chemistry will be held during August 2–5, 1961, and will be followed by the eighteenth International Congress of Pure and Applied Chemistry during August 6–12. Both meetings will be held in Montreal. Further information is available from the Secretariat, National Research Council, Ottawa, Canada.

A THREE-DAY symposium on Control of the Mind is being organized by the Medical Center of the University of California at San Francisco during January 28–30, 1961. The symposium is being organized with financial aid from the Schering Foundation. Further information can be obtained from the Department of Continuing Education in Medicine, University of California, Medical Center, San Francisco 22.

ORGANIZATION AND FINANCING OF BIOCHEMICAL RESEARCH IN BRITAIN

A JOINT session of the Biochemical Society and Section I (Physiology and Biochemistry) of the British Association was held in the Department of Biochemistry, University College, Newport Road, Cardiff, during the afternoon of September 7, the closing day of the annual meeting of the British Association. The session was organized on behalf of the Biochemical Society by K. S. Dodgson and W. J. Whelan and took the form of a colloquium, with contributions by nine principal speakers, on "The Organization and Financing of Research in Biochemistry and Allied Sciences in Great Britain". The meeting was under the chairmanship of Prof. John Pryde and was attended by about a hundred members of the two organizations.

Prof. A. Haddow, director of the Chester Beatty Research Institute, introduced the subject in a general way, pointing out the unfavourable and widening gap between the research efforts of Britain and those of the United States and the Soviet Union, and then turned more specifically to the organization and financing of the British Empire Cancer Campaign. Dr. F. J. C. Herrald, Sir William Slater and Mr. C. Jolliffe described the activities of the Medical Research Council, Agricultural Research Council and Department of Scientific and Industrial Research respectively, while Dr. G. F. Marrian gave an interesting account of the work of the Imperial Cancer Research Fund and of the new research laboratories now under construction in Lincoln's Inn Fields. Prof. F. C. Happold had collated information from professors of biochemistry in Britain, and spoke of the problems, particularly financial, which are facing university biochemists. The activities of industry (particularly the pharmaceutical industry) in the field of biochemistry were outlined by Dr. F. A. Robinson, of Allen and Hanburys, Ltd., while Dr. J. B. Bateman, deputy scientific attaché to the American Embassy, spoke of the contributions of the United States in providing support for biochemistry and related sciences in Britain. Finally, Prof. A. Neuberger summarized the proceedings and pointed to the steps which need to be taken if Britain is to maintain its high position in the field of biochemical research.

Contacts with numerous members of the audience prior to the meeting suggested that the real problems surrounding biochemical research are financial rather than organizational. In this connexion, a glance at the list of participants might have indicated that the speakers could be separated into two categories, namely, those distributing financial aid and those receiving it. The possibility of the meeting dividing sharply into two factions thus existed but, happily, did not materialize. Indeed, there was a general appreciation of the considerable assistance which various bodies have provided for all fields of biological research with the funds at their disposal, and of the sympathetic way in which applications are handled by them. In turn, it was clear that officials of these bodies are well aware of the problems facing research biochemists, particularly those working within the universities.

Several points of importance emerged during the course of the meeting. In the first place, it was clear from figures presented by Prof. Haddow that, in spite of the difficulty of translating the currency figures of various countries into absolute and meaningful terms, there is a widening gap between the amount of financial aid available for research in biological and medical sciences in Britain compared with that available in the United States or the U.S.S.R. Prof. Haddow reminded his audience of the blunt words of Sir Harry Melville earlier this year: "Whether we like it or not, the age of string and sealing wax has come to an end, and the pursuit of scientific knowledge is now a rather expensive and complex affair in which substantial resources in men, material and facilities are needed". Apart from the discrepancy in financial effort, there is also some degree of contrast between the principles applied in financing research in the United States and those applied in Britain. In the United States, money is being provided for medical research, including biochemistry, on a scale which we in Britain would regard as lavish. There is a tendency to assume that expansion on this scale must inevitably result in a dilution of scientific standards and attainments. In fact, there is increasing evidence to show that the great and rapid expansion resulting from the American system has not diluted scientific standards, but rather has elicited talent which might otherwise not have become manifest.

In contrast, financial assistance for research in Britain is not so readily available, and the case must be forcefully and compellingly presented to the appropriate organization in order to obtain the necessary financial support. In considering applications for financial assistance, the Medical Research Council, the Agricultural Research Council and the Department of Scientific and Industrial Research attach great (perhaps too much) significance to the ability and reputation of the grant-seeker and the 'timeliness and promise' of the proposed research work. However, what might appear to be of timeliness and promise at the moment may not appear so twelve months hence. Other work which appears to have little import or significance at the time (and which may therefore remain unsupported) may well provide the vital answer to a problem which develops in five or ten years time. In order to cope with this problem, so far as university departments of biochemistry and allied sciences are concerned, Prof. Happold pleaded that the universities themselves should be given more adequate sums for distribution among their departments. The distribution of such sums should be under the control of an internal university committee composed of those in a position to judge the needs. Prof. Happold pointed out that it is the universities (the source of a large proportion of the research in biochemistry and other biological sciences) which are particularly affected by inadequate financial support. Indeed, the head of a department had informed him that, "If the apparatus which has been bought with gifts from the Royal Society, the Rockefeller Foundation or the M.R.C. were taken

away from this department, I can safely say that every single major line of research at present being pursued here would stop at once". Support for Prof. Happold's plea came from the body of the meeting during discussion periods, and it was clear that a strong feeling existed that university departments urgently need greater financial support from within the universities themselves.

Two further inter-related points which emerged from the colloquium were, first, that biochemistry is still primarily a research subject, and secondly, that there is already a shortage of trained biochemists in Britain. In relation to the first point, Dr. Robinson produced some interesting figures which suggested that comparatively few biochemists are employed in industry and that, generally speaking, they tend to take subordinate roles. However, Dr. Robinson did stress that his figures related particularly to the pharmaceutical industry, and it seems to the present writers that reference to other industries, for example, the food industry, might provide a more favourable picture. On the second point, Sir William Slater pointed out that it has become increasingly difficult to obtain suitably qualified research biochemists and that the brakes on the progress of the biochemical work of the Agricultural Research Council have not been shortage of funds but shortage of the right men. Further point was given to this statement by Dr. Marrian, who said that the development of the work of the Imperial Cancer Research Fund and the opening of its new Institute will mean that the number of qualified research workers employed by the Fund will increase from the present level of about 30 to between 80 and 100 by 1964–65. Approximately one-third of these will probably be biochemists. At the present rate at which trained biochemists are emerging from the universities, one suspects that Dr. Marrian will experience difficulty in recruitment on this scale.

In his summarizing remarks, Prof. Neuberger struck at the very root of this problem by pointing out that several British universities do not yet have departments of biochemistry, and he appealed to the universities to see that this defect is speedily remedied. In his own University of London, although there are a number of biochemistry departments concerned with the instruction of medical students, there are only two departments catering for a science degree in the subject, and the combined intake of these departments is limited to about twenty students a year. Prof. Neuberger further stressed the frustration felt by university biochemists of high standing who are unable to progress to senior status because of the rigidity of establishment. He pleaded for the speedy creation of new chairs of biochemistry and the introduction of personal chairs in this and related subjects. Citing the case of Harvard University, with its five professors within what is probably the best organic chemistry department in the world, Prof. Neuberger said that this is one aspect of the American university system that we should be prepared to adopt.

Bearing in mind the comments of Dr. Robinson regarding the subordinate position of biochemists in industry, Prof. Neuberger suggested that it might be time to do some re-thinking as to the way in which biochemists in Britain are trained. For example, is a training in organic chemistry being given which is sufficient for the needs of industry? Should the universities encourage the biochemist who is perhaps not ideally suited for a research position to think of a teaching post in a grammar or public school? The student population of the schools might then become more aware of the possibilities of biochemistry as a career, and this in turn might stimulate the flow of recruits to the profession.

During the two periods which were allocated to discussion, many members of the audience took the opportunity to ask questions and to state their own views. From later discussions which took place during an informal supper, it was clear that the colloquium had been a most successful venture and, in particular, many people expressed their appreciation of the co-operation of the various research councils and similar organizations in providing such interesting accounts of their activities. The meeting has raised a number of points which appear to merit further investigation and a number of problems which, it seems to the present writers, should now be actively pursued by the Biochemical Society for the good of British biochemistry and, indeed, for science as a whole.

K. S. DODGSON
J. PRYDE

RESEARCH FOR INDUSTRY

"RESEARCH for Industry 1959"* follows the general pattern of the previous year's report. The report of the Industrial Grants Committee, which this year discusses the coverage of the Government scheme and co-operation in three specific areas—creep research, fatigue of metals and shipbuilding research—is accompanied by a review of the achievements of a dozen of the Associations, the terms of grant of which have been reviewed during the year; and, under "The Research Associations To-day", there is the now customary list of Associations, giving their officers, income, publications and a brief indication of the present scope of the work of each Association. To the total income of the Associations in 1959 of £7·3 million, the Department of Scientific and Industrial Research contributed £1·7 million.

In place of the two special chapters in last year's report dealing with the place of the research associations in the evolution of scientific endeavour and the service of co-operative research to the textile industry, there is a chapter by Dr. J. Thomson on instrumentation and automatic control in industry, which surveys briefly recent progress in this field in various industries, particularly under the headings of detecting elements, indicators and recorders, and controllers. The British Scientific Instrument Research Association seeks first to serve the scientific instrument industry and secondly, to bring large users of instruments into contact with manufacturers. Besides current investigations into the structure and control of thin films, of glassy phosphors, particularly

* Department of Scientific and Industrial Research. Research for Industry 1959: a Report on work done by Industrial Research Associations in the Government Scheme. Pp. iv+126+12 plates. (London: H.M. Stationery Office, 1960.) 8s. net.

as detectors of high-speed neutrons, and of the parameters of optical receiving systems with particular reference to frequency response measurements, the Association has just completed the development of an ultrasonic flowmeter, under the sponsorship of the National Research Development Corporation. The Industrial Grants Committee stresses its anxiety to foster a free exchange of information in this field between the many research associations concerned.

In regard to coverage, the Industrial Grants Committee notes that the admission of the Water Research Association, which in its new premises at Medmenham, Bucks, will be concerned with rapid methods of water filtration, algal growth in stored waters, and the disposal and reclamation of waterworks sludge, brought for the first time the number of organizations in the Government scheme to fifty. Only forty-one of these bodies, however, have the formal and permanent status of a research association; the others, with the title, usually, of research council, committee or organization, being as a rule young concerns in an experimental stage. Stress is laid on the need to increase greatly the scale of research on creep. The new building being erected at the National Engineering Laboratory for completion in 1961 will permit basic researches to be expanded with the view of obtaining a better understanding of the creep process and of those properties relevant to the successful use of engineering materials at high temperatures; in the meantime, a Creep Information Centre has been opened to enable industrial designers to obtain creep data not at present readily available in a co-ordinated form. The Electrical Research Association is also planning an extended programme of tests to provide new information on those ranges of steels and temperatures of particular relevance to modern steam-raising plant and turbines, especially for generating electric power. The National Physical Laboratory will analyse and evaluate the relevant metallurgical data obtained on a range of selected steels, and co-operative creep tests are being made by several steel firms organized through a committee of the British Iron and Steel Research Association.

A committee of nine members, under the chairmanship of Sir Alfred Pugsley, has been set up to consider what research needs to be done into the fatigue of engineering structures made of metal, to survey existing research facilities and to make recommendations to the Department. In regard to shipbuilding research, besides the work of the British Shipbuilding Research Association and Parsons and Marine Engineering Turbine Research and Development Association, which is specially reviewed in the report, much useful work on ship hydrodynamics has been done at the National Physical Laboratory, and it is intended to concentrate in the new laboratory at Feltham all research and commercial tests relating to rough water and all work on steering and manœuvring problems, and to conduct smooth-water tests at Teddington. The Industrial Grants Committee is encouraging as much flexibility as possible in the programmes of the two research associations, and the report refers to the virtual completion by the British Shipbuilding Research Association of an extensive methodical series of hydrodynamic experiments on models of ocean-going merchant ship forms, the charts compiled from which should provide naval architects with a standard work of reference for estimating the resistance and power required for propulsion of any new form of ship's hull within a wide range of variables. The Association also operates an establishment for testing full-scale components of ships' structures and is concerned with all types of propelling and auxiliary machinery on ships, other than steam and gas turbines, which are dealt with by the Parsons and Marine Engineering Turbine Research and Development Association. Research and design studies by this Association have led to the production of turbine machinery of advanced design, with a 27·5 per cent reduction in overall fuel consumption and a 53 per cent reduction in the weight of marine turbines and gearing between 1945 and 1958. A special hydraulic transmission has been developed with ahead and astern units, together with a friction clutch for running ahead under steady conditions. Tests on a small steam turbine at temperatures up to 1,150° F. have yielded much valuable information, and an experimental liquid-cooled single-stage gas turbine has been designed which shows promise of giving appreciably better performances than the steam turbine. Full-scale tests of hardened and ground naval gears, and through-hardened merchant-marine gears have permitted designs of higher loading to be applied to the propulsion of merchant ships.

Among recent achievements of the British Cast Iron Research Association noted in this report may be mentioned outstanding progress in work on the causes and elimination of defects in iron castings, its development of a successful external system of dust control for stand grinders in fettling shops, the establishment of much more precise correlations between mechanical properties and structure of cast iron and between melting processes and properties, and the complete definition of the conditions for producing shock-resistant nodular cast iron. The British Steel Castings Research Association's steel-making section has constructed control curves permitting prediction, for any temperature of steel-bath and any initial oxygen content, of the amount of oxygen to be injected after the carbon flame appears in order to give a predetermined reduction in the carbon content of the bath. Other work seeks to provide basic data on the physical properties of cast steel, and the Association is also studying the control of both dust and noise when using portable fettling tools.

The File Research Council has established a maximum forging temperature by studying the metallurgical treatment of high-carbon file steel, and a study of metal flow during tooth-cutting has enabled the relation between tooth shape and chisel angles to be determined. The British Welding Research Association's tests of welded steel plates 3 ft. wide and 1 in. and 3 in. thick have established the relative importance in brittle fracture of weld defects, residual stresses, and quality of steel, and extensive work on the welding metallurgy of aluminium alloys has facilitated the selection of filler alloys. Fatigue tests have confirmed the serviceability of butt-welded pipes provided the root-run is sound and the penetration bead is smooth. The Chalk, Lime and Allied Industries Research Association, now in its fifth year, has been concerned chiefly with possible new uses for lime, the examination of factors affecting the quality of lime, and with the manufacture and use of sand-lime bricks. The Research Council of the British Whiting Federation has clearly indicated the possibility of considerable improvements in whiting manufacture by producing a range of

more uniform and finer-quality powders, and its work on quality control and grading has led to the adoption of a comprehensive system of grading by size characteristics, with limits for chemical impurities.

Basic research by the British Leather Manufacturers' Research Association in the past five years has been concerned with the hide and skin proteins and the isolation and identification of constituents of vegetable tanning materials. In applied research the advantage of sodium chlorite over sodium hypochlorite as an antiseptic in soaking has been demonstrated, and a water-proofing process developed in which the addition of rubbery polymers to the silicone solution greatly reduces the amount and cost of silicone needed. An intensive study of batch tannages in the laboratory and on the small-works scale enabled the duration of vegetable tanning to be reduced from 6–12 weeks to 14–21 days. The Hosiery and Allied Trades Research Association has given considerable help in the development of new knitting and wet-processing techniques for tailored synthetic fibre yarns, and suggested a scheme for the continuous processing of nylon hose. The British Launderers' Research Association has established the practicability of medium-temperature washing and cold-water rinsing, and has set up a Special Projects Group to investigate and develop new methods and equipment which should permit laundering on a continuous-flow basis. Psychological tests on apprentices in nineteen firms by the National Institute of Industrial Psychology have yielded a good correlation between performance at the tests and performance at technical colleges, and the tests should give a valuable forecast of probable performance during apprenticeship. Work still in progress includes inquiries into relations between satisfaction and efficiency at work, between management structure and managers' satisfaction and effectiveness in their work, methods of measuring 'personal' values relevant to people's occupations and the development of new tests of colour vision and colour-matching skills.

THE FRANKLIN INSTITUTE

At the annual meeting of the Franklin Institute held on January 20, the president, Mr. W. L LePage, gave a summary of the activities of the Institute during 1959, and presented the annual report of the board of managers for 1959*.

The year 1959 marked the one hundred and thirty-fifth anniversary of the founding of the Institute and the twenty-fifth of its fine building on the Parkway, Philadelphia, and the report makes special mention of the remarkable growth of the Institute's activities since its modest beginning in 1824 as an organization for the mutual benefit of a few citizens of Philadelphia. To illustrate the Institute's present wide sphere of influence, the highlights of the activities for 1959 are presented in the annual report in the form of a spiral, the focus of which is taken as at the Institute's headquarters in Philadelphia and the unbroken curves of which reach out through the Delaware Valley, the nation, the world, and the universe beyond our planet. Each of these areas is taken as the title of one of the sections of the report, and the Institute's activities are discussed according to the area in which their contributions to science were the largest.

Five of the Institute's main activities—the Science Museum, the Astronomy Department, the educational radio and television programmes, the science meetings, and the Library—are confined almost entirely to Philadelphia and the Delaware Valley. The number of visitors to the Museum during 1959 was 410,433, of whom approximately 290,000 were school children. Sixteen permanent exhibitions were added during the year, of which the two most spectacular were the full-size *Matador* missile and the smoke tunnel in the Hall of Aviation. The demonstration, "Our Biggest Satellite—the Moon", which was shown in the Astronomy Department during September–October, proved extremely popular since that period coincided with the launchings of the *Lunik* II and *Lunik* III. Other exhibits included a *Vanguard* exhibit and a model of the 600-ft. radiotelescope which is being erected in Virginia. The radio and television programmes for schools in the area consisted of a weekly series of radio broadcasts covering science subjects and six television broadcasts featuring aspects of work being carried out in the Institute's laboratories. The titles of the twenty-one lectures presented at the Institute's meetings are listed in the report. They include, "The Impact of the International Geophysical Year on Science and Engineering" given by H. Odishaw; "Fundamental Particles" by H. A. Bethe; "The Fuel Cell" by H. A. Liebhafsky; and "The Science of Yesterday, To-day and To-morrow" by W. F. G. Swann. The number of accessions to the Library during the year was 4,281, bringing the total of holdings to 167,135, and the number of journals currently received rose to 1,336, including nineteen Russian journals and fourteen English translations of Russian serial publications.

In recent years the part played by the Institute in the scientific life of the United States of America has grown greatly in importance, mainly because of the work of the Institute's Laboratories and the series of technical symposia and conferences sponsored by the Institute. The symposium on space medicine electronics, held in the spring, and the international symposium on gas-lubricating bearings, held in the autumn, attracted large audiences from afar. The Computing Centre, which completed its third year of operation in 1959 and its first year as a separate activity, drastically reduced its machine-use charges and many more industrial firms availed themselves of its services. Contracts received during 1959 by the Institute's Research and Development Laboratories passed the four million dollar mark for the first time. New equipment included the latest model electron-microscope and Varian instruments used in studies of nuclear and electron-spin resonance. Projects undertaken included the production of an ultra-pure iron bar of 1-in. diameter by zone refining; apparatus to measure speed by detecting the light of an ionized gas at two points along the travel of a

* A summary and full text of the illustrated report appear in the April issue of the *Journal of the Franklin Institute* (269, 315; 1960).

wave; the preparation of a text-book on thermal stresses in nuclear reactors; and several projects related to missiles and satellites, including the design and construction of an advanced type of satellite.

By its Committee of Science and the Arts, its *Journal*, and by the work of the Biochemical Research Foundation, for which the Institute serves as trustee, the Institute is best known throughout the world. The Medal Day ceremonies organized by the Committee were held on October 21, 1959. The seventeen individual recipients included H. A. Bethe, C. H. Townes, and C. M. Zener, and one industrial company. One of the achievements of the Biochemical Research Foundation in its concentrated attack on cancer was the successful isolation of a unique streptomycin-independent strain of *E. coli* which can be used as a screening organism in a search for anti-mutagens. Long-term studies of the effects of nutrition on cancer growth were continued, as well as studies of the metabolic processes of cancer cells. In addition to the *Journal* the Institute now issues *The Institute News* eleven times a year, and although intended primarily for Institute members, this four-page newspaper is also distributed to schools, libraries and others interested in science education.

The cosmic ray group of the Bartol Research Foundation of the Institute participated in the International Geophysical Co-operation, and constructed a new cosmic ray monitor for installation at McMurdo Naval Air Facility in Antarctica, to complement the one in operation at Thule, Greenland. The detector for heavy nuclei contained in the satellite *Explorer* VII was designed by the Foundation. The Foundation's headquarters are located on the campus of Swarthmore College, and in addition to providing an active programme of scientific colloquia and public lectures, undergraduate students of the College have been encouraged to participate in the Foundation's research programme.

The report concludes by emphasizing that, though the Institute's Laboratories and the Foundation are self-supporting, the accounts indicate that the educational and general activities of the Institute, which must expand to meet the growing need, will soon face a critical financial situation. A total of approximately 204,000 dollars was received in 1959 in gifts, bequests and from other sources, but the net loss for educational and general activities, though reduced from the 1958 figure of 100,000 dollars, was still more than 20,000 dollars, and will rise as the planned expansion gets under way during the next decade. The managers of the Institute appeal to the increased generosity of members and friends of the Institute to provide the necessary additional funds.

THE ATOMIC ENERGY OF CANADA LIMITED

THE need for, and the extent of, a nuclear power programme in Canada is one of the main topics of discussion in the annual report of the Atomic Energy of Canada Limited for the year ended March 31, 1960, which has recently been published*. Although Canada has vast resources of oil, gas, coal and untapped water power, these are not uniformly distributed across the country and already some regions are approaching the point where the conventional power resources will need to be supplemented by nuclear power. The industrial area of southern Ontario is likely to be the first of these regions, and it is fortunate that conditions in this area are favourable to the early introduction of nuclear power, for not only is the generating capacity of the Hydro-Electric Power Commission which serves Ontario capable of absorbing the additional 200 or so megawatts, but also there are present in the province of Ontario extensive uranium deposits and large uranium mines.

After considerable examination of the various alternatives and several years experience in the operation of such reactors, it is still the conviction of Atomic Energy of Canada Limited that the type of reactor which is fuelled by natural uranium and moderated by heavy water offers the best promise for early, low-cost nuclear power in large units. The four nuclear power projects which the authority has in hand are described in detail in the report. The first two, the Nuclear Power Demonstration Station being built at Rolphton some twenty miles west of Chalk River, and the Douglas Point plant, are closely related. The reactor at the Nuclear Power Demonstration Station is moderated and cooled by heavy water and uses pressure tubes instead of a pressure shell to contain the coolant. The fuel consists of natural uranium dioxide pellets sheathed in 'Zircaloy' tubes, and the tubes are grouped together in bundles. The Station, which is expected to have an output of 20 MW. (electrical) and to go into operation during 1961, is a prototype, and the results of tests carried out at the Station will be used to improve and modify the design of the Douglas Point Station, the construction of which was authorized in June 1959. The clearing of the 2,300-acre site on the eastern shore of Lake Huron began in February 1960, and the Station is scheduled for completion by mid-1964. Provision has been made for two 200-MW. units, but at present only one unit *Candu* (Canadian deuterium uranium) has been authorized and is under construction.

The third nuclear project, called *Ocdre* (organic cooled, deuterium moderated, reactor experiment), consists of the development of a nuclear power reactor of medium size which it is hoped will prove attractive to industrial concerns. A preliminary report on the design of such a reactor, which was to be available in August 1960, is to include an estimate of cost of the construction of an experimental reactor. The fourth project is devoted to the study of information relating to small nuclear plants suitable for use in remote regions of Canada.

At the Chalk River Research Establishment both the *Nry* and *Nru* reactors were in routine operation during the year, being fully occupied with research experiments, the production of radioisotopes and plutonium, and engineering testing. The several 'loops' in the reactors have been used by both the United States Atomic Energy Commission and the United Kingdom Atomic Energy Authority. The

* Atomic Energy of Canada Limited. Annual Report, 1959–1960. Pp. 36. (Ottawa: Queen's Printer, 1960.) 25 cents.

two small experimental reactors, *Zeep* and *Ptr*, were also in constant operation, and a new zero energy, heavy-water moderated reactor, *Zed*-2, is being constructed and is nearing completion. One of the important lines of fundamental research carried out at Chalk River is the investigation of the structure of the atomic nucleus for which special facilities, such as the experimental reactors and particle accelerators, are provided. During the year under review major ancillary equipment was added to the 10-MeV. tandem accelerator for this particular investigation. In the Physics Division a new spectrometer, which employs the neutron beam from the *Nru* reactor as a probe to examine the forces holding together liquids and solids, was installed. The Research Chemistry Branch was mainly concerned with investigations on the breakdown of molecules exposed to intense radiation and the bombardment of metals with heavy ions. Fuel development, the physical properties of reactor materials, field tests of the method of disposal of fission products by fixing them in glass, and the development of new radiation monitoring instruments, including a tiny radiation detector which uses semiconductors, were some of the applied research problems investigated by the research establishment.

The directors and management of Atomic Energy of Canada Limited gave consideration during the year to the long-range expansion of research and development in the field of atomic energy, and recommended that Chalk River should not continue to expand, but that a new site should be selected at which future expansion could take place. In October 1959, the Government announced the establishment of a new research and development centre in Manitoba, on the east bank of the Winnipeg River between Seven Sisters and Lac du Bonnet, to be known as the Whiteshell Nuclear Research Establishment. The first major facility to be provided at the new site is likely to be the *Ocdre* reactor. During October also, Canada and Euratom signed an agreement for co-operation in the peaceful uses of atomic energy and a technical agreement for a joint programme of research and development in heavy-water reactors. A group of Euratom industrialists visited Canada in the autumn to see the various atomic energy facilities. Close co-operation with the United Kingdom Atomic Energy Authority and the United States Atomic Energy Commission continued, as well as with the authorities in Australia, Japan and Pakistan. The number of staff from other countries attached to Atomic Energy of Canada Limited during the year was sixty-two, and was limited only because of lack of working and housing accommodation. The construction of the Canada-India reactor at Trombay, India, is now essentially complete and the initial start-up is scheduled for mid-1960.

The report concludes with the financial accounts of Atomic Energy of Canada Limited and with details of the Commercial Products Division which is responsible for the production, planning, processing and marketing of the radioisotopes produced in the Chalk River reactors. More than half the curies of radioactivity sold by Canada has been for the cobalt therapy machines for the treatment of cancer which were originally developed in Canada. One hundred and eighty-five machines have been installed in thirty countries. Another device recently developed is the *Gammacell* 220, which is a portable facility for the gamma-irradiation of materials, and fourteen of these units are in service in eight countries.

CONCENTRATION OF PLANKTON PIGMENTS IN AUSTRALIAN WATERS

ESTIMATIONS of the quantity of plankton pigments are widely used as a measure of the biomass of phytoplankton. They have achieved this popularity through the ease and accuracy of the chemical estimation, and they give results more reliable than most other techniques. However, as G. F. Humphrey emphasizes in a recent paper issued by the Australian Commonwealth Scientific and Industrial Research Organization, they have many disadvantages. For example, there is a variable and uncertain relationship between pigments and the chemical composition of the organism, and so they are a poor measure of, say, the cellular carbon. Nevertheless, the pigments are the potential absorbers of the energy used in photosynthesis and the widespread usage of one particular method commends it further (Division of Fisheries and Oceanography. Technical Paper No. 9: The Concentration of Plankton Pigments in Australian Waters. Pp. 27. Melbourne: Commonwealth Scientific and Industrial Research Organization, 1960).

The author, Dr. G. F. Humphrey, who is chief of the Division of Fisheries and Oceanography, has gone to some length in perfecting a satisfactory modification of the Richards and Thompson technique for pigment measurements. He has also ascertained the precision obtained with the method, and for the analyses this amounts to $\pm$ 10 per cent, but the variation between replicate plankton samples is much larger and particularly at greater depths it is shown even to exceed previous estimates of $\pm$ 33 per cent.

The results described were obtained mainly from the Tasman Sea and in particular from two stations at 50 and 100 m. depth off Sydney. The ratios of the pigments varied during the year, with either chlorophyll *a* or *c* predominating. Chlorophyll *c* was frequently in excess and it appeared to be a pigment of major importance in the deeper waters. It should be mentioned, however, that the units used to express chlorophyll *c* values cannot be compared in absolute terms with the milligrams of chlorophyll *a*, for the specific absorption coefficient of pure chlorophyll *c* is not yet known and the determination of the actual weight of chlorophyll *c* is therefore not possible.

No smooth seasonal variation is evident in the results, but from late winter to late summer there were a series of sharp increases in pigment. There is some evidence that these peaks may be correlated with the prevailing hydrological conditions. The depth distribution suggests that the inorganic

phosphate content was inversely proportional to the chlorophyll, but neither nitrate nor total phosphate showed any correlation with the pigments.

The quantities of pigments found off Sydney covered the range found on more extensive cruises in the Coral and Tasman Seas and in the Indian Ocean. On these cruises the importance of chlorophyll *c* was again evident.

The results described in this paper are the first detailed observations of plankton pigments from Australian waters, collected in the extensive oceanographical programme which the Commonwealth Scientific and Industrial Research Organization in Australia is now undertaking, and they form an interesting basis for comparison with other regions.

R. I. CURRIE

CENOZOIC MAMMALS IN NORTH AMERICA

JUST over one hundred years ago Charles Moore, an amateur geologist of Bath, washed and sieved three tons of clay to obtain 30 multicusped teeth · the clay was a Rhaeto–Liassic fissure infilling and the teeth were of *Microlestes*, and they remain to-day almost the only record of this rare group of animals astride the frontier that separates mammals and reptiles.

Despite this promising beginning, few vertebrate palæontologists have taken to the labours of washing and sieving on a big scale. Dr. McKenna has been one and it has paid handsome dividends; the washing and sieving of Wasatchian claystones and sandstones has yielded him 11,000 complete mammal teeth from a formation otherwise almost barren, and a horizon astride the Eocene and Palæocene all too poorly known. The complete dissociation of the remains is a considerable limitation of the technique and Dr. M. C. McKenna does not appear to have attempted any concentrating methods, the fossils being hand picked from sieved fractions (University of California Publications in Geological Sciences. 37, No. 1: Fossil Mammalia from the Early Wasatchian Four Mile Fauna, Eocene of Northwest Colorado. Pp. 1–130. (Berkeley and Los Angeles: University of California Press; London: Cambridge University Press, 1960.) 2.50 dollars).

A fauna of 58 species from 12 mammalian orders is described; these include four multituberculates, a marsupial, several primates and insectivores. The fauna shows close similarity with those of early Gray Bull fauna of Wyoming, though there are notable absentees, and is considered early Wasatchian, that is, basal Eocene. The paper has no plates, but the text-figures are ample and exceptionally clear.

Pantodonta is an order of mammals the systematic study of which is fraught with difficulties; while distinction as an order is clear, the internal and external affinities remain debatable. Recent work by Dr. E. L. Simons is confined largely to the Palæocene species of North America, albeit this comprises most of the described forms; the European Eocene and Asiatic Oligocene forms are mentioned in his discussions (*Trans. Amer. Phil. Soc.* (New Series), 50, Part 6: The Paleocene Pantodonta. Pp. 99. (Philadelphia: American Philosophical Society, 1960.) 2.50 dollars). Detailed diagnoses are given for North American Palæocene species only. The post-cranial skeleton is described for most genera where it is known, with differences noted, but few comments on their significance: although approximately half this paper is devoted to skeletal anatomy, there is only one illustration of pelves. The wealth of material available makes it difficult to accept the quotation "they [Pantodonta] defy interpretation of their mode of life because they are so totally unlike anything now living"; they are no more remote than Titanotheres and mammal-like reptiles.

Biostratonomic work threw little light on the ecology of the pantodonts; this is not surprising since their life habitat was probably quite different from their place of entombment. Concerning the relations to other orders, the author restates the main arguments used by earlier writers.

R. J. G. SAVAGE

EARTH SATELLITE OBSERVATIONS AND THE UPPER ATMOSPHERE

Temperature Inversion in the *F*1-Layer

SUFFICIENTLY reliable values of atmospheric density—including the diurnal variations—in altitudes 200–700 km. have been derived from the variations of the acceleration of artificial Earth satellites[1–3]. Measurements from rockets[4,5] gave density values up to about 200 km.

The densities obtained from rocket measurements and the satellite data could not be represented satisfactory by a single curve with monotonically varying gradient. Therefore, H. K. Kallmann[6] suggested a model which contains a 'wiggle' in the logarithmic density curve at altitudes 150–200 km. It is model *C* in her paper.

From the data[7] from satellites 1958δ2 (*Sputnik* 3) and 1959ζ (*Discoverer* 6), it now became possible to derive the exact form of the 'wiggle'. Twenty values for atmospheric density at altitudes 180–235 km. from the satellite 1959ζ and the numerous results from the satellite 1958δ2 during August 1959–April 6, 1960, were available for this purpose. During this period the altitude of the perigee of the latter satellite decreased from 215 km. to 147 km. In order to eliminate seasonal effects, only values with $|\Delta\delta| = |\delta_\pi - \delta_\odot| < 60°$ were used (where δ is declination, π is perigee, $\odot$ is Sun).

The atmospheric densities were first derived according to a method described in detail in our earlier paper[1]; that is, preliminary values for atmospheric density were computed using the scale heights of H. K. Kallmann's "preliminary model"[6]. Then a linear approximation to the logarithmic density curve was derived graphically for altitudes where the major air drag on the satellite occurs. The gradient of this linear approximation was employed to determine the final atmospheric densities, so that we have an itera-

tion process. Because of the diurnal density variation, the gradient depends on local time. This was taken into account in the last step of the iteration.

Even the preliminary atmospheric densities derived showed a well-developed 'wiggle' in the logarithmic density curve which varied only slightly in shape when changing to the final atmospheric densities. Finally, the atmospheric densities above 180 km. were corrected to a standard value of solar activity. It is based on a flux of solar 20-cm. radiation of $S = 170 \times 10^{-22}$ W./m.^{2}c./s.

As has been shown in an earlier paper[1], the atmospheric densities are practically proportional to the flux of the 20-cm. radiation. This correlation was called the 'solar effect' or (better) 'effect of solar activity'. It has since been confirmed by L. G. Jacchia[2]. The reduction was performed using the relation:

$$\Delta \log \rho = \log \rho_{\text{obs.}} - \log \rho = \log (S/170) \qquad (1)$$

where ρ is the atmospheric density and S the solar flux at wave-length 20 cm. in units 10^{-22} W./m.^{2}c./s. The measurements were obtained by the Heinrich-Hertz-Institut, Berlin-Adlershof. We used values averaged over ten-day intervals since the satellite data also represent averages over several days. Since the solar values showed little scattering about the standard value of 170 during the period of interest, the correction had little influence on the shape of the curve.

For the ratio of mass to area we used $m/A = 40 \cdot 8$ gm.cm.$^{-2}$ for 1958δ2 and $m/A = 12 \cdot 9$ gm.cm.$^{-2}$ for 1959ζ. From this follows $AC_DF/m = 0 \cdot 0465$ cm.^{2}/gm. and $0 \cdot 154$ cm.^{2}/gm., where C_D is the drag coefficient and F a factor between $0 \cdot 9$ and $1 \cdot 0$ caused by rotation of the atmosphere, using the notation of D. G. King-Hele[3]. We found that the ratio of mass to area for the satellite 1959ζ gave atmospheric densities fitting those obtained from *Sputnik* 3 very closely.

The computed atmospheric densities are shown in Fig. 1. The circles and triangles represent the densities obtained from the *Space Track Bulletins* of *Sputnik* 3. The circles marked the data for $|\Delta\delta| < 20°$ and the triangles values for $20° < |\Delta\delta| < 60°$. The open symbols are day-time values (8–20 hr. local time), the filled symbols night-time values (20–8 hr.)

Below 170 km. the data of the Smithsonian Astrophysical Observatory deviate from the Space Track data. In this region the Smithsonian data are represented by crosses. The solid curve is valid for 14 hr. local time, the dotted curve for 6 hr. local time. Data from *Discoverer* 6 are marked by vertical crosses.

The rocket measurements by LaGow *et al.*[5] have been inserted in the diagram. The data were obtained from rocket launchings at Fort Churchill on July 29, 1957, 4.00 p.m. C.S.T. and October 31, 1958, 2.00 p.m. C.S.T., giving atmospheric densities at altitudes up to 210 km. and 188 km. respectively. These results, too, were corrected for the solar effect. The daily averages of the 20-cm. radiation were $S = 256$ and 188 after calibration (letter from the Heinrich-Hertz-Institut).

As will be seen, the 'solar effect' originates in the region of the 'wiggle' (F1-layer of the ionosphere) as a result of absorption of ultra-violet radiation. At 150 km. the influence on the atmospheric density becomes negligible. Thus the rocket data for $h \geqslant 180$ km. were corrected using equation (1); the data for $150 < h < 180$ km. were corrected using the following relation:

$$\Delta \log \rho = \frac{1}{30} (h_{\text{km.}} - 150) \cdot \log (S/170) \qquad (2)$$

Thus we obtained an increase in the correction from 0 at 150 km. to the full value at 180 km.

The agreement between the rocket data and the curve is excellent. In interpreting the data, however, one has to take into account the position of the rockets in 59° north latitude, with $\Delta\delta = 40°$ on July 29, 1957, and $\Delta\delta = 73°$ on October 31, 1958.

The very close correlation between atmospheric density variations ($h > 180$ km.) and the solar 20-cm. radiation emitted from the hot condensations of the solar corona points to the fact that the origin of the solar effect may lie in the absorption of solar ultra-violet radiation, which is also part of the thermal emission of the hot condensations. The Lyman alpha line of He$^+$ (304 Å.) may be mainly responsible for that, because of the high ionization potential of helium. H. E. Hinteregger *et al.*[9] were able to measure the absorptions of the He$^+$ line in altitudes 150–210 km. from a rocket on March 12, 1959. From their results we find that the Earth's atmosphere has at 304 Å. an optical thickness $\tau \approx 0 \cdot 1$ at 210 km. but $\tau = 1$ at 160 km. The increase in optical thickness is almost linear in the log τ, h diagram for altitudes 210–150 km. At 150 km. the He$^+$ line is almost completely absorbed.

From the atmospheric density curve between 180 and 200 km. we find a temperature inversion in the F1-layer. The quantitative representation of the

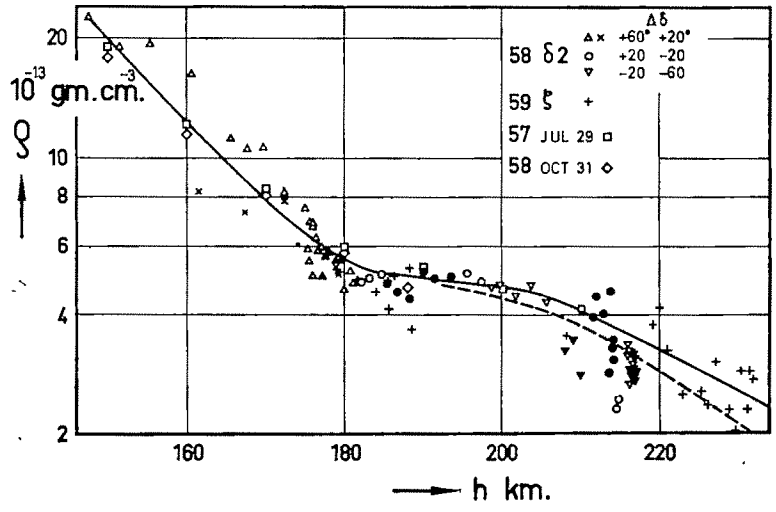

Fig. 1. Atmospheric densities at altitudes 150–230 km. above the Earth ellipsoid. The solid line refers to 14 hr. local time, the dotted line to 6 hr. local time. The results were obtained from the satellites 1958δ2, 1959ζ and the rocket launchings (ref. 5) of July 29, 1957, and October 31, 1958. The results from 1958δ2 are subdivided into three groups according to their $\Delta\delta$-values ($\Delta\delta = \delta_\pi - \delta_\odot$) (where δ is declination, π is perigee, $\odot$ is Sun). Open symbols give day-time values (8–20 hr. T.L.T.); filled symbols give night-time values (20–8 hr.)

temperature will be given elsewhere[10]. Because of the small heat conduction at 200 km. the density curve changes little between day and night (see Fig. 1).

It is not possible at present to decide whether solar ultra-violet radiation as well as the solar He^+ line and solar X-ray radiation contribute to the heating of the $F1$-layer. Furthermore, heating by a steady flux of solar corpuscular radiation may be expected at 200 km. according to L. G. Jacchia's observations on satellite 1958δ1 during the magnetic storms of July 1958 and September 1958. The diurnal variation of atmospheric density may indicate a contribution of corpuscular radiation to the heating (see ref. 11, Fig. 1). The increase in density seems to start before sunrise; that cannot be explained by electromagnetic radiation. However, because of the large scattering of the values, this result seems unreliable.

A second 'wiggle' depending on solar activity may be expected in the E-layer. It remains to be shown whether it has an observable value. A third 'wiggle' could be expected at 300–500 km. ($F2$-layer). It will be smoothed out by the large heat conductivity that has been deduced by M. Nicolet[12]. This problem will be discussed in more detail in the following communication[11].

We are grateful to Dr. H. K. Kallmann, who suggested this problem, and to Mr. D. G. King-Hele for discussion of the data of *Discoverer* 6.

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Diurnal and Seasonal Density Variations in the Upper Atmosphere

CONTINUING our earlier investigations[1,2], we have been able to derive the diurnal and seasonal density variations at altitudes of 210, 562 and 660 km. from variations in the acceleration of the satellites 1958δ2 (*Sputnik* 3), 1959α1 (*Vanguard* 2) and 1958β2 (*Vanguard* 1). The computation of atmospheric densities by an iteration process has been described in the preceding communication and will be given in detail in a subsequent publication[3]. The air densities given in Figs. 1–3 are the final values obtained after the last step in the iteration process.

The numerous values of atmospheric density from satellite 1958δ2 were grouped according to their dependence on $\Delta\alpha$ and $\Delta\delta$ respectively since the variations of density are relatively small at 210 km. above the Earth ellipsoid. The differences $\Delta\alpha$ and $\Delta\delta$ are defined by $\Delta\alpha = \alpha_\pi - \alpha_\odot$, $\Delta\delta = \delta_\pi - \delta_\odot$ (where α is right ascension, δ is declination, π is perigee, $\odot$ is Sun).

The diurnal variation of density is a function of $\Delta\alpha$ and thus of true local time. Since during the lifetime of the satellite $\Delta\alpha$ traversed 360° eight times, the group averages of the diurnal variations are taken from different dates within the period May 15, 1958–October 1, 1959. Observations of the last six months of the satellite, during which its perigee traversed the 'wiggle' of the $F1$-layer, were not included in the derivation of the group averages. The seasonal effect is a function of $\Delta\delta$. The group averages are plotted in Fig. 1. The diurnal variation curves for $\Delta\delta = 0°$ and $-40°$ were obtained with the aid of a special adjusting method using all group averages.

The variation of the atmospheric density at 562 km. above the Earth elipsoid is plotted in Fig. 2. These results were obtained from satellite 1959α1, and each

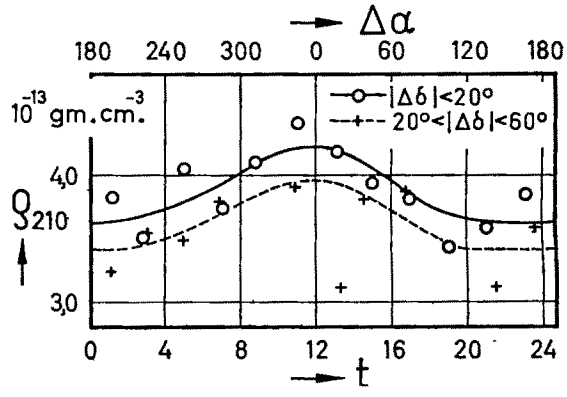

Fig. 1. Diurnal and seasonal variations in atmospheric density at 210 km. derived from observations of the satellite 1958δ2. The lower α-scale gives true local time, the upper $\Delta\alpha = \alpha_\pi - \alpha_\odot$. The parameter of the curves is $\Delta\delta = \delta_\pi - \delta_\odot$, where α is right ascension, δ is declination, π is perigee, $\odot$ is Sun

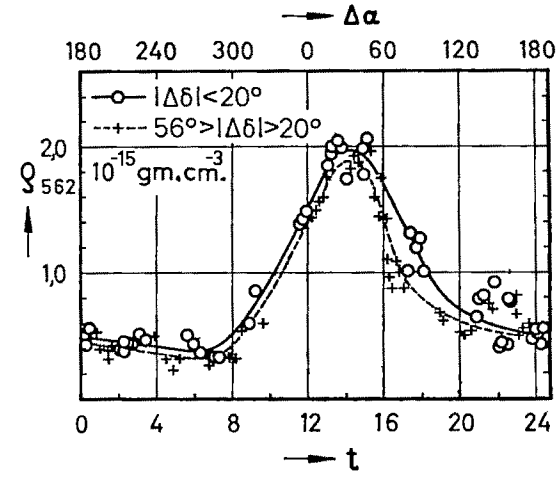

Fig. 2. Variations in atmospheric density at 562 km. above the Earth ellipsoid derived from the observations of satellite 1959α1. Scales as in Fig. 1

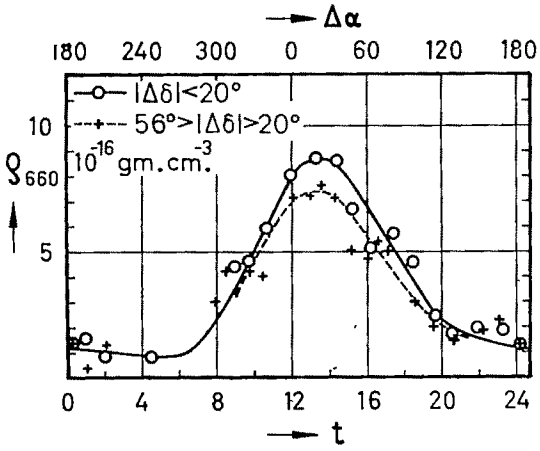

Fig. 3. Variations in atmospheric density at 660 km. derived from the observations of satellite 1958β2. Scales as in Fig. 1

one is plotted. They are derived from the orbital elements of the Smithsonian Astrophysical Observatory and the dP/dt values by L. G. Jacchia[4].

The variation of the atmospheric density at 660 km. was obtained from the orbital elements of the satellite 1958β2 (Fig. 3) (Orbital elements by NASA Computing Center, dP/dt values by L. G. Jacchia[5]). Each dot represents a group average. All diurnal variation curves have similar shapes, especially at high altitudes. The peak of density is reached at about 14 hr. true local time. Then a steep decline follows until sunset. During the night, the density continues to decline though more slowly and almost linearly. After sunrise the curve begins to rise steeply until it reaches its peak.

The amplitude of the variation increases with increasing altitude. Above 300 km. it becomes the most important characteristic of the atmospheric model. In Fig. 4 the variation of atmospheric density is plotted against true local time for the zone $|\Delta\delta| < 20°$. The model was obtained using the curve shown in Fig. 2. This curve was selected because it was obtained from results between February 24, 1959, and March 20, 1960. During this period, the 20-cm. observations obtained by the Heinrich-Hertz-Institut, Berlin-Adlershof, showed no intense drifts of long duration as was the case in 1958. An explanation of the drift in 1958 has not yet been given. M. Nicolet[6] assumes that the drift results from instrumental errors; this means, however, that in order to understand the satellite observations one must postulate an important effect of unknown cause the variation of which corresponds to the variation in the 20-cm. radiation (see also L. G. Jacchia[4]).

The shape of the curves in Figs. 2 and 3 as functions of the position of the Sun (local time) shows clearly that the diurnal variation results from the absorption of electromagnetic radiation (ultra-violet-radiation) and from heat conduction, which is very rapid at high altitudes. The diurnal variations which occur at altitudes higher than 250 km. cannot result from the heating by absorption of the He^+ line 304 Å. at 200 km. because heat conduction is very slow at this altitude. Thus one may conclude that a further absorption of high-energy solar radiation occurs at altitudes 300–500 km., possibly in the $F2$-layer. Because of the rapid heat conduction, no well-developed 'wiggle' is to be expected. The day-time heating simply results in a larger curvature of the logarithmic curve of density. This may be seen in comparing the curvatures above 400 km. for 14 hr. and 6 hr. in Fig. 4. The effect of both heating and heat conduction results in the 'fan shape' of the density model (Fig. 4).

The isothermal atmosphere which is caused by rapid heat conduction begins above 500 km. The temperature there is a function of local time analogous to the density function. One may suppose that the heating results mainly from the absorption of the helium line at 584 Å. at altitudes of 300–500 km. The line was barely detectable at 210 km. according to measurements by H. E. Hinteregger *et al.*[7]. Measurements of the solar ultra-violet radiation and the X-ray spectrum between 300 and 500 km. are urgently needed. At the same time, measurements of the helium content of the upper atmosphere would be highly desirable.

The diurnal variation of density for $|\Delta\delta| \geq 20°$ gives an insufficiently uniform picture. Furthermore, from the above theory we must expect the density to be a function of geographical latitude as well as $\Delta\delta$.

The physical condition in the upper atmosphere may be summarized in the following simplified picture: The 'solar effect' originates in the $F1$-layer as a result of heating by the solar He^+ line at 304 Å. This explains the good correlation between density variations above 200 km. and solar decimetre radiation

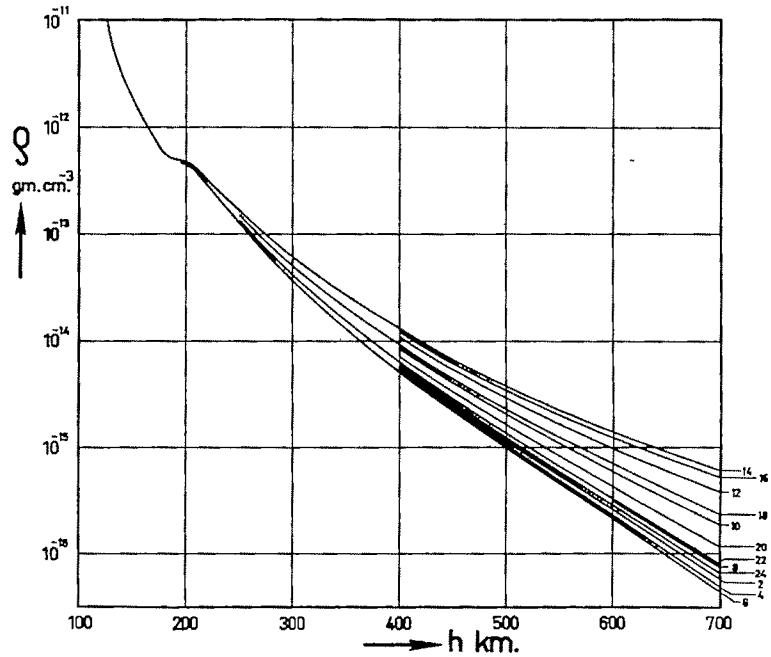

Fig. 4. Diurnal variations of the atmospheric density at altitudes 150–700 km. above the Earth ellipsoid for $|\Delta\delta| < 20°$. All values are corrected to mean solar activity (solar flux of 20-cm. radiation $S = 170 \times 10^{-22}$ W./m.^{2} c./s.). The parameter of the curve gives the true local time. In addition to the satellites mentioned in the text, we used 1958α and 1958ε in computing this atmospheric density model

(3–30 cm.). The period of the density variations agrees largely with the rotational period of the Sun. The heating of the $F1$-layer determines the boundary conditions for the upper atmosphere at 210 km. This explains why the logarithmic curves for density appear to be shifted parallel as a function of 20-cm. radiation (see ref. 1, Fig. 10). The diurnal variation of density at 210 km. is only a few per cent. Absorption of solar electromagnetic radiation in the $F2$-layer together with the large heat conductivity cause the intense diurnal density and temperature variations above 300 km. ('fan shape' of the air density model, Fig. 4).

We gratefully acknowledge the continuing dispatch of 20-cm. data by the Heinrich-Hertz-Institut, Berlin-Adlershof, prior to publication. We are also indebted to Dr. H. K. Paetzold for unpublished dP/dt values of *Sputnik* 3. Furthermore, we wish to thank the Space Track Center and the Smithsonian Astrophysical Observatory for supplying the orbital elements.

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Bonn.
June 27.

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SOME GEOCHEMICAL ASPECTS OF A COLUMBITE-BEARING SODA GRANITE FROM SOUTH-EAST UGANDA

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AS part of the exploratory programme of the Research Institute of African Geology in the University of Leeds, a unique radioactive soda granite from the Lunyo area in south-east Uganda has been investigated. This granite was first recorded and named the Lunyo granite by Dr. K. A. Davies[1], a former director of the Uganda Geological Survey. Late in 1951 a number of specimens of the Lunyo granite were examined in this Institute, and at the request of Dr. Davies a mineral separation was carried out in order to analyse an unusual mica in the granite. The mica was identified as zinnwaldite, rich in lithium and with an exceptionally high fluorine content. During 1956 the concentrates of the Lunyo granite were re-examined, and in addition to the main magnetite and zircon, columbite, cassiterite and thorogummite were found. The discovery of these important accessories prompted a closer investigation of the Lunyo area, and a summary of this work is communicated here.

The general geological configuration of south-east Uganda has been previously described by Davies[1]. Subsequent geological observations have shown that the main rock types occurring within this region can be conveniently correlated with the Nyanzian rocks on the eastern side of Lake Victoria in Kenya. The minimum absolute age for the Nyanzian as deduced from lead isotope determinations in galena is 2,200 ± 150 million years. The rocks of the Nyanzian System are therefore comparable in age with the oldest rocks known from the Precambrian.

The area under discussion lies in the south-easternmost corner of Uganda, bounded by the Kenya border to the east and Lake Victoria to the south. Granitic and dioritic rocks constitute the main geological element, and are seen to be intrusive into remnants of older supracrustal rocks comprising leptites and amphibolites with an east–west trend. The Lunyo granite is exposed in a few separate units occupying a total area of some 10 sq. miles.

The following tentative geological succession has been established in the area: 1, leptites and amphibolites; 2, granodiorites; 3, Lunyo granite; 4, Masaba granite; 5, late doleritic dykes.

The leptites are the metamorphic equivalents of Precambrian acid volcanics, usually of rhyolitic–dacitic composition. Banded structures consisting of coarse- and fine-grained layers suggesting alternating lava and tuff material are frequently seen. Among the leptite varieties there may be both soda and potash extremes, as well as rocks with a silica content greater than 80 per cent. The leptites in this area are generally porphyritic meta-dacites and are dominantly soda-bearing. The highest metamorphism attained corresponds to the amphibolite facies. The volcanic character of these rocks is very apparent and, in places hypabyssal equivalents, either fine-grained felsites or coarser feldspar porphyries, are observed. Some of the leptites have conspicuous corroded phenocrysts of sapphire-blue quartz, a feature which persists over wide areas. Pyrite and pyrrhotine mineralization is widespread among the leptitic rocks.

The meta-rhyolites have been observed only in isolated hills rising above the normal flat terrain. They are extremely siliceous rocks, and in their present metamorphic state resemble fine-grained sericite schists of sedimentary origin; however, some exposures show distinct igneous flow structures, and in thin sections the rocks are seen to contain corroded bipyramidal crystals of quartz. In places, quartzites associated with these latter rocks and especially those which bear andalusite or are interbanded with graphitic shales and hæmatite ore, may well have formed under different conditions, for example,

alternating sedimentation of colloidal silica, clay and iron hydroxides in water.

The amphibolites are either interbanded with the leptites or form separate lenticular bodies. In some parts they occupy larger areas, for example, Bulamba and Isindi hills, and are frequently accompanied by coarse doleritic types. At several exposures pillow structures are developed locally, and some thin sections exhibit distinct flow texture.

The granodiorites form a characteristic group of rocks, and in one case a lenticular body extends for several miles along the southern boundary of the Lunyo granite. The granodiorites consist of lath-shaped crystals of zoned plagioclase, together with larger reddish grains of microcline-perthite, amphibole and smaller amounts of biotite and quartz. Contacts between the granodiorite and the leptites indicate a later emplacement of the former rocks, while pegmatite veinlets which apparently have been derived from the Lunyo granite are seen to intersect both the leptites, amphibolites and the associated granodiorites.

The main type of the Lunyo granite as found in the Lunyo hill area is a leucocratic, medium-grained rock, with a distinct foliation produced by the parallelism of ellipsoidal quartz grains, especially clearly seen on the weathered rock surface.

Observations in the field show, however, considerable variations both in colour and size of grain, and often the granite appears to be porphyritic with large, rounded phenocrysts of quartz, angular porphyroblasts of feldspar and aggregates of mica set in a fine-grained matrix of albite.

Direct contacts with surrounding granites or other rock types have not been observed. In many places within the Lunyo granite, pods and schlieren of greisen are common. These are at times of considerable size and consist mainly of a fine-grained greenish-yellow mica (phengite) with some feldspar, quartz and variable amounts of fluorite. A partly greisenized Lunyo granite contains some 4 per cent fluorite. Pegmatites and aplites are common associates of the granite. Indeed, in places they are so numerous that the rock resembles a veined gneiss. The pegmatites occur as sheets or bands which are either cross-cutting or conformable. They are not uniform in thickness, but pinch and swell to various degrees. Zoning has been observed in some cases, but on the whole is rare. The pegmatites consist chiefly of a coarse-grained white or red microcline-perthite with varying amounts of quartz and fine-grained albite and only occasionally some mica is present. The aplites are intermixed with the pegmatites and are composed of the same minerals, but the soda/potash ratio is much higher. Microscopic examination of the Lunyo granite shows ovoid-shaped grains of quartz with highly undulose extinction and often with inclusions of minute albite laths at times in concentric arrangement. The microcline porphyroblasts almost always contain inclusions of albite, commonly aligned and forming a regular pattern, and stringers of albite in a flame-perthite fashion. Grains of a crypto-perthite, thought to be anorthoclase, also have been noted. Fine-grained albite constitutes the ground-mass, and frequently the laths are seen to be in parallel orientation. Zinnwaldite, which is the main mica of the rock, shows a distinct light-green to blue-grey pleochroism. A dark-green mica is locally present forming spherical aggregates.

The following accessory minerals have been identified so far: magnetite, columbite, cassiterite, zircon, thorogummite, fluorite and pyrite in the granite, and in addition to these betafite, kasolite, galena, zinc-blende and cerussite in the pegmatites. An interesting feature is that both the granite and the associated pegmatites, aplites and greisens contain practically the same rare-mineral assemblages.

The Masaba granite borders the Lunyo granite and the meta-volcanics to the north, east and south. The granite intrudes in the leptites and the amphibolites and forms a contact zone of hybrid rocks which retain many of the textural features of the original volcanics; they also include xenoliths of leptites and amphibolites. There does not appear to be any genetical relationships between this granite and the Lunyo granite proper, and it is perhaps significant that pegmatites are totally absent.

Late dolerite dykes cut all the previous rocks. It is often difficult, however, to distinguish these dykes from older doleritic rocks associated with the amphibolites.

A series of chemical and spectrographic analyses have been made on rocks from the Lunyo area, including various types of the Lunyo granite, aplites, meta-volcanics, granodiorites, amphibolites and other granitic rocks from the surrounding area, and a part of these results is reproduced in Table 1.

The outstanding rocks, from a geochemical point of view, are the Lunyo granite, together with the

Table 1. Chemical Analyses of Rocks from the Lunyo Area and Surroundings, South-east Uganda

	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SiO_2	73 67	73·01	70·79	74·97	73 67	69 33	65·89	84 24	72·35	70·30	68 36	65 98	52 30	50 73
TiO_2	tr.	nil	nil	0·17	0·26	0 48	0·37	0·17	tr.	0·45	0·55	0·39	1 27	1·24
Al_2O_3	15 24	16·14	14·99	12 63	13·57	14·78	15·40	10·16	14 60	13·93	15 59	15 30	15·52	14 09
Fe_2O_3	0·35	1 04	0·08	0·62	0·52	0·64	1·25	0 58	0·73	1·27	0·64	1·05	1·64	6 55
FeO	0·36	0·21	0·53	0·89	1·26	2·63	1·58	0 13	1·16	3 33	2·87	2 65	9·04	6·61
MnO	0 01	0·02	0·06	0·03	0 03	0·05	0·10	tr.	0·02	0 06	0·06	0·06	0·30	0·20
MgO	0·02	tr.	tr.	0·35	0·23	1·30	2 31	0·15	0 10	1·49	1·33	1·39	4·68	6·05
CaO	0·07	0·20	3·47	1·52	0·97	3·50	2·89	tr.	1·44	4·79	2·46	3 05	11·40	10·51
Na_2O	7·04	7·11	3·38	4·15	3 66	4·78	5 05	0·29	5·79	2·60	6·00	5·36	2·47	2 48
K_2O	3·20	1·50	4·26	3·46	5·34	0·77	4·22	3·12	3·01	0·96	0·75	3·15	0·21	0·42
H_2O+	0·07	0·43	0·45	0·66	0·55	1·00	0·56	1·20	0·33	0·75	0·98	0·75	1·08	1·36
H_2O-	0·10	0 17	0·21	0·04	0·09	0 04	0·08	0 08	0·07	0 07	0·05	0·05	0·04	0·08
P_2O_5	tr.	0·13	0 05	0·07	0·12	0 48	0·20	0·08	0·07	0 19	0 13	0·61	0·08	0·14
Total	100·26	99·96	99·52	99·99	100 27	99 78	99 90	100·15	99·96	100·19	99 77	99 98	100·03	100·46

1. Lunyo granite (fresh) from Lunyo hill (Li_2O = 0·13 per cent). 2. Aplite from Nakinu. 3. Fluorite-bearing granite from Namaingo (F = 2·15 per cent; less O ≡ F = 0 90 per cent). 4. Masaba granite near Masaba (CO_2 = 0·43 per cent). 5. Buteba granite from Buteba near Busia. 6. Granite-gneiss (hybrid rock) from Nasigombe. 7. Granodiorite from Bullali. 8. Meta-rhyolite from Siavona hill. 9. Fine-grained porphyry, upper Nalioba (CO_2 = 0·29 per cent). 10. Leptite from Luangosia. 11. Leptite (soda-extreme) from Butenge. 12. Feldspar porphyry from Luangosia (S = 0·30; less O ≡ S = 0 11 per cent). 13. Amphibolite (pillow lava) from Isindi hill. 14. Dolerite from Isindi hill.

Nos. 1 and 4: analysis by O. von Knorring. Nos. 2 and 3: analysis by Mrs. E. Padget. Nos. 5, 8 and 11: analysis by Miss J. R. Baldwin. Nos. 6–7, 9–10, and 12–14: analysis by Mrs. M. H. Kerr.

Table 2. SPECTROGRAPHIC ANALYSES OF ROCKS FROM THE LUNYO AREA AND SURROUNDINGS (IN P.P.M.)
Analysis by Miss J. M. Rooke and Mrs. A. M. Fisher

	Li	Rb	Sr	Ba	Ga	Y	Zr	Pb	V	Nb	Cr	Ni
Lunyo Granite (Fresh)	>1,000	900	<30	<30	65	<30	700	50	<3	350	10	6
Lunyo Granite (Weath)	>1,000	1,000	<30	<30	70	<30	500	5	<3	170	45	10
Aplitic Granite, Bugaya	>1,000	1,300	<30	<30	85	<30	>1,000	400	<3	170	60	35
Aplitic Granite, Buhah	>1,000	1,400	<30	<30	60	<30	>1,000	45	<3	600	40	20
Fluorite Granite, Namaingo	400	1,000	60	40	45	45	>1,000	55	<3	700	40	17
Buteba Granite, Buteba	90	450	85	450	35	<30	170	30	5	<10	75	10
Masaba Granite, Masaba	8	<100	160	1,500	20	<30	130	12	8	<10	10	10
Granite-gneiss, Nasigombe	30	<100	170	200	30	<30	170	13	60	<10	40	30
Leptite, Luangosla	15	<100	100	200	30	<30	160	10	50	<10	130	110
Leptite (soda-extreme), Butenge	25	<100	250	300	30	<30	190	6	75	<10	65	30
Meta-Rhyolite, Siavona	<3	<100	<30	500	25	<30	200	14	<3	<10	45	9
Granodiorite, Buhah	18	<100	>1,000	1,300	30	<30	140	15	90	<10	350	75
Granodiorite, Budidi	40	<100	450	1,100	30	<30	200	16	100	<10	250	60
Fine-grained porphyry, Nahoba	<3	<100	450	1,300	25	<30	95	13	<3	<10	50	5

In all analyses: Be < 3, La < 100, Ge < 30, Ta < 100, Co < 10 and Mo < 3.

allied rocks within its boundaries. The chemical composition of the Lunyo granite, analysis 1, shows some affinities to the metasomatic late-kinematic ideal granites as defined by Eskola[2], providing the alkalis are reversed. Geochemically, there are marked similarities with the Nigerian younger granites, especially with the late suite of albite–riebeckite granites[3].

Among the major constituents, alumina is much higher than in ordinary granites. This is mainly due to the high soda, as there is no corresponding increase in lime. Coupled with the high soda and potash, the sum of the normative feldspars is more than 70 per cent, while the albite component is approximately 60 per cent. The cafemics are exceptionally low, and usually amount to less than 1 per cent.

Among the minor elements, lithium and rubidium are comparatively high. Spectrographic estimates of lithium and rubidium indicate that the amounts of these constituents are higher than is usual for granitic rocks, apart from those of the pegmatitic phase. Lithium is contained in zinnwaldite and other micas, and rubidium is concentrated mainly in the microcline–perthite of the pegmatites, where the rubidium content is approximately 1 per cent. Fluorine is constantly present and is abundant in the fluorite-bearing granite. In the Lunyo granite most of the fluorine is accommodated in the zinnwaldite, which carries 8 per cent fluorine. The content of beryllium is low and beryl has not been met with in the pegmatites of the area. Lead and zinc are distinctive trace elements of this complex and both are represented by independent minerals: galena, sphalerite (yellowish-green in colour), cerussite, kasolite (a lead–uranium–silicate) and an unidentified lead–uranium mineral. All these minerals have been introduced during a late stage and at relatively low temperatures. There is a much lower concentration of the rare earths as compared with the Nigerian province; consequently monazite and xenotime have not been found. The content of the trivalent gallium, however, is greater than average. Zirconium, tin and thorium are represented by the accessories zircon, cassiterite and thorogummite. The latter mineral is found in various stages of alteration and may be green, yellow, orange or brown in colour. The titanium content is exceptionally low and no independent titanium minerals have been noted. The high niobium content is a characteristic feature of the Lunyo granite and its associated pegmatites, aplites and greisens. In the granite itself the niobium content in terms of columbite varies from 0·05 to 0·1 per cent, in the greisens there is approximately 0·1 to 0·2 per cent, and in the aplites and pegmatites the columbite may be as high as 0·5 per cent. These columbite values are comparable with those of the Nigerian younger granites[4]. The Nb_2O_5/Ta_2O_5 ratio is about 13 to 1. Another niobium mineral, betafite, has been identified from various pegmatites.

In addition to the conspicuous deficiency of titanium, there is also an apparent lack of boron and phosphorus. Tourmaline and apatite appear to be absent in the Lunyo granite and its associates, and even the greisens are devoid of these minerals.

When the values for trace elements of the Lunyo granitic suite are compared with those of the surrounding rocks, the former show a completely distinct geochemical pattern (Table 2).

The characteristic textural features of the Lunyo granite, together with its position within the belt of porphyritic volcanics, strongly suggest some genetic relationship with the latter rocks. The granite is considered to have been formed by metasomatic granitization of soda-rich volcanics of the Butenge type, and the unique mineralization involving lithium, fluorine, zinc, lead, zirconium, tin, thorium, niobium and uranium in the form of accessory minerals is believed to be connected with the granitization process. The metasomatism appears to have involved little addition of soda, but potash was certainly introduced, particularly during the later stages of granitization now marked by the dominantly microcline-rich pegmatites and micaceous greisens.

The Lunyo granite, together with its pegmatites, aplites and greisens, are distinctly radioactive over large areas. The main cause of this radioactivity was initially attributed to the accessory thorogummite, but recent observations have shown that, among the accessory minerals, kasolite and betafite are of common occurrence and thus contribute to the radioactivity. A sympathetic relationship seems to exist between the important minor accessories and the radioactivity observed. Thus higher radioactivity not only denotes an increase in radioactive minerals but also indicates higher concentrations of columbite.

This work has been undertaken in close collaboration with the Geological Survey of Uganda. I am indebted to Mr. A. Cawley, director of the Geological Survey, for his assistance during field-work and permission to publish this communication.

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ULTRASONIC DEGRADATION OF WOOL AND HAIR

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ULTRASONIC vibrations have been used for the disruption of cells[1], micro-organisms[2], and for the modification of soluble proteins and amino-acids[3-5]. The evidence on wool is conflicting, since it has been reported that virgin wool is not degraded by ultrasonics[6,7], although shrink-proofing can be effected by this means[8], and Andrews[9] has since found that cuticular material is liberated. Because of the need for a purely mechanical method of degradation of the fibre (other than the laborious method recently developed[10,11]), it was decided to investigate this possibility. It is reported here that wool and hair can be degraded mechanically by ultrasonic treatment, with no appreciable amount of chemical attack, into cuticle material and cortical cells.

Two different types of ultrasonic instruments were used. The first was a 60-watt, *MSE*-Mullard ultrasonic disintegrator in which waves of 16–24 kc./s. were transmitted by a ¾-in. diameter stainless steel probe immersed directly in the solution containing the sample. Samples of wool and hair (0·05–1 gm.) were treated at < 35° about 1–4 cm. below the probe, which disintegrated slowly in aqueous solutions. The second was a 60-watt, Narda Ultrasonics Corporation, Sonblaster, series 600, in which the contents of a 3-litre capacity stainless steel tank were treated with ultrasonics at 40 kc./s. Samples of up to 10 gm. of wool and hair were treated in about 1-litre of solution which was kept at < 30° by a cooling coil.

After treatment the residual fibres were dried, snippets were cut in a representative manner and mounted in 'Sellotape'[12,13]. These were examined under the microscope and ≮ 200 classified into four different groups as follows: (0) scales undamaged, (1) slight removal of scale edges, (2) considerable removal of scale edges, (3) complete removal of scale edges. The percentage of fibres in each category was multiplied by the number in brackets and the figures summed to give a weighted total indicative of damage to the cuticle.

The milky solution obtained after treatment was centrifuged, and if the Mullard instrument had been used, metal particles were sedimented by centrifugation in 2 *M* potassium dihydrogen phosphate, 2 *M* dipotassium hydrogen phosphate solution while the protein remained suspended. The latter was weighed, examined microscopically and in a few cases amino-acid analyses were carried out by the dinitrophenylation method[11].

Samples of virgin wool ranging from Merino 90's to Lincoln 36's, and human hair were cleaned[14] and 3-gm. samples treated in the Sonblaster for 16 hr. in 500 ml. distilled water. A yield of 0·6 per cent of degraded material was obtained from each of the four samples of wool and 1·5 per cent from the human hair. The material from wool and hair consisted of about 90 per cent of small flat pieces of cuticle material and about 10 per cent of needle-like cells of sizes up to that of cortical cells. The treated fibres were examined microscopically and there was a gradation from no apparent damage with Merino 90's to a value of 62 for Lincoln 36's and 103 for human hair. This would be expected in view of the progressive decrease in the surface area to weight ratio of the fibres in this series. It is not clear why the cuticle of human hair breaks down more rapidly than that of wool, particularly as the former overlap along about 5/6 of their length compared with only about 1/6 for Lincoln wool[15].

Three-gm. samples of Lincoln 36's top were treated for 2 hr. in the Sonblaster in 500 ml. of solutions buffered at *p*H 1, 3, 5, 7, 9 and 11. The percentage yields of degraded material were 0·1, 0·1, 0·2, 0·4, 0·6 and 0·6 respectively. The rate of breakdown was not increased by treatment in concentrated ammonia or hydrazine hydrate but was rapid in 0·1 *N* sodium hydroxide, with considerable chemical degradation of the wool. Treatment in aqueous solutions of lithium bromide (100 per cent w/v), guanidine hydrochloride (50 per cent w/v), urea (sat.) or glacial acetic acid, dichloroacetic acid, formamide or dimethyl formamide produced only small changes in the amount of breakdown, but there was a large increase in 98 per cent formic acid. Breakdown was slight in organic solvents such as *n*-butanol, ethanol and a petroleum fraction, b.p. 150–200°.

Samples of Lincoln 36's top chemically modified by acid chlorination, hydrogen peroxide, reduction with sodium hydrogen sulphite or treatment with alcoholic sodium hydroxide showed no greater rate of ultrasonic breakdown during 24-hr. treatment in water using the Mullard instrument than the untreated top. Also wool from the tip of the fibre showed no difference in behaviour from that taken from the base.

Two samples of human hair treated for 4 hr. and 40 hr. in the Mullard instrument in water produced material in about 0·3 and 4 per cent yields respectively. On amino-acid analysis[11] it was found that the latter sample contained more Arg (26 per cent) Cys (29 per cent) and less Gly (19 per cent) than the former, but both were entirely proteinous. The differences may be due to the continuous mechanical degradation of the fibre, producing material of a continuously changing composition, and/or chemical degradation of the material. This point was resolved by amino-acid analyses on a finely powdered sample of Lincoln 36's top (obtained by grinding in a pestle and mortar under liquid oxygen) before and after a 40-hr. ultrasonic treatment as above. There was no detectable change in the amino-acid content after the ultrasonic treatment, hence the amount of chemical degradation was negligibly small.

The ultrasonic method should make possible a much more detailed investigation of the chemical composition and structure of the various cuticle layers of virgin and treated wools than has been possible by the descaling method[11] or by methods based on chemical degradation of the cuticle. It should also be possible to probe deeper into the wool fibre and separate chemically unchanged cortical cells for detailed investigation.

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BIAS IN BASE-PAIR ORIENTATION IN DEOXYRIBONUCLEIC ACID

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A COMPLEMENTARY base-pair within a double-helical deoxyribonucleic acid molecule may be oriented in one of two ways. This article reports the finding of a relatively uniform bias in the orientation of the adenine–thymine complementary base-pair in human deoxyribonucleic acid.

KB cells[1] were cultured in the presence of 5-bromodeoxyuridine together with 5-fluorodeoxyuridine and uridine for 48 hr. at 36° C. Under these conditions a fraction of the cells undergo a single replication-cycle of their deoxyribonucleic acid[2]. Since 5-fluorodeoxyuridine blocks the endogenous synthesis of the deoxyribonucleic acid thymine precursor, thymidylic acid[3], all the newly synthesized deoxyribonucleic acid strands contained 5-bromouracil in the place of thymine. The cæsium chloride density gradient analysis[4] of the deoxyribonucleic acid from these cells revealed two bands of the acid (Fig. 1). The less-dense band (modal density = 1·702 gm.cm.$^{-3}$) consists of unreplicated deoxyribonucleic acid molecules (that is, 'parental' acid) The more dense bimodal band (inter-modal density = 1·758 gm.cm.$^{-3}$) comprises those molecules of deoxyribonucleic acid which have engaged in one cycle of replication in the presence of 5-bromodeoxyuridine, and thus contain density-increasing 5-bromouracil instead of thymine in their newly synthesized strands They are 'hybrid' molecules with respect to their 5-bromouracil content. It is proposed that the bimodality of the hybrid deoxyribonucleic acid band arises from a uniform bias in the orientation of the adenine–thymine complementary base pair in most of, if not all, the deoxyribonucleic acid molecules in the cell complement.

By scoring the two possible orientations of a particular base-pair as + 1 and − 1, respectively, along a deoxyribonucleic acid molecule, the bias (β) for that base-pair is defined as the absolute value of the mean score for the molecule. Obviously, $0 \leqslant \beta \leqslant 1$.

The 5-bromouracil content of the two hybrid progeny molecules derived from a single replication in 5-fluorodeoxyuridine–5-bromodeoxyuridine of a molecule of deoxyribonucleic acid, will be different when it possesses an adenine–thymine bias greater than zero, providing the replication is semi-conservative[5–7]. Then the two hybrid molecules will have different buoyant densities.

Similarly, the 5-bromouracil hybrid progeny molecules derived from the semi-conservative replication of a population of deoxyribonucleic acid molecules of heterogeneous base composition, but possessing a uniform adenine–thymine bias, will consist of two equal sub-populations differing in their mean 5-bromouracil content and hence differing in their mean buoyant density.

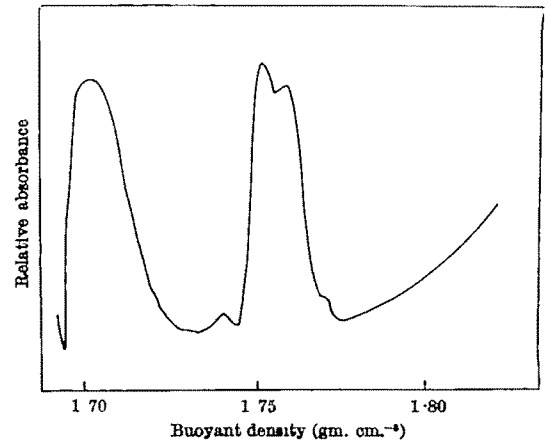

Fig. 1. Spinco 'Analytrol' trace from an ultra-violet absorption photograph of the deoxyribonucleic acid concentration distribution obtained from human *KB* cells. Cells were cultured for 48 hr. in lactalbumin hydrolysate–Earle's saline with 15 per cent heat-inactivated human serum, containing 6×10^{-5} *M* 5-bromodeoxyuridine, 10^{-4} *M* 5-fluorodeoxyuridine and 10^{-4} *M* uridine. Cells were lysed by adding 0·05 ml. of 20 per cent aqueous sodium dodecyl sulphate to 3×10^{8} cells in 1 ml. of physiological saline *p*H 8·5 and 0·01 *M* in ethylenediaminetetracetic acid. A 0·5 ml. aliquot of this lysate made up to 57·7 per cent (w/w) with respect to cæsium chloride, and centrifuged at 20° C. for 22·5 hr. at 44,770 r.p.m. The density gradient was 0·122 gm.cm.$^{-4}$.

The mean buoyant density of the parental population (ρ_P) may be written in terms of mean base composition as:

$$\rho_P = \rho_0 + k_1 r_{GC} \text{ gm.cm.}^{-3}$$

where ρ_0 is the intercept at $r_{GC} = 0$, and r_{GC} is the mean molar ratio of guanine–cytosine, and k_1 is the density increment for the total substitution of adenine–thymine by guanine–cytosine.

Similarly, since the substitution of thymine by 5-bromouracil leads to a linear change in buoyant density[4], the mean buoyant density of each population of hybrid progeny molecules (ρ_{H_I} and $\rho_{H_{II}}$) may be written as:

$$\rho_{H_I} = \rho_p + k_2\left(\frac{1+\beta}{2}\right)(1 - r_{GC})\alpha \text{ gm cm.}^{-3}$$

and:

$$\rho_{H_{II}} = \rho_p + k_2\left(\frac{1-\beta}{2}\right)(1 - r_{GC})\alpha \text{ gm.cm.}^{-3}$$

where k_2 is the density increment for total substitution of thymine by 5-bromouracil, β is the adenine–thymine bias and α the proportion of available thymine sites occupied by 5-bromouracil (here α is assumed to be 1). From the above equations adenine–thymine bias may be evaluated as:

$$\beta = \frac{\rho_{H_I} - \rho_{H_{II}}}{k_2(1 - r_{GC})\alpha}$$

For ease of computation the mode rather than the mean values of buoyant density and guanine–cytosine content were chosen to estimate the adenine–thymine bias of human *KB* cell deoxyribonucleic acid. Substituting 0·184 gm.cm.$^{-3}$ for k_2, 0·39 for r_{GC}, and 0·007 gm.cm.$^{-3}$ for the difference in density between the two modes of the hybrid deoxyribonucleic acid band, one obtains 0·06 as an estimate of the adenine–thymine bias.

In each hybrid sub-population, the uniform incorporation of density-increasing 5-bromouracil is expected to decrease the buoyant density heterogeneity due to variation in guanine–cytosine content. The expected transformation factors (γ_I and γ_{II}) relating guanine–cytosine content to buoyant density for the two hybrid sub-populations (H_I and H_{II}) are respectively:

$$\gamma_I = 1 - \frac{(1+\beta)k_2\alpha}{2k_1}$$

and:

$$\gamma_{II} = 1 - \frac{(1-\beta)k_2\alpha}{2k_1}$$

For this experiment $\gamma_I = 0{\cdot}02$ and $\gamma_{II} = 0{\cdot}14$, using $k_1 = 0{\cdot}100$ as given by Rolfe and Meselson[8].

The variance of buoyant density in the parental deoxyribonucleic acid (σ_p^2) may be written as:

$$\sigma_p^2 = \sigma_T^2 + \sigma_D^2$$

where σ_T^2 is the variance due to thermal motion and σ_D^2 is the variance due to heterogeneity of base composition[10]. Similarly the expected variance of each hybrid sub-population can be written as:

$$\sigma_{H_I}^2 = \sigma_T^2 + \gamma_I^2\sigma_D^2$$

and:

$$\sigma_{H_{II}}^2 = \sigma_T^2 + \gamma_{II}^2\sigma_D^2$$

The expected variance of the hybrid distribution is therefore:

$$\sigma^2_{[H_I + H_{II}]} = \sigma_T^2 + \left(\frac{\gamma_I^2 + \gamma_{II}^2}{2}\right)\sigma_D^2 + \left(\frac{\rho_{H_I} - \rho_{H_{II}}}{2}\right)^2$$

From Fig. 1 it can be clearly see that the variances of the hybrid sub-population would each be less than the variance of the parental deoxyribonucleic acid band, as one would expect.

The inequality of the modal concentrations of the hybrid deoxyribonucleic acid where the major mode is on the low-density side of the distribution is expected if the less-dense hybrid sub-population (H_{II}) has a γ_{II} value less than γ_I. This would imply a mean γ value less than 0. These expectations do not agree with the calculated values of $\gamma_I = 0{\cdot}02$ and $\gamma_{II} = 0{\cdot}14$. The discrepancy may arise entirely from the gratuitous assumption that the molecular volume is not affected by 5-bromouracil substitution. Indeed, the observed k_2 value (0·184 gm.cm.$^{-3}$) exceeds the k_2 value (0·121 gm.cm.$^{-3}$) expected from the mass increment due to 5-bromouracil substitution, assuming no change in molecular volume. Thus the appropriate k_1 value for computing the γ values may well be less than 0·100 gm.cm.$^{-3}$.

Further studies have been made with the *KB* cell system using aminopterin instead of 5-fluorodeoxyuridine to block endogenous thymidylic acid synthesis[2] and with HeLa cells using the 5-fluorodeoxyuridine-5-bromodeoxyuridine system. Bimodal distributions of the hybrid deoxyribonucleic acid were obtained in each case, confirming the postulate that human deoxyribonucleic acid contains a uniform bias in the orientation of its adenine–thymine base-pairs.

A more detailed account of this work will be published elsewhere.

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CORRELATION OF VIRAL RIBONUCLEIC ACID AND PROTEIN COMPOSITION

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In 1952 Dounce[1] suggested that the sequence of nucleotides in nucleic acid constitutes a code which determines the sequence of amino-acids in proteins. He did not, however, draw any conclusions as to how such a code could be deciphered. In 1954, without knowledge of Dounce's suggestion, Gamow[2] made a similar proposal, and pointed out that information on sequences of amino-acid might make it possible to determine the nature of the code, using elementary cryptographic methods.

About this time considerable information on amino-acid sequences of proteins became available. Numerous efforts were therefore made, mainly by Gamow and his collaborators, to solve the coding problem. These efforts failed[3]. It was found that all proposed solutions were either incompatible with known amino-acid sequences or were not subject to test by evidence then available.

The reason for this failure became clear as information on amino-acid sequences accumulated. Gamow's

original proposal assumed that enough information is available in nucleic acid to determine completely the amino-acid sequence in the corresponding protein. Since there are 20 kinds of amino-acids and only four nucleotides, at least three nucleotides would be needed to specify each amino-acid. As the nucleic acid was visualized to act as a template in protein formation, it was felt that there should not be too great a disparity in length between the nucleic acid and the protein produced. It was therefore assumed that neighbouring configurations of nucleotides, each determining an amino-acid, shared some of their nucleotides, and this, of course, would produce restrictions on possible sequences of amino-acids. 'Decoding' consisted, essentially, of a search for such restrictions, from which the nature of the code could be deduced. Unfortunately, as more amino-acid sequences were published, it was found that there were no restrictions, either absolute or statistical, on which amino-acid could neighbour one another[3]. It was therefore concluded that amino-acid determinants were not configurations of overlapping nucleotides[4]; but no further progress in decoding was possible by the method proposed by Gamow.

These negative results do not necessarily imply that all forms of the coding hypothesis are false, but do suggest the need for developing criteria other than those used by Gamow and his collaborators. It is my purpose to point out that information already available provides evidence on the type of code carried by ribonucleic acid. In what follows, only the 'non-overlapping' types of codes will be discussed.

The most obvious and reliable method of determining the nature of the code would be inspection of sufficiently long sequences of ribonucleic acid and the corresponding protein. The nearest approach to this is provided by the ribonucleic acid viruses, the ribonucleic acid of which apparently codes a single molecular species of protein[5]. As information is available on the approximate compositions of viral proteins and ribonucleic acids the problem is to determine what correlation exists between their compositions, and if such a correlation is found, to deduce the nature of the code. It is possible, of course, that a significant part of the ribonucleic acid has some other, non-coding, function, in which case its composition would bear no necessary relation to viral protein. Demonstration of a correlation would indicate the absence of such a fraction.

To correlate the change in ribonucleic acid associated with change in protein, it is first necessary to define a suitable quantitative measure of the amount of difference between two proteins or ribonucleic acids. This is the molar difference or change Δ_a which is defined as $\frac{1}{2}\,\Sigma|D_a|$, one half the sum of the absolute values of the differences between the quantities, expressed as moles per cent, of corresponding amino-acids in two proteins. The analogous molar difference for ribonucleic acid Δ_n is $\frac{1}{2}\,\Sigma|D_n|$. The reason for choosing these quantities is that they express how many mole fractions of residues in a protein (or ribonucleic acid) have to be replaced by others to obtain a second protein (or ribonucleic acid) of specified composition. Since the unit used is the mole fraction, valid estimates of compositional differences can be made even if the molecular weights are different.

The initial problem is to determine the 'coding ratio' n, or the number of nucleotides required to specify an amino-acid. Since the molar differences between ribonucleic acids or proteins are experimentally determinable quantities, it is useful to consider what relation their ratio Δ_n/Δ_a, which will be referred to as r, bears to the coding ratio n. The nature of this relation can be seen from the following considerations.

Let each amino-acid be determined by n nucleotides. If a protein consists of k residues, the corresponding ribonucleic acid will have nk nucleotides. Each configuration of n nucleotides will then be the same mole fraction of ribonucleic acid as each amino-acid residue is of the protein. If a single amino-acid is replaced by another, the corresponding nucleotide configuration is also replaced, and the molar change in protein will then be the same as the molar change in ribonucleic acid, using nucleotide configurations as a unit. What can be observed, however, are variations in the quantities of individual nucleotides, and the observable molar change in ribonucleic acid will therefore depend on the compositions of the nucleotide configurations which replace each other. For example, a nucleotide configuration Ad-Ad-Ad* could be replaced by Gu-Gu-Gu. In such a case the molar change in ribonucleic acid will be the same as the molar change in protein, $r = 1$. If Ad-Ad-Ad is replaced by Ad-Ad-Gu, $r = 1/3$. A configuration Ad-Gu-Cy could also be replaced by Cy-Gu-Ad, in which case $r = 0$.

Therefore, if one considers a single amino-acid replacement, r can range from 0 to 1; but if the coding hypothesis is correct r cannot exceed 1, and can be 1 only if the amino-acids which replace each other are determined by configurations which have no nucleotides in common. Configurations which have this property will be referred to as 'nucleotide-exclusive' sets. (Examples of such sets would be triplets Ad-Ad-Ad, Gu-Gu-Gu, nucleotide exclusive with respect to Cy-Cy-Cy, Ur-Ur-Ur, or Ad-Ad-Gu with respect to Ur-Cy-Cy.)

The situation is modified if one considers a change in protein involving several different residues. In such a case, r could be 1 only if the configurations in a ribonucleic acid molecule as a group were a nucleotide-exclusive set with respect to the configurations replacing them in the second ribonucleic acid molecule. There is a maximum of four such configurations, so that if five or more amino-acids differ in the two proteins r must be less than 1. This is assuming, of course, that each amino-acid corresponds to a different nucleotide configuration. Usually a random set of configurations would tend to have an overall composition rather similar to most other random sets which would replace them, so that r would tend to be of the order of $1/n$ or less, the exact value depending on the compositions of the nucleotide configurations involved.

It is now possible to consider the experimental evidence, consisting of data on six ribonucleic acid viruses (Table 1). From the foregoing, it will be evident that maximal but not minimal values of r are of interest, and therefore proteins and ribonucleic acids of other viruses are compared to turnip yellow virus, the ribonucleic acid of which differs radically from the others. Molar differences for protein and ribonucleic acid are calculated on this basis.

The ratio of molar difference in ribonucleic acid to molar difference in protein, taking turnip yellow virus as a standard, has the following values: southern bean mosaic virus, 0·90; tomato bushy stunt virus, 0·75; cucumber virus, 0·66; tobacco mosaic virus, 0·83; and poliovirus 1·09. Two of these ratios, for southern bean mosaic virus and poliovirus, are close to 1, the maximum possible if the coding hypothesis

Table 1. Composition in Moles per cent of Viral Ribonucleic Acid and Protein

	SBM(6)	D_a	TBS(7)	D_a	CV(8)	D_a	TMV(5)	D_a	PV(9)	D_a	TY*
ALA	7·7	0·3	8·5	1·1	9·0	1·6	9·2	1·8	7·8	0·4	7·4
ARG	6·4	4·8	5·8	3·7	7·0	5·4	6·7	5·1	4·7	3·1	1·6
ASX	7·3	2·2	11·1	6·0	12·9	7·8	11·6	6·5	11·9	6·8	5·1
CYS	0·9	1·6	0·8	1·7	0·0	2·5	0·6	1·9	0·8	1·7	2·5
GLX	6·8	0·3	5·7	1·4	5·8	1·3	10·4	3·3	7·7	0·6	7·1
GLY	9·0	4·7	8·6	4·3	2·6	1·7	3·7	0·6	6·8	3·1	4·3
HIS	1·3	0·1	1·2	0·2	0·0	1·4	0·0	1·4	2·4	1·0	1·4
ILEU	6·0	2·2	3·3	4·9	4·6	3·6	5·5	2·7	4·8	3·4	8·2
LEU	8·5	0·0	10·9	2·4	9·4	0·9	7·9	0·6	8·5	0·0	8·5
LYS	3·0	3·4	3·4	3·0	2·1	4·3	1·2	5·2	4·7	1·7	6·4
MET	2·6	0·6	0·8	1·2	0·0	2·0	0·0	2·0	1·5	0·5	2·0
PHE	3·4	0·7	3·6	0·9	7·8	5·1	4·8	2·2	4·4	1·7	2·7
PRO	4·7	6·9	3·9	7·7	6·5	5·1	4·8	6·7	7·2	4·4	11·6
SER	9·0	0·7	8·6	0·3	11·7	3·4	11·0	2·7	7·0	1·3	8·3
THR	12·4	1·2	11·0	2·6	7·7	5·9	10·4	3·2	9·1	4·5	13·6
TRY	—	—	0·5	0·2	0·3	0·4	1·2	0·5	—	—	0·7
TYR	4·3	2·8	2·8	1·3	2·7	1·2	2·4	0·9	3·9	2·4	1·5
VAL	6·8	0·6	10·0	2·6	10·0	2·6	8·5	1·1	7·2	0·2	7·4
Δ_a		16·6		22·8		28·1		24·2		18·4	

	RNA (12)	C	RNA (12)	C	RNA (12)	C	RNA†	C	RNA (17)	C	RNA (12)	C
AD	26	28	28	29	26	26	29	28	30	27	23	23
CY	23	24	21	20	19	16	19	17	19	23	38	36
GU	26	25	28	27	26	29	26	27	26	24	17	18
UR	25	24	25	24	30	29	27	28	27	26	22	23
Δ_a	15		17		19		20		20			

D_a—difference in amino-acid composition between protein of specified virus and turnip yellow virus protein. C—Ribonucleic acid composition computed from amino-acid composition. The sums of amino-acids and nucleotides deviate slightly in some cases from 100, due to rounding off of all numbers to two places.

* Mean values from (10) and (11).

† Mean of four determinations (13, 14, 15, 16).

RNA, ribonucleic acid; SBM, southern bean mosaic virus; TBS, tomato bushy stunt virus, CV, cucumber virus; TMV, tobacco mosaic virus, PV, poliovirus; TY, turnip yellow virus.

is correct. If $r = 1$ this implies that all amino-acids differing between two viruses are determined by configurations which are nucleotide-exclusive as between the two ribonucleic acids. Now as the molar difference between the ribonucleic acids of turnip yellow virus and poliovirus and southern bean mosaic virus is due entirely to a large excess of cytidylic acid in turnip yellow virus, and this excess is quantitatively about the same as the molar difference between the proteins, it follows that all, or virtually all, amino-acids which are more abundant in turnip yellow virus protein than in the proteins of southern bean mosaic virus and poliovirus must be determined exclusively by cytidylic acid. At least four amino-acids (*iso*leucine, lysine, proline and threonine) are significantly more abundant in turnip yellow virus than in either southern bean mosaic virus or poliovirus. It would thus appear that more than one amino-acid must be determined by configurations of nucleotides containing only cytidylic acid. This is an unexpected result as it suggests that the coding ratio may be 1, and that viral ribonucleic acid does not carry sufficient information to specify the viral protein completely.

Once a coding ratio of 1 is suggested, there is available a method, quite independent of any of the above arguments, for testing the validity of the proposal, the 'assignment test'. It should be possible to assign to each amino-acid a nucleotide in such a way that the composition of the corresponding ribonucleic acid can be calculated from the composition of the protein. This test is the more stringent as the number of ribonucleic acid-protein pairs increases. Failure to meet this test is, of course, a telling argument against the hypothesis.

The following assignments are suggested: Adenylic acid; glutamic acid, glutamine, glycine, leucine, phenylalanine and tryptophan. Cytidylic acid; cysteine, lysine, methionine, proline, and threonine. Uridylic acid; aspartic acid, asparagine, *iso*leucine, histidine, and serine. Guanylic acid; alanine, arginine, tyrosine, and valine. The sum of amino-acids in each group is the predicted mole fraction of the corresponding nucleotide in the ribonucleic acid, shown in Table 1. In spite of the fact that the compositions of ribonucleic acid and protein of most viruses are only approximately known, concordance of the calculated and experimentally determined abundance of nucleotides in ribonucleic acid is good (Table 1). The Bravais–Pearson coefficient of correlation is 0·92 ($N = 24$), a very significant value. So far as the available evidence goes, the assignment test supports the hypothesis.

In assessing the validity of the proposed amino-acid–nucleotide assignments two sources of possible error should be considered. All the viruses in Table 1, other than turnip yellow virus, are of rather similar composition, and the objection can be raised that the correlation is merely between these viruses as a group and turnip yellow virus, effectively involving only two rather than six independent sets of determinations. That this is not the case, however, is shown by calculating the correlation coefficient without the data from turnip yellow virus, which is 0·87 ($N = 20$) still highly significant. Concordance of the predicted and determined ribonucleic acid composition is therefore still good within this group of similar viruses, although the range of variation is less.

A second, more serious, objection is that from the nature of the case the assignments of amino-acids to nucleotides are selected to give a good correlation, and that the concordance is therefore artificial. This objection is of course quite valid when only one or two cases are considered. But the probability that such a selection will be possible, when no real correlation exists, falls sharply as the number of cases increases. It is indeed a merit of the proposed hypothesis that it can be readily tested by refining analyses and applying them to viruses not yet investigated. So far only the composition of tobacco mosaic virus has been determined with the accuracy modern methods allow.

If the coding ratio of 1 is supported by further data it will be evident that viral ribonucleic acid does not carry all the information required to specify the corresponding protein, and the virus must be considered a joint product of both viral ribonucleic acid and the host. Nothing now known contradicts such a possibility.

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Note added in proof. A recent more extensive redetermination of the composition of poliovirus ribonucleic acid[18] gave Ad, 0·285; Cy, 0·220; Gu, 0·240; Ur, 0·253, which is in much better agreement with the predicted ribonucleic acid composition than the earlier results quoted in Table 1. The coefficient of correlation between predicted and found ribonucleic acid composition for all viruses, using these new data, is 0·95.

*The following abbreviations are used. Ad, Cy, Gu, Ur—adenylic, cytidylic, guanylic and uridylic acids respectively. Amino-acid abbreviations as in ref. 3.

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HÆMOGLOBIN DIFFERENCES IN INBRED STRAINS OF MICE

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THE existence of genetically determined differences in the electrophoretic patterns of hæmoglobin of inbred strains of mice has been reported previously[1,2]. When filter paper[1,2] or starch granules[3] were used as supporting media for zone electrophoretic analyses in veronal buffer *p*H 8·6, two types of hæmoglobin pattern were seen: type 1, also called 'single', was a homogeneous single hæmoglobin, and type 2, also called 'diffuse', contained at least two components, an electrophoretically rapid one with mobility comparable to that of type 1, and a quantitatively smaller electrophoretically slower component. These hæmoglobin patterns appeared to be controlled by a pair of alleles, Hb^1 and Hb^2. Of eleven strains of mice tested, three showed the type 1 pattern only, five the type 2 pattern and three strains segregated for both. The hæmoglobin of mice of the F_1 generation, from crosses of type 1 with type 2 resembled, on electrophoresis, the pigment of the type 2 parent. Recently hæmoglobin differences have been demonstrated in different inbred strains of mice with various electrophoretic methods, for example, starch granules[3], starch gels[4] and agar gels[5].

That the relationship between hæmoglobin genes and hæmoglobin types in the mouse was perhaps more complex than assumed originally was suggested by the observation of five different hæmoglobin bands in the work of Rosa *et al.*[4], who used starch-gel electrophoresis. For this reason two observations made in the course of our work on mouse hæmoglobin seemed to require further investigation:

(1) Aqueous solutions of carbonmonoxyhæmoglobin from mice of the *DBA* strain with hæmoglobin type 2 developed a precipitate on prolonged standing at 4° C. whereas no such precipitate developed in hæmoglobin solutions from mice of the Kink strain with hæmoglobin type 1.

(2) Different mice of the *DBA* strain with hæmoglobin type 2 as well as of the F_1 generation from crosses of *DBA* × Kink (resembling hæmoglobin type 2) showed great variability in the amount of the electrophoretically slow component of the diffuse type 2 hæmoglobin.

The present work was an attempt to investigate further these two observations and their possible relationship to the presence of several hæmoglobin bands in certain mice as reported by Rosa *et al.*[4].

Blood was obtained by cardiac puncture of anæsthetized mice, and hæmoglobin was prepared by the method of Drabkin[6]. Oxyhæmoglobin was prepared for solubility studies, and carbonmonoxyhæmoglobin was used for electrophoretic and ultracentrifugal analyses.

The appearance of a precipitate in stored hæmoglobin solutions from *DBA* and F_1 mice and the absence of precipitation in stored Kink hæmoglobin suggested that the two hæmoglobins might differ in solubility. Therefore solubility studies were carried out using a modification of Itano's[7] method. In 3·17 *M* phosphate buffer, and sodium hydrosulphite, Kink hæmoglobin was more soluble (Table 1) than *DBA* hæmoglobin; a value approximately intermediate between these two was obtained for F_1 hæmoglobin.

Starch-gel electrophoresis of carbonmonoxyhæmoglobin was carried out on horizontal and vertical gels

Table 1 SOLUBILITY OF HÆMOGLOBIN OF INBRED MICE IN 3·17 *M* PHOSPHATE BUFFER, *p*H 7·2

Strain	Amount Hb added* O.D.	Amount Hb soluble O.D.
DBA/1	0·335	0·164
Kink	0·335	0·262

* These values were obtained by recording the optical density of the hæmoglobin in 2·5 molar phosphate buffer and hydrosulphite[7]; no precipitation occurred under these conditions

according to the methods of Smithies[8,9], within one week after bleeding the animals. This analysis of hæmoglobin of Kink mice (type 1) revealed a single hæmoglobin band. *DBA* (type 2) hæmoglobin included the same and three additional bands, one faster than the main component and two faint slower components. These same three bands, as well as the 'single' band, were visible in F_1 (*DBA* × Kink) hæmoglobin although the electrophoretically slow components were very faint. A semiquantitative method for measuring the relative amounts of hæmoglobin components was based on dissolving a known volume of starch gel with its hæmoglobin in concentrated hydrochloric acid, and the preparation of a blank of the same volume of starch gel in hydrochloric acid without hæmoglobin. Concentrated acid was used, because the presence of excessive amounts of water was associated with turbidity of the resultant solutions. The optical densities of the hydrochloric acid–starch-gel solutions at 400 mμ were obtained on a Bausch and Lomb spectrophotometer. The average amount of slow components in 16 *DBA* animals was 20 per cent and in 40 F_1 animals 4 per cent of the hæmoglobin; no slow component was detectable in Kink hæmoglobin (Table 2). However, when *DBA* and F_1 specimens were stored at 4° C. as either carbonmonoxy- or oxy-hæmoglobin, slow components became apparent in those F_1 specimens in which they were initially lacking, and increased in quantity in other F_1 and in all *DBA* specimens. Hæmoglobin solutions of Kink (type 1) animals stored in identical circumstances failed to accumulate a slow component.

Table 2 ELECTROPHORETICALLY SLOW COMPONENTS OF HÆMOGLOBINS OF INBRED STRAINS OF MICE

Strain	No of animals	Slow components % of total Hb	Main component % of total Hb
DBA/1	16	5 to 58 (av. 20)	80 (av.)
Kink	10	0	100
F_1	40	0 to 20 (av. 4)	96 (av.)

In order to study the effect of storage on the amount of electrophoretically slow component, pooled hæmoglobin solutions were prepared separately from five *DBA*, from five F_1, and from five Kink animals. Electrophoretic and ultracentrifugal analyses of the hæmoglobin solutions were carried out three days after bleeding and repeated after 28 days of storage at 4° C. (Fig. 1).

Initial starch-gel electrophoresis of the different mouse hæmoglobins gave the picture described before. When the electrophoretic analyses were repeated after 28 days, Kink hæmoglobin appeared unchanged, whereas marked changes were noted in *DBA* and in F_1 (*DBA* × Kink) specimens. Electrophoresis of the *DBA* (type 2) specimen now revealed only two components: (1) the electrophoretically slowest band which had increased markedly in amount, and (2) the electrophoretically most rapid component. Electrophoresis of F_1 (*DBA* × Kink) hæmoglobin after storage revealed changes similar to, but not identical with, those in the parent *DBA* (type 2) hæmoglobin: the electrophoretically slowest component had increased markedly, and a rapid component comparable in electrophoretic migration to the rapidly migrating component of *DBA* hæmoglobin was seen. However, in the stored F_1 hæmoglobin, an electrophoretic component of the same mobility as that of hæmoglobin of the Kink (type 1) parent was still evident.

The initial ultracentrifugal analyses revealed a single peak in Kink and F_1 hæmoglobin in contrast to

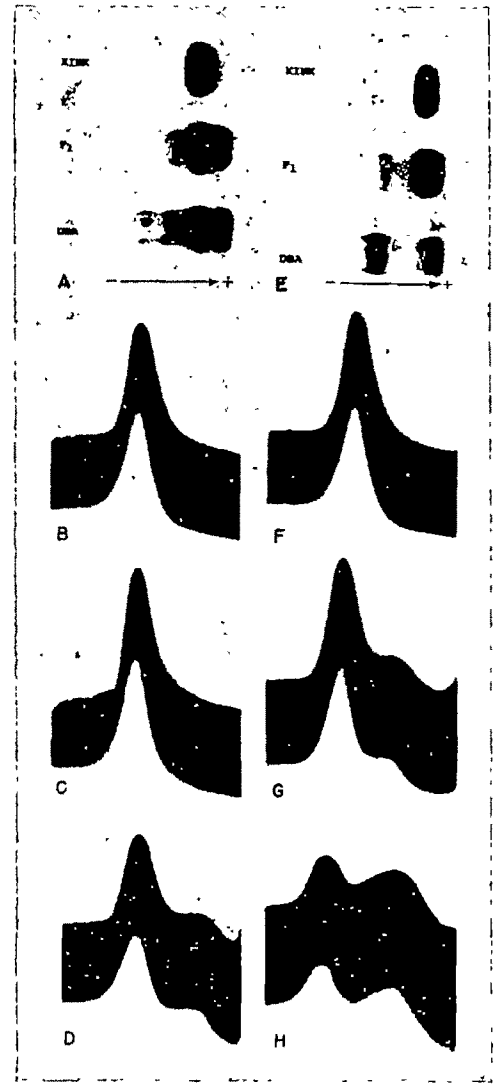

Fig. 1. Electrophoretic and ultracentrifugal analyses of carbonmonoxyhæmoglobin of inbred strains of mice
A, Initial vertical starch-gel electrophoreals[9] of Kink, F_1, and *DBA* hæmoglobins. *E*, electrophoretic analysis of the same solutions after 4 weeks of storage at 4° C. Electrophoretic analyses were carried out for 16 hr. in borate buffer, photographs taken without staining
B, *C*, *D*, initial sedimentation diagrams of Kink, F_1, and *DBA* hæmoglobins respectively
F, *G*, *H*, sedimentation diagrams of same solutions after 4 weeks of storage. Ultracentrifugal analyses were carried out at a concentration of 2 gm. per cent in a 3-mm. cell at 59,780 r.p.m. in a Spinco model *E* analytical ultracentrifuge. Photographs taken in mid-period of each run

the *DBA*, which contained in addition a smaller more rapidly moving peak. On ultracentrifugal analysis after the four-week storage period, a small rapidly moving peak appeared in the pattern of the F_1 hæmoglobin which now resembled the initial pattern observed in *DBA* samples, and the height of the rapidly moving peak of *DBA* hæmoglobin increased markedly during this period.

The sedimentation constant for the main peak of mouse hæmoglobin was $S_{20} = 4{\cdot}2 \times 10^{-13}$, which is within the range of values given for other animal hæmoglobins by Svedberg and Pedersen[10].

A possible interpretation of the changes in the electrophoretic analysis of type 2 hæmoglobin after a

storage period may be derived from the data of Smithies[8], who showed that in starch gels the rate of electrophoretic migration is apparently dependent on size as well as on electrical charge of the proteins. Thus, the observations reported here may be due to the fact that part of the hæmoglobin of *DBA* mice (type 2) may tend to aggregate in solution while that of Kink (type 1) does not. The increase in amount of an electrophoretically slow component in stored *DBA* and F_1 (*DBA* × Kink) hæmoglobin solutions further suggests that the slow components may be the products of aggregation of hæmoglobin molecules.

The results of ultracentrifugal analyses of *DBA* and of F_1 hæmoglobin also provide evidence for aggregation of these hæmoglobins during storage. In F_1 (*DBA* × Kink) hæmoglobin, a rapidly sedimenting, heavy component appeared during the storage period, and, in *DBA* (type 2) hæmoglobin, the heavy component present in the initial runs increased markedly in amount during the same 28-day period.

The faint electrophoretic bands of slowly migrating hæmoglobin of the initial F_1 (*DBA* × Kink) specimens probably represented material quantitatively insufficient to be detected on ultracentrifugal analysis. However, after storage and at a time when the electrophoretically slow component of F_1 hæmoglobin had increased in amount, a new component appeared in the sedimentation diagram of the ultracentrifugal analysis. Similarly during the storage period there was correlation between increase in amount of the electrophoretically slow component of the *DBA* (type 2) hæmoglobin and that of the heavy component in the ultracentrifuge. The simultaneous changes in behaviour of these hæmoglobins on electrophoretic and ultracentrifugal analyses suggest the identity of the electrophoretically slow component with the rapidly sedimenting component in the ultracentrifuge; we have designated this component 'aggregated hæmoglobin'.

In order to demonstrate that aggregation is a property of *DBA* (type 2) hæmoglobin but not of Kink (type 1) hæmoglobin, Kink hæmoglobin labelled with iron-59 was mixed with an equal amount of unlabelled *DBA* hæmoglobin. The absence, after six weeks of storage, of a significant amount of radioactivity in the slow component suggests: (1) that aggregation is indeed a property of the *DBA* hæmoglobin molecule and not of Kink hæmoglobin, and (2) there is no component of the *DBA* hæmolysate which facilitates aggregation of Kink hæmoglobin.

Large variations in the amount of electrophoretically slow component of different specimens of *DBA* and F_1 (type 2) hæmoglobin are recorded in Table 2. Since the amount of this 'aggregated hæmoglobin' seems to increase with storage time, some of the variation may be explained on the basis of time differences. However, differences in amount of hæmoglobin aggregation during storage may depend on other factors such as the hæmoglobin concentration of the hæmolysate. Whether this slow component exists in the circulating erythrocyte is uncertain: we have repeatedly failed to demonstrate the electrophoretically slowest component when starch gel electrophoresis of *DBA* hæmoglobin was carried out within 2–3 hr. after the animals were killed. In these circumstances, only the three electrophoretically rapid components were observed in the *DBA* hæmoglobin specimen. When electrophoretic analysis of *DBA* hæmoglobin specimen was carried out after storage at 4° C. for several months, somewhat more aggregated hæmoglobin appeared, but the rapid component (Fig. 1) was still present. Further studies of factors affecting the rate of hæmoglobin aggregation are under way in our laboratory.

The appearance of aggregated hæmoglobin in the stored hæmolysate of *DBA* and F_1 (*DBA* × Kink) mice may be related to the spontaneous denaturation of mouse hæmoglobin observed by Rosa *et al.*[4]. The observations on aggregated hæmoglobin in the present report were made on hæmoglobin solutions in which no visible precipitation had occurred. On more prolonged storage, a hæmoglobin precipitate appeared in the *DBA* and F_1 (*DBA* × Kink) hæmolysates: both the supernatant hæmoglobin solution and a solution of the precipitate in veronal buffer *p*H 8·6 were found to exhibit the characteristic spectroscopic absorption bands of carbonmonoxyhæmoglobin. After appropriate treatment of the solutions, the absorption bands of oxyhæmoglobin and of reduced hæmoglobin were readily seen in both.

At least part of the differences between *DBA* (type 2) and F_1 (*DBA* × Kink) hæmoglobin could be explained by the presence of Kink (type 1) hæmoglobin in F_1 mice. The smaller amount of aggregated hæmoglobin in stored F_1 (*DBA* × Kink) hæmolysates may reflect the presence of a smaller amount of *DBA* hæmoglobin in these animals than in the *DBA* parent. Whether this aggregation is a property of the hæmoglobin of all mouse strains which were originally classified in the type 2 hæmoglobin group is uncertain[1,3]; the present work was confined to hæmoglobin of *DBA* and Kink animals and their F_1 offspring.

Our own work[1,2], considered together with that of others[3,4], seems to indicate that the genetic control of mouse hæmoglobin type may be fundamentally analagous to that described for human hæmoglobins in that the phenomenon of co-dominance obtains. The two alleles, Hb^1 and Hb^2, each determine the presence of one particular type of hæmoglobin, that is, 'single' or 'diffuse' and heterozygotes contain a mixture of these two electrophoretically separable hæmoglobin types. The 'diffuse' hæmoglobin type from *DBA* mice determined by the allele Hb^2 contains several components, at least one of which may undergo aggregation. The 'single' hæmoglobin type from Kink mice used in this work, on the other hand, exhibits a homogeneity comparable to that of human hæmoglobin A_1 when subjected to various electrophoretic conditions. Hæmoglobin from F_1 ('single' × 'diffuse') mice representing a mixture of the parent hæmoglobins differs from either parent type, both in quantity and quality of components. It is difficult to carry further the comparison of genetic control of mouse hæmoglobins with that of human hæmoglobins in the absence of further knowledge of the chemical differences between hæmoglobins of type 1 and type 2.

This investigation was supported by Grants *A* 1017 and *B* 931 from the National Institutes of Health and by a grant-in-aid from the American Cancer Society.

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LETTERS TO THE EDITORS

ASTRONOMY

A New Correlation of the Mayan and Christian Calendars

BECAUSE solar and lunar eclipses and certain other lunar phenomena tend to repeat themselves in a periodic fashion, it has often been stated that it will be impossible to determine the correlation of the Mayan and Christian calendars from astronomical data alone. As a result, the two most generally accepted correlations, the Spinden[1] ($A = 489,384$) and the Goodman–Thompson[2] ($A = 584,283$) depend in part on historical records; A, the Ahau equation, is the Julian Day Number of the zero date of the Mayan calendar. This communication puts forward a correlation which rests on astronomical data and the assumption that the Spinden and Makemson[3] ($A = 489,138$) correlations are within 100 years of the truth, an assumption suggested by early radiocarbon results.

This assumption and a new interpretation of certain pages of the Dresden Codex allow one to proceed to a determination of A with only slight ambiguity. I suggest that the second line on page 24 of the Dresden Codex indicates dates common to a Venus ephemeris and a solar eclipse table, and that the three lines of month names and numbers on pages 46–50 of the Codex, instead of providing three separate ephemerides for Venus, were designed to give dates of solar eclipses preceding and following particular solar eclipses associated with some special dates in the Venus ephemeris.

Let us assume (*a*) that the initial date of the Venus tables, 9–9–9–16–0, 1 Ahau 18 Kayab, as given on page 24 of the Dresden Codex, is also the date of a solar eclipse visible in Central America; (*b*) that the interval from this date to 9–14–2–6–0, 1 Ahau 18 Uo (page 47, Dresden Codex), 33,280 days (line 2, page 24, Dresden Codex), is an interval between two solar eclipse syzygies as well as the interval between two important Venus dates, namely, from a first appearance of Venus as a morning star to a somewhat later disappearance as an evening star; (*c*) that A lies between $489,384 - 36,524$ and $489,384 + 36,525$, which is equivalent to assuming that 9–9–9–16–0 lies between A.D. April 12, 263, and A.D. April 12, 463, both dates in the Gregorian Calendar. Assumption (*c*) is a re-statement of the one offered in the first paragraph above, namely, that the Spinden correlation is within a hundred years of the truth.

One can now examine the list of solar eclipses in Oppolzer's "Canon Der Finsternisse", looking between A.D. 263 and A.D. 464 for a solar eclipse which was visible in Central America, and which occurred very near a date at which Venus was in inferior conjunction with the Sun. In this interval, there were two solar eclipses meeting this description. The first was an annular eclipse on A.D. December 22, 344, G.C., the second a total eclipse on A.D. December 1, 392, G.C. Equating the former date with 9–9–9–16–0 yields an Ahau equation, $A = 482,699$. The latter date gives $A = 500,210$.

In this brief communication, it does not seem wise to try to give all the reasons for discarding the second value of A; rather it appears more desirable to present some of the reasons for adopting the first, namely, $A = 482,699$.

Consider now the three sets of numerals and month names in the lower part of pages 46–50 of the Dresden Codex. The three initial dates, or 'lubs', are 3 Xul, 18 Kayab, 13 Mac, reading from the bottom up. Let us now examine the six dates:

I. 9–8–3–16–0, 1 Ahau 3 Xul
II. 9–9–9–16–0, 1 Ahau 18 Kayab
III. 9–11–3–2–0, 1 Ahau 13 Mac
IV. 9–12–16–6–0, 1 Ahau 8 Chen
V. 9–14–2–6–0, 1 Ahau 18 Uo
VI. 9–15–15–10–0, 1 Ahau 18 Pax

Using $A = 482,699$, each represents a date within about one day of a solar eclipse syzygy. Venus was 4 days past and 1 day before inferior conjunction with the Sun at (II) and (V) respectively; 286 and 282 days past inferior conjunction and hence near superior conjunction at (III) and (VI); 13 and 14 days before inferior conjunction at (I) and (IV). The consecutive intervals between the dates as listed in order above are: 9,360; 11,960; 11,960; 9,360; and 11,960 days. The interval from (II) to (V) is 33,280 days, one of the numbers on line 2, page 24, of the Dresden Codex. All these intervals are close approximations to intervals between solar eclipse syzygies.

Let us next consider three of the dates given on page 52*a* of the Dresden Codex:

VII. 9–16–4–10–8, 12 Lamat 1 Muan
VIII. 9–16–4–11–3, 1 Akbal 16 Muan
IX. 9–16–4–11–18, 3 Eznab 11 Pax

These dates have often been considered as important items in the interpretation of the lunar tables of the Dresden Codex. The Ahau equation, $A = 482,699$, makes these dates A.D. 477 September 23, October 8 and October 23, G.C. The first date is that of the autumnal equinox, and the third is a solar eclipse syzygy date. The second date is that of a full Moon, one month before a lunar eclipse.

Finally, among the 92 different dates given by Teeple[4], if one omits Nos. 10, 85 and 94, the differences between the age of the Moon, as computed using modern tables (using $A = 482,699$) and as given by the Mayans (in the sense Computed–Mayan), all lie between $+1 \cdot 65$ and $-4 \cdot 25$. There is some evidence that solar eclipses visible in Central America were used to adjust lunar counts; in some cases, corrections of opposite sign were made about the same time in Copan and Piedras Negras, near the time of a solar eclipse visible in those cities.

I wish to acknowledge the generous assistance, particularly in the matter of reprints, of Dr. H. J. Spinden, Dr. M. W Makemson and Mrs. Howard D

Day, a niece of Prof. R. W. Willson. I have been fortunate in having an excellent group of students who have tackled the astronomical computing with enthusiasm.

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ASTROPHYSICS

The Possibility of Detecting a Gravitational Red Shift in 21-cm Radiation from the Galaxy

THE interesting suggestion has recently been made by Landovitz and Marshall[1] that a gravitational red shift might be detectable in observations of the 21-cm. hydrogen line from the inner regions of the Galaxy. The effect is proportional to the difference in gravitational potential between the point of emission and the Earth's surface, and so could give independent information on the mass of the Galaxy. Currently accepted values for the mass and scale of the Galaxy would lead to a frequency shift of -3 kc./s. for radiation originating near the galactic centre; this corresponds to a Doppler velocity of $+0{\cdot}7$ km./sec.

Landovitz and Marshall point out that this shift would have to be isolated from the much larger Doppler shifts (typically 50–100 km./sec.) arising from the differential rotation of the Galaxy, and suggest methods by which the separation might be made. There are, however, some other effects which appear to have been overlooked by Landovitz and Marshall, and these add considerably to the difficulty of picking out the gravitational effect.

The proposed tests involve a search for asymmetries in the velocity pattern of the 21-cm. radiation over the galactic plane. Rotational effects will be symmetrical about the direction to the galactic centre, but gravitational effects will not. I have recently been concerned with some closely related symmetry questions, through comparisons between our own 21-cm. survey of the southern part of the Milky Way strip[2] and the corresponding Leyden survey for the northern part[3]. Some degree of asymmetry does exist, and in consequence a simple rotation picture cannot give a satisfactory interpretation of the observational results. It seems probable, however, that the asymmetry is related to imperfectly understood motions, rather than to a gravitational shift.

A rotational velocity curve can be derived from 21-cm. observations by the method of Kwee, Muller and Westerhout[4], which they applied to the Leyden data for the northern side of the Sun-centre line. An application of the same method to the southern data is found to give slightly lower velocities. (The reality of this difference between the two velocity curves has also been confirmed by other lines of approach.) The difference of velocity between the southern and northern curves varies with galactic longitude in the way which would be produced by an additional motion of the Sun of about 7 km./sec. outwards from the galactic centre.

In all 21-cm. reductions to date, the observed velocities have been corrected to allow for the so-called 'standard' solar motion relative to the local centre of rest. This value for the solar motion has in effect been determined from the mean motion of stars within 2–3 kiloparsecs of the Sun, and the above result implies that the Sun and the local centre of rest are moving outwards at 7 km./sec. with respect to a larger galactic frame of reference.

Some other considerations suggest that the gas at the Sun's distance from the centre is also streaming outwards with about the same velocity. This motion is presumably connected with the large 'expansion' velocities which have been found in the nuclear region of the Galaxy[5], with the inference that all the gas in the galactic disk is moving outwards, with a velocity which decreases with increase of distance from the centre.

These motions produce substantial asymmetries in the Doppler shifts on the two sides of the direction of the galactic centre, overshadowing the somewhat similar asymmetry which Landovitz and Marshall hoped to use to separate the gravitational and rotational effects. Admittedly, there will be second-order differences in the pattern of the various effects over the galactic disk, but these are likely to be hidden by the random motions and local irregularities.

We should of course consider the possibility that the observed asymmetry, which has been attributed to other causes, might in fact be a gravitational shift. For this to be so, the mass of the Galaxy would need to be increased by 10–20 times from the present estimates, and this seems very unlikely. Furthermore, the variation of the effect over the galactic plane is more in keeping with solar motion as a cause.

The test proposed by Landovitz and Marshall for recognizing the gravitational effect has the further difficulty that the integrated brightness in any direction is weighted heavily in favour of the nearby gas, where the effect is smaller still. One way to concentrate attention on the central region is to consider the small central disk and ring, which have recently been discovered by Rougoor and Oort[6]. These appear to be rotating at nearly 300 km./sec., and a $0{\cdot}7$ km./sec. asymmetry would be difficult to detect. The observed distribution pattern of the radiation in velocity and longitude does show a marked asymmetry, of rather complex form, but it seems more likely that structural factors are responsible for this.

So far we have only considered the potential variation in the galactic plane; but there is also a gradient of gravitational potential in a direction normal to the galactic disk. This would lead to a 'blue shift' in observations towards the galactic poles. A blue shift of a few kilometres per second is in fact observed over most of the high-latitude regions (ref. 7, and unpublished work by R. X. McGee), but it is about two orders of magnitude too large for the potential difference which would be expected over the few hundred parsecs where most of the gas is believed to be.

An observation of the gravitational red shift in our own or an external galaxy would be very valuable; but there seems to be little possibility of recognizing

it, until the detailed structure and motions have been established more definitely.

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RADIOPHYSICS

Identification of Mode in Low-Frequency Sweep Ionospheric Sounding, and Interference Patterns between Overlapping Echoes

To help determine the origin of ionospheric echoes received on low-frequency sweep equipment it is very desirable to know their polarization, but unfortunately such information is not easy to record or display in a convenient manner. However, one of the most important parameters of the polarization is the sense of rotation of the wave vector, and a method has been developed which displays this in a simple way on a normal $h'f$ record.

A conventional pulse transmitter is used, operating over the swept range of 100 kc./s.–1,000 kc./s. The echo is received on a pair of crossed coplanar horizontal dipoles and analysed into its two circular components by means of a two-channel receiver with appropriate phase shifters[1] (see Fig. 1). The resulting video signals are electrically subtracted and applied to the grid of a conventional recording cathode-ray tube with its quiescent brightness adjusted to a level midway between zero and full intensity. Thus any particular echo, which will in general be elliptically polarized, will be displayed either as a light trace or dark trace, depending on its sense of rotation. A linearly polarized echo will not be displayed.

In the examples, a dark trace represents $N \rightarrow E$ (right-handed) polarization and a light trace $N \rightarrow W$ (left-handed); Fig. 2 shows a record in which echoes of both polarizations are clearly visible. The form of this particular record is similar to that described by Watts[2] and the polarization is that which we would expect theoretically if the N_0-levels for all frequencies in the range are at heights greater than the ν_0-level. (The terminology is that of Ratcliffe[3].)

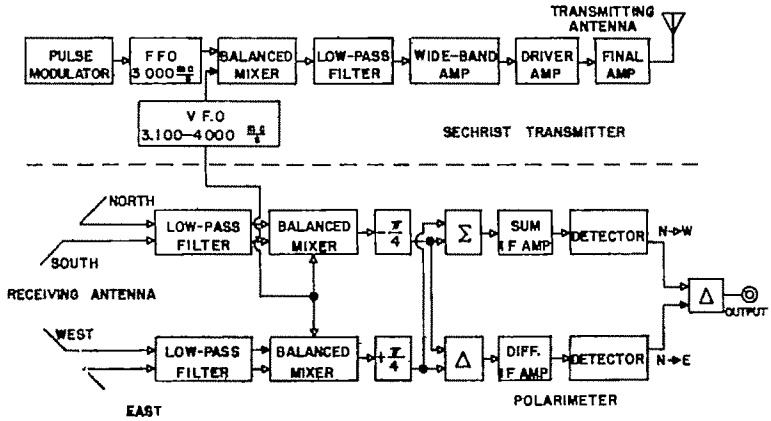

Fig. 1. Equipment block diagram

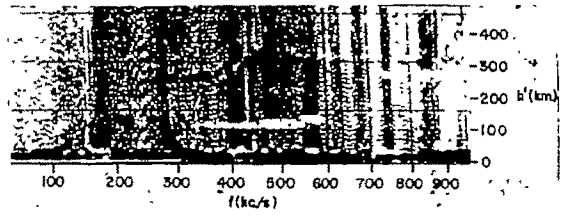

Fig. 2 0415 January 24, 1960

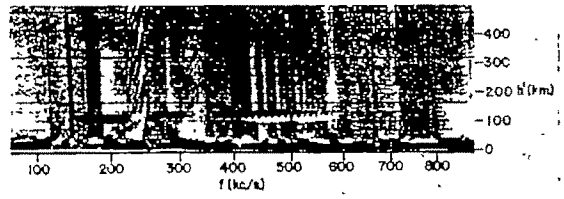

Fig. 3. 0615 March 26, 1960

A particularly interesting effect sometimes observed is the appearance of interference fringes (see Fig. 3). These can be produced if either or both of two overlapping echoes have non-circular polarization, since interference can then take place in either interference fringe channel. Now the fringes are produced as the frequency varies, and hence are a representation of the rate of change (with frequency) of the difference in phase between the two echoes. But, as is well known, the rate of change of phase, φ, with frequency is just equal to the pulse delay of a system, so that in this case it should correspond to the time-interval between the reception of the two echoes. Or, in terms of group height, h', we have:

$$\left(h'_1 - h'_2\right) = \frac{c}{2}\frac{\partial}{\partial\omega}\left(\varphi_1 - \varphi_2\right)$$

There are two possible reasons for the occurrence of a double trace:

(i) If the electron density increases monotonically with height and the gradient is not too great, then ray theory applies, and two magneto-ionic components will be reflected from the layer provided $\nu \ll \nu$ and $\nu \ll \omega$. In this case we expect the upper of the interfering echoes to have $N \rightarrow E$ polarization and the lower to have $N \rightarrow W$. This is just what is observed in Fig. 3. The separation of height of the echo computed from the observed fringe width agrees with that actually observed, namely, 12·5 km. and 12 kc./s.

(ii) If the electron density profile contains sharp gradients, partial reflexions will occur and may give rise to split echoes. In this case, the polarization which the echoes will

have is not at all obvious, but we still have the possibility of production of interference fringe. Examples have been observed of interference fringes between echoes, which, because of their polarization, can only be explained by this mechanism.

It should be noted that whenever fringes are observed, their separation can be measured with precision, and this gives a much more accurate measure of the group-height separation of the echoes than could be obtained by direct measurement of a conventional $h'f$ record. In fact, sometimes fringing can be observed when the existence of a split echo might not otherwise be evident, thus providing independent information about the fine structure of the E-region.

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PHYSICS

Small-Angle Scattering of X-Rays from Deformed Natural Graphite

EXAMINATION of deformed metals using techniques of small-angle scattering of X-rays[1], stimulated by the development of theories and experiments on defects in crystals, has been made. Some results obtained along these lines with natural graphite are reported in this communication. In order to obtain deformed graphite it was treated either mechanically or chemically as follows:

(1) *Rolling*. 1 gm. of Ceylon graphite powder was pressed into a copper tube, 5 mm. external diameter and 3 mm. internal diameter, and sealed by turning down both ends. Afterwards the tube was pressed between plates to 4 mm. thick by rolling in a hand mill (5 cm. diameter). The thickness was reduced to 3·35 mm. after 4 passes through the first setting of the roller gap, and it was successively reduced to 2·8 mm., 2·4 mm., and 1·8 mm. by passing through, respectively, the second, third and fourth roller gap. The narrow solid strips of graphite obtained in this manner were carefully dispersed by lightly rubbing in boiling water.

(2) *Extruding*. Graphite powder was pressed into a cylinder, 4 mm. internal diameter, with a load of 200 kgm. The resulting solid graphite rod was introduced into a cylinder of the same diameter and extruded through a nozzle, 1 mm. or 1·5 mm. in diameter, at varying speed.

(3) *Pressing* 50 mgm. of graphite powder was pressed each time with a piston in a cylinder of hard steel of 4 mm. internal diameter. The ultimate load applied was 3 tons.

(4) *Lamellar compounding*. Lamellar compounds with bromine[2] and potassium[3,4] were prepared as usual since these compounds are reproducible and easy to prepare. It was debrominated at 100° C. in air and at 650° C. *in vacuo*. Potassium was driven off at 400° C. in a sealed glass tube for 12 hr. Then the residue was transferred to a porcelain boat and heated at 800° C. for 1 hr. in an evacuated furnace. Use was made of a slit collimated camera having the sample to the photographic film distance of 28 cm. The determination of the scattering from the different samples was achieved by exposure, under constant operating conditions, on the same photographic film by means of the rotation of the film holder. The sample (100 mgm.) was situated immediately behind the collimating slit uniformly pressed in a holder 2 × 24 mm.[2] and while irradiating oscillated longitudinally with an amplitude of 14 mm. The crystallites in the holder were preferentially oriented so that the layer planes were at right angles to the X-ray beam. Cobalt radiation filtered through Ross-type filters was used.

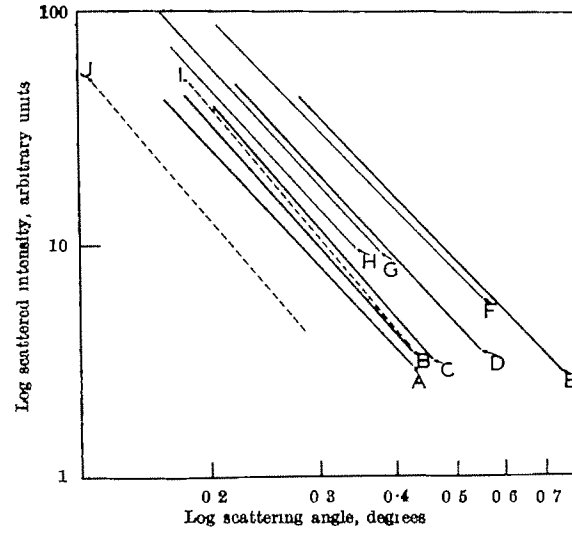

Fig. 1. *A*, Normal Ceylon graphite; *B*, rolled graphite, first stage; *C*, second stage; *D*, third stage; *E*, fourth stage, *F*, extruded through 0·1-mm. nozzle; *G*, pressed at 16,000 atm.; *H*, pressed at 8,000 atm., *I*, residue of brominated graphite, *J*, residue of potassium compound

The representative scattering curves are plotted in Fig. 1. The intensities of scattering increase with the degree of rolling from curves *A* to *E*. The degree of deformation of the graphite crystal may be expressed with Franklin's p-value[5] and estimated as in my previous work[6] to be, respectively, 0·05, 0·05, 0·055, 0·057 and 0·074. Besides this a slight progressive decrease of the grain-size L was observed and estimated to be, respectively, 827, 804, 741, 647 and 473 Å. from the half-peak width of the 0008 line and using nickel K radiation. For extruded graphite (F) the values are $p = 0·055$ and $L = 714$ and for pressed graphite (G) $p = 0·053$, $L = 755$. In the case of graphites treated mechanically the intensities of scattering were correlated with the p and L values. Abnormally small intensity (J) was obtained in the case of the sample treated with potassium, whereas p and L values were normal. The result was confirmed with the samples prepared under slightly different conditions. However, with the rolled samples treated and untreated with potassium, identical intensities of small-angle scattering were observed.

It will be apparent from Fig. 1 that the curves obtained are very nearly linear over the range of angles observed and approximately parallel to each other. From this the angle dependence of the

scattered intensity has been found to be $(2\theta)^{-2.5}$, which would correspond to $(2\theta)^{-3.5}$ in the case of pinhole collimated camera. $(2\theta)^{-3}$ dependence was observed by Grosskreutz and Rollins[7] with stressed copper and aluminium in the same range of angles.

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Townsend Ionization Constants in *n*-Alkanes

WE recently measured the first Townsend ionization coefficient, α, in a series of *n*-alkyl chloride gases[1], and found that the dependence of α on molecular structure in these gases was similar to, but different in detail from, that indirectly inferred in the hydrocarbon gases by Devins and Crowe[2] and Heylen and Lewis[3] from measurements of sparking potentials. In order to determine whether these differences are real or are the result of errors in analysis of the results for sparking potentials, we have undertaken the direct measurement of the first Townsend ionization coefficients in the *n*-alkane gases containing 1–6 carbon atoms.

Crowe, Bragg and Devins[4] have, on theoretical grounds, related the ionization coefficient, α, to pressure, p, field, E, and to molecular structure through the relationships:

$$\alpha/p = Af(E/p)\exp(-BP/E) \qquad B = k\theta\varepsilon_i^{3/2} \tag{1}$$

A is a constant for a given gas, ε_i is the ionization potential, θ the Ramsauer cross-section, and k, while not necessarily a constant for different gases, was found from measurements of sparking potential to be so for the hydrocarbon gases[2]. The pre-exponential factor $f(E/p)$ in equation (1) was assumed to be equal to E/p for the hydrocarbons[2], although the range of E/p covered with the measurements of sparking potentials was insufficient to distinguish between $f = E/p$ and $f = 1$. Our measurements for the alkyl chlorides[1] showed that equation (1) gave a much better fit for those results if $f = 1$.

The experimental apparatus and procedure have already been described[1]. The gases were more than 99 per cent pure. Pressures were varied from 0·5 to 20 mm. mercury and electrode spacings from 0·2 to 3 cm.

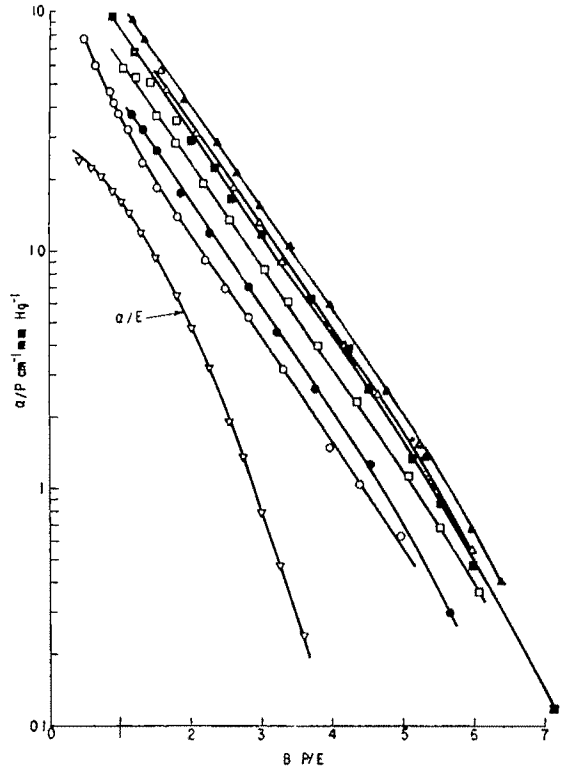

Fig. 1. Dependence of α/p on B/p for the *n*-alkanes: ○, methane; ●, ethane; □, propane; ■, butane; △, pentane; ▲, hexane; ▽, α/E for butane

In Fig. 1 we have plotted our experimentally determined ionization coefficients for the *n*-alkanes containing 1–6 carbon atoms. The abscissa was chosen to separate the individual curves; values of B were obtained from individual plots of log α/p against P/E and are listed in column 3 of Table 1. The curves all show linear regions over a variation in α/p of approximately fifty-fold, with some curvature below $BP/E = 1$ and above $BP/E = 5$. Such deviations are to be expected according to the theory[4]. If $f = E/p$ in equation (1), then the logarithm of α/E should be a linear function of P/E. In Fig. 1 such a plot is shown for butane, arbitrary units being chosen for convenience in plotting. The pronounced curvature suggests that, for the alkanes, as for the alkyl chlorides, equation (1) describes the results better if f is chosen to be unity.

Values of B for the alkanes were re-calculated from sparking potential data[2], assuming $f = 1$ in equation (1). The values, shown in column 4 of Table 1, are 10–25 per cent lower than those obtained in the present work.

Table 1. IONIZATION CONSTANTS IN *n*-ALKANES

Gas	A (cm⁻¹ mm. Hg⁻¹)	(*a*) $B(a)$ (V. cm.⁻¹ mm. Hg⁻¹)	(*b*) $B(V_s)$ (V. cm.⁻¹mm. Hg⁻¹)	(*c*) $B(V_s)$ (V. cm.⁻¹ mm. Hg⁻¹)	(*d*) ε_i (eV.)	$\frac{B(a)}{\varepsilon_i^{3/2}}$ (V. cm.⁻¹ mm. Hg⁻¹ eV.$^{3/2}$)
Methane	8 3	198	181	195	13·04	4 2
Ethane	11·7	226	188	235	11 76	5 6
Propane	17·2	302	235	292	11 21	8 1
Butane	22·5	358	294	336	10 80	10·4
Pentane	24·5	416	336	388	10·55	12 2
Hexane	29 2	476	385	442	10 43	14·1

a, This work; *b*, heavy illumination (ref. 2); *c*, light illumination (ref. 6); *d*, ref. 2.

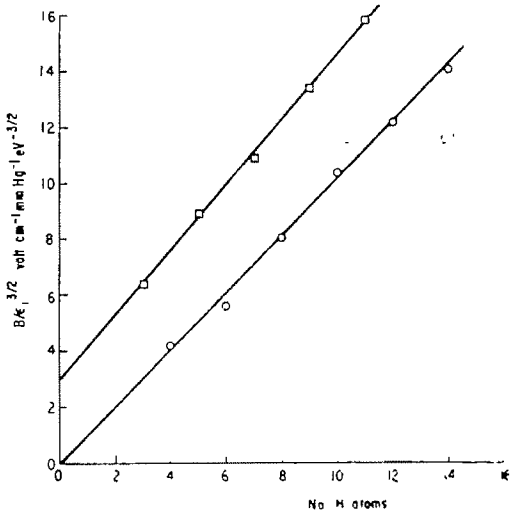

Fig. 2. Relationship between $B/\varepsilon_i^{3/2}$ and the number of hydrogen atoms for the normal alkanes, O, and the normal alkyl chlorides, □

An essential feature of the Townsend mechanism is the independence of the sparking potential on the level of cathode illumination, provided that adequate time is allowed for breakdown to occur. As Heylen and Lewis[3] point out, however, for hydrocarbons, decreases in sparking potential of 10–20 per cent are readily observable on relatively moderate ultraviolet illumination of the cathode. Although with low levels of illumination they observed the same values of B for the alkanes as did Devins and Crowe[2], their values for the alkenes were distinctly lower[5]. In Table 1, column 5, we have included earlier measurements of B of Devins and Crowe[6] made with a 'Pyrex' cell irradiated with a $BH4$ lamp. The effective level of illumination was therefore much lower than in their later work. These values of B agree much more closely with those obtained from measurements of α than do those obtained using a more heavily illuminated gap.

Utilizing our measurements of α, we can calculate from measurements of sparking potentials values for the second Townsend coefficient, γ, assuming the Townsend sparking criterion to be valid. For the relatively heavily illuminated gaps[2], values of γ increase approximately exponentially with decreasing E/p, and lie in the range of 10^{-2}–10^{-6}. With the lightly illuminated gaps of Heylen and Lewis[3] and of Devins and Crowe[6], values of γ are more nearly independent of E/p and much lower (10^{-8}–10^{-9}). These results are consistent with the hypothesis of Heylen and Lewis[3], which suggests that if γ is very low for the hydrocarbons, appreciable distortion of the field by space charge may occur below the Townsend threshold, even with moderate illumination.

Measurements of sparking potentials[2] had indicated that the cross-section θ was a colligative function of the number and types of atoms in a molecule if the contribution of the singly bonded carbon atoms is zero. In Fig. 2 we plot $B/\varepsilon_i^{3/2}$, obtained from our direct measurements of α for the n-alkanes and n-alkyl chlorides[1], versus the number of hydrogen atoms. The least-square lines are: for the n-alkane gases, slope $= 1{\cdot}03 \pm 0{\cdot}05$, intercept $= -0{\cdot}1 \pm 0{\cdot}14$; for the n-alkyl chloride gases[1], slope $= 1{\cdot}16 \pm 0{\cdot}03$, intercept $= 2{\cdot}97 \pm 0{\cdot}07$. The zero intercept for the n-alkane curve indicates a zero contribution to θ from the carbon atoms, as was reported earlier[2], and the 12 per cent difference in slope suggests either a slightly different contribution of the hydrogen atom or different values of k for the n-alkane and n-alkyl chloride series.

The constant A for the n-alkane gases appears to be proportional to the number of hydrogen atoms per molecule. An understanding of the dependence of A on molecular structure must await further theoretical work.

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Tungsten-185 in Precipitation and the Seasonal Variations in Fall-out

The introduction of tungsten during the U.S. 'Hardtack' nuclear test series in 1958 provided a unique opportunity of identifying nuclear debris of known origin. From June 1958 until August 1959, tungsten-185 (half-life, 74 days), the tungsten isotope of most interest, was detected in precipitation occurring at Westwood, New Jersey and other stations[1]. Data on both tungsten-185 and strontium-90, and other short-lived isotopes such as barium-140 and strontium-89, in rain-water cast light on the mechanism of stratospheric fall-out, and if suitable corrections for radioactive decay of the short-lived isotopes are made the fraction of debris from 'Hardtack' tests may be estimated. An initial activity ratio tungsten-185/strontium-90 of 500 on July 15, 1958, as suggested by Lockhart *et al.*[2], has been used in this work.

The deposition of tungsten-185 and strontium-90 in precipitation at Westwood, New Jersey, is shown in Fig. 1 together with the rainfall amounts. These curves were constructed by adding the activities in each rain within overlapping 30-day periods, each interval being advanced in 10-day steps. All tungsten-185 results were corrected for radioactive decay to August 15, 1958. Fig. 2 shows a similar graph

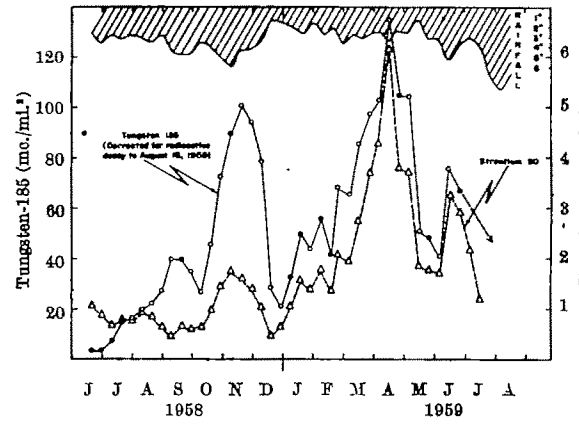

Fig. 1. Levels of tungsten-185 and strontium-90 deposition in precipitation at Westwood, New Jersey, during the period June 1958–July 1959

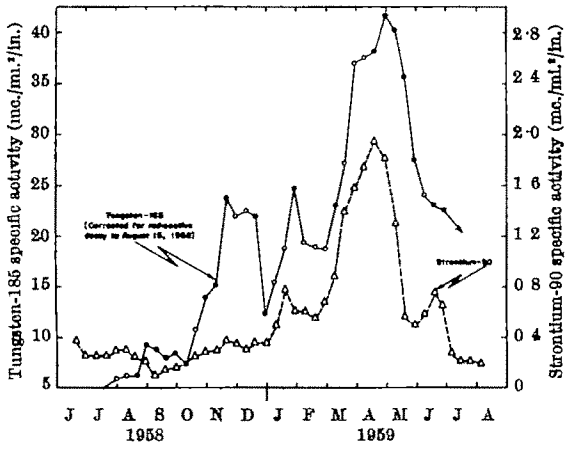

Fig. 2. Variations of the specific activities of tungsten-185 and strontium-90 in precipitation at Westwood, New Jersey

of the variation in specific activity of strontium-90 and tungsten-185 in rains for the period June 1958–July 1959.

It is clear that the deposition of these nuclides varies considerably during the period chosen for discussion. Furthermore, these variations are not due to differences in rainfall amounts as can be seen from the precipitation data in Fig. 1 and the specific activity results in Fig. 2. Perhaps two major peaks in tungsten deposition can be seen, one in November–December 1958, and a second in the spring of 1959. The latter is accompanied by a similar increase in deposition and specific activity of strontium-90, but with the former peak the increased strontium-90 deposition is not so pronounced. The abrupt rises in tungsten-185 and strontium-90 specific activities, commencing in early 1959 and attaining their peaks in mid-April, provide good evidence for the seasonal variation in fall-out first observed by Stewart *et al.*[3]. However, the tungsten curve supports the theory that this spring rise in fall-out is not wholly attributable to the Soviet testing schedule, as postulated by Martell[4], but is rather a meteorological phenomenon and is independent of the geographical origin of the debris[5,6]. The continuous deposition of tungsten-185 during the late autumn of 1958, two to three months after the last

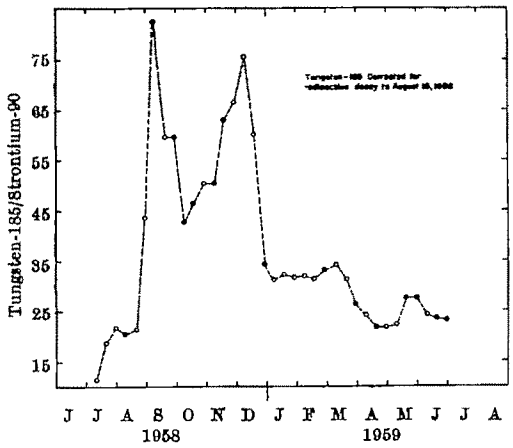

Fig. 3. Tungsten-185/strontium-90 ratios in precipitation at Westwood, New Jersey

major 'Hardtack' tests, is unlikely to be tropospheric debris and we must therefore attribute it to delayed stratospheric fall-out.

Fig. 3 shows the change in the tungsten-185/strontium-90 ratio with time. During early 1959 this ratio remained relatively constant over a six-month period. This indicates that the 'Hardtack' and other debris in precipitation were quite well mixed, and calculations, using the tungsten-185 results to obtain the accompanying 'Hardtack' strontium-90, reveal that only about 8 per cent of the strontium-90 was 'Hardtack' in origin. During earlier periods, that is, in late 1958, this contribution rose as high as 20 per cent. These findings are in good agreement with the conclusions of Lockhart *et al.*[2] from ground-level air measurements. Considerable changes in the tungsten-185/strontium-90 ratio occurred, however, during 1958, probably due to the Soviet testing at that time. Other isotope data (for example, strontium-89/strontium-90 ratios) obtained at this laboratory[7] indicate that 70–80 per cent of the debris sampled during spring 1959 could be attributed to Soviet tests in the autumn of 1958.

The tungsten-185 data have demonstrated, therefore, that material injected into the stratosphere in the equatorial regions is involved in the seasonal variations of fall-out. The spring peaks in fall-out are therefore not entirely a result of the testing schedule nor are they entirely related to the area where detonations have occurred. Furthermore, it appears that the 'residence times' of material injected into the equatorial stratosphere can be relatively short, as discussed recently by Feely[8].

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Elimination of a Glow Discharge in an Induction-heated Vacuum Furnace

WHEN metals and other conductors are heated by induction at low gas pressures, difficulty is sometimes experienced due to electrical breakdown of the gas by the high-frequency electromagnetic field of the induction coil. The effect is most pronounced in the pressure-range, 0·01–0·5 mm. mercury[1]. Occasionally the discharge becomes so intense that effective heating by the work-coil can no longer be obtained, particularly if high temperatures are required.

There has been little reported in the literature on the quenching of high-frequency discharges. McDonald *et al.*[2] found that by using traps cooled in liquid nitrogen to remove mercury vapour, the

discharge could be eliminated. Tokube *et al.*[3] also found this to be effective. Bach *et al.*[4] used a step-down transformer to reduce the voltage across the work-coil from 1,000 V. to 100 V. and found that this entirely eliminated the discharge.

The problem of eliminating such discharges was encountered in this Laboratory in the application of the isotope dilution method to the determination of gases in metals[5]. The technique involved the heating of a graphite crucible approximately 1 in. in diameter by 1 in. in length suspended by platinum wires in a vertical cooled tube 2 in. in diameter, in an atmosphere of carbon monoxide in the pressure-range 0·05–0·5 mm. mercury. Work coils 3 in. in diameter, with 5–10 turns of ¼-in. copper tubing, were used in conjunction with an electronic generator of maximum output of 10 kV. amp. at a nominal frequency of 350 kc./sec. In earlier work[5] in which a 2·5-kV. amp. generator was used and for which better coupling between coil and crucible was obtained, only a faint discharge was occasionally encountered.

In view of the scarcity of data, an outline of several approaches to the problem which have been made in this Laboratory may be of help to present and future users of induction-heated vacuum furnaces.

(*a*) *Gas pressure.* As a result of limitations on the weights of steel samples which can be used in this apparatus, the partial pressure of $C^{16}O$ and $C^{18}O$ is restricted to 0·05–0·5 mm. mercury. An attempt was made to quench the discharge by increasing the total pressure by adding an inert gas. Argon (I. potential 15·7 V.) and helium (I. potential 24·46 V.) were used at pressures up to 20–30 mm. mercury. In both cases an improvement was obtained at low power output; but at the power output which would be used during an isotope dilution run a strong discharge was still obtained.

(*b*) *Mercury Vapour Traps.* The furnace was isolated from any mercury vapour in the system by the use of solid carbon dioxide–acetone traps. Unlike other workers, McDonald and Tokube (*loc. cit.*), I did not find that this was significantly effective in quenching the discharge.

(*c*) *Use of Short Generator-Coil Leads.* The initial experiments were performed with the generator remote from the coil. Because of the possibility of poor grounding due to the long leads, the generator was placed as close as possible to the work coil. A massive earth connexion was also made between the generator and work coil. This assembly gave much better coupling and removed the discharge at low currents. However, it had no significant effect on the discharge at higher power output.

(*d*) *Grounding.* It was observed that there was a certain amount of grounding of the discharge through the clamps supporting the furnace. This produced dark spots on the glassware at these points, probably due to deposition of carbon and platinum particles carried by the ionized gas from the graphite crucible and supporting wires. Following this observation, attempts were made to ground the discharge by grounded wires dipping into the furnace cooling water, without any success.

(*e*) *Use of a Metallic Film.* During the course of the grounding experiments, it was discovered that the discharge was reduced most effectively by hanging unconnected copper wires in the furnace cooling water. The discharge was progressively decreased by increasing the number of wires. Thomson[6] has suggested that the rapidly oscillating electric field is required to initiate a high-frequency discharge and this was confirmed by later workers[7]. It seems likely, therefore, that the successful use of free-hanging wires to quench the discharge may be due to a shielding of the electric field, so that the field strength is reduced below that necessary to produce electrons, by being spread over a greater area of the furnace tube.

The effect of increasing the conductivity of the cooling water was then examined, since from the above argument this should also eliminate or decrease the discharge. It was found that very low concentrations ($<10^{-3}$ *M*) of strong electrolytes, such as sodium chloride, hydrochloric acid, or nitric acid, completely eliminated the discharge. Large pieces of very insoluble substances suspended in the cooling water (calcium fluoride, barium sulphate, silver chloride) had no effect on the discharge.

The final solution to the problem has been obtained by silver-plating, in strips, the inner wall of the furnace water-cooling jacket. When this has been done, no discharge is observed, even at maximum power output from the generator.

In conclusion I would like to acknowledge my thanks to members of the High-Temperature Group of this Laboratory and to Prof. A. D. McDonald of Dalhousie University for helpful discussion of this problem.

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CRYSTALLOGRAPHY

A New Case of Crystallographic Stacking Fault: U_3O_{8-x}

BY the use of modern electron optical techniques, the study of structures involving periodic stacking faults (or 'out-of-steps' between 'anti-phase domains') is making remarkable advances. Some of the most recent reports are referred to refs. 1–5. However, many contributions to this field have hitherto been confined mainly to physically ordered states of binary alloys. Now, in the course of electron diffraction investigation of uranium compounds, I have encountered a new case of fault structure which is connected with a chemical decomposition.

In Fig. 1 the electron diffraction pattern of a single crystal of orthorhombic uranium oxide (U_3O_8) is reproduced. The sample is very thin along [001], and the incident beam is in this direction. The pattern is compatible with the crystal structure of orthorhombic U_3O_8 proposed by Andresen[6], and Chodura and Malý[7]. Since the uranium ions in the crystal are all arranged on (001) in a nearly hexagonal manner[6,7], the pattern exhibits a hexagonal feature as a whole. Moreover, the crystal consists presumably of inevitable twins, oriented at 60° to each other around the *c*-axis.

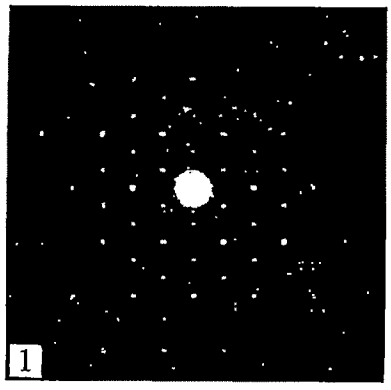

Fig. 1. Electron diffraction pattern of a single crystal of U_3O_8

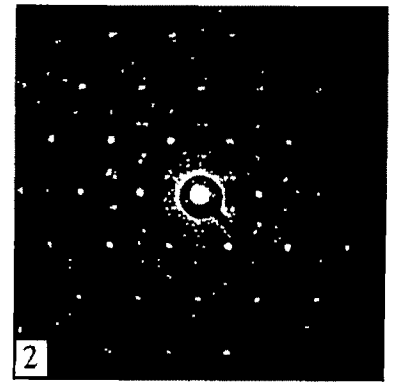

Fig. 2. Electron diffraction pattern of the sample of Fig. 1 after being heated *in vacuo*

When such a single crystal of U_3O_8 is heated *in situ* in the electron optical apparatus, it is reduced eventually to uranium dioxide (fluorite-type cubic) in a special orientation. However, prior to the appearance of the uranium dioxide phase the comparatively weaker spots of Fig. 1 suffer an anomalous splitting as shown in Fig. 2. The splitting becomes more pronounced as the reduction proceeds, while the comparatively stronger spots of Fig. 1 remain almost unchanged. Thus, it seems that before conversion of the orthorhombic lattice of U_3O_8 to the cubic lattice of UO_2 the former undergoes a modification. The chemical formula for the modified stages should be U_3O_{8-x}, where x is a small positive variable.

In Fig. 3*a* the line-up of U^{6+}- and U^{5+}-planes in orthorhombic U_3O_8 with respect to the *b*-direction is depicted schematically. It is to be noted that actually the U^{5+}-planes trisect only approximately the spacing between adjacent U^{6+}-planes. Now, suppose that a particular mode of valency conversions of uranium ions (U^{6+} to U^{5+} or U^{4+}, and U^{5+} to U^{6+}) takes place so as to lead to the sequence, for example, of Fig. 3*b*. Suppose, moreover, that the spacings between adjacent U^{6+}-planes in Fig. 3*b* be either 1 or 4/3 (taking the spacing in Fig. 3*a* as the unit), owing to slight changes in position of uranium ions accompanying the valency conversions. This is an out-of-step structure, where stacking fault takes place at every M-th step of the U^{6+}-plane. For Fig. 3*b* M is 3. It will be readily understood that M decreases as the reduction proceeds, since smaller M means lower density of the U^{6+}-plane in the crystal (Fig. 3*c* and *d*). The asymmetric splitting of spots in the direction above–below in the patterns, such as Fig. 2, can be accounted for by such stacking fault structures, the amount of splitting depending on the value of M. That the split spots in Fig. 2 show an elongation is presumably due to the fact that the M values in the crystal fluctuate considerably around a predominant value. By introducing to the above a triad operation, corresponding to the presence of the 60° twinning, all the anomalous spots of Fig. 2 can be accounted for. The reduction of U_3O_8 to U_3O_{8-x} in this way is supposed to proceed until M decreases to unity (Fig. 3*d*).

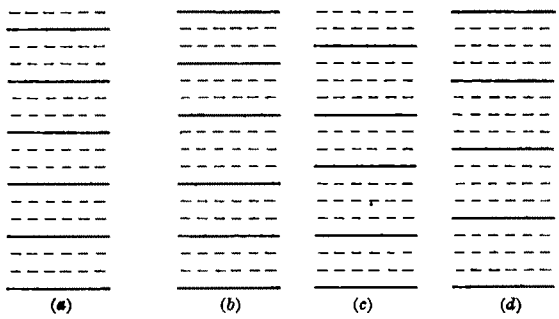

Fig. 3. Successive stages of line-up of U-planes in the reduction of U_3O_8 to U_3O_{8-x}. Solid lines indicate U^{6+}-planes, and broken lines U^{5+}-(or U^{4+}-) planes. (*a*) corresponds to U_3O_8 (Fig. 1). The M values are ∞, 3, 2 and 1 from left to right

A detailed account of this work will be given elsewhere.

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MINERALOGY

Formation of Hydrogarnet by Chemical Reaction among Calcium Carbonate, Ammonium Chloride and some Silicates

THE Lawrence Smith method, which is well known as a procedure for the chemical analysis of alkali ions, has not been considered in the light of structural chemistry. Here we are considering the chemical reaction from the structural chemistry point of view and show that hydrogarnet is frequently formed, which suggests that the reaction should await further studies in relation to the natural skarnization.

As starting materials, we used specimens of feldspars (orthoclase, adularia, microcline, and sanidine) which are free from impurities other than feldspars. The known mixture of $KAlSi_3O_8/CaCO_3/NH_4Cl$ in the ratio (by weight) of 2 : 3 : 2 was heated at the temperatures 100° C., 200° C. . . . 800° C. for 1 hr., immediately cooled, and then washed about ten times with hot water to remove water-soluble salts. The residue was dried at room temperature and analysed by X-ray (Table 1) and chemically (Table 2).

Feldspar and calcite structures are persistent up to nearly 600° C. Wollastonite structure begins to be formed from about 500° C., and garnet structure begins to be formed from about 700° C. The spacing of this garnet structure deviates slightly from that of grossularite. Owing to this fact, coupled with a considerable amount of ignition loss as revealed in the

Table 1. X-RAY POWDER DATA FOR THE RESIDUE OBTAINED FROM ORTHOCLASE HEATED AT 600° C. (COPPER $K\alpha$: 1 5418 Å.)

d (Å.)	I			d (Å.)	I		
7 69	7	W		2·442	18		G (422)
4·90	8			2 340	15	W	G (431)
4 29	5	W	G (220)	2 304	9		
3·83	14	W		2 186	13	W	G (521)
3 58	6			2 058	5		
3·52	17	W		2 023	5	W	
3 39	5			1 981	5	W	
3·31	24	W		1 941	7		G (611–532)
3·23	10	W		1 918	5	W	
3·20	8	W		1 881	4	W	G (620)
3·09	17	W		1 852	6	W	
3·04	11	W		1·834	6	W	
2·988	39	W	G (400)	1 762	6	W	
2 984	6			1 725	7	W	
2·805	5			1·687	4		
2 730	9	W		1 658	9		G
2 675	50		G (420)	1 629	3		G
2 550	10	W	G (332)	1·598	10	W	
2 481	9	W					

W, wollastonite; G, reflexions corresponding to those of grossularite. Numerals in brackets mean indices of reflexions.

Table 2. CHEMICAL COMPOSITION OF THE RESIDUE OBTAINED FROM SANIDINE HEATED AT 650° C.

	Per cent
Silica	35 30
Alumina	12·33
Calcium oxide	43·27
Ignition loss (> 105° C.)	7 20
Water (−)	1 23
Total	99 33

chemical composition, it can be anticipated the garnet may belong to hydrogrossularite.

Earlier papers[1] indicated that the a_0-parameter gradually increases through increasing amount of hydrogen replacing silicon in the grossularite–hydrogrossularite series.

In the present case, the spacing of the garnet structure has nearly a fixed value even in the specimen not having been with hot water. Hence, it can be considered that the hydrogrossularite structure has been formed in the chemical reaction and has nearly a fixed chemical composition. The a_0-parameter was obtained as 11 9, Å., which is near to that of plazolite:

$$3CaO.Al_2O_3.2SiO_2.2H_2O = Ca_3Al_2(Si_2H_4)O_{12}$$

From the above data, the chemical compositions can be represented as:

$$3\ CaO.Al_2O_3.1{\cdot}5\ SiO_2.3{\cdot}3\ H_2O + 3{\cdot}4(CaO.SiO_2)$$

and the amount of wollastonite obtained from this formula was about 47 per cent, which agrees with that obtained in the natural standard wollastonite specimen.

Heating the known mixture of leuchtenbergite/calcium carbonate/ammonium chloride in weight ratio of 1 : 1 : 1, we were able to obtain periclase and hydrogrossularite structures. Leuchtenbergite and calcite are persistent up to about 700° C., and periclase and garnet structures begin to be formed at about 600° C. The a_0-parameter was obtained as 12·10 Å.

Table 3. CHEMICAL COMPOSITION OF THE RESIDUE OBTAINED FROM LEUCHTENBERGITE HEATED AT 800° C.

	Per cent
Silica	24·37
Alumina	17·32
Titanium dioxide	0 05
Ferric oxide	0·98
Ferrous oxide	0·24
Magnesium oxide	21·66
Calcium oxide	29·22
Sodium monoxide	0 35
Potassium monoxide	0·19
Water (+)	5·77
Water (−)	0·13
Phosphorus pentoxide	0 16
Manganous oxide	0·06
Total	100 50

The chemical composition (Table 3) can be represented by the following formula:

$$3{\cdot}0CaO.Al_2O_3.2{\cdot}4SiO_2.1{\cdot}9\ H_2O + 3\ 2\ MgO$$

These results may indicate that hydrogarnet can be formed even in a normal atmosphere at about 700° C. or above it, and ammonium chloride may play an important part in its formation. Probably, chlorine acts on calcium ions forming calcium chloride, which reacts on silicates, exchanging potassium ions with calcium ions, and the residue transformed into the following materials as wollastonite, garnet, and periclase. Hydrogen released from ammonium chloride may play an important part in the formation of grossularite.

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RADIATION CHEMISTRY

Reactions of Nitric Oxide or of Oxygen with Benzene Selectively Excited to the Triplet State

WE have recently described[1] a method of studying the reactivity of aromatic molecules in their lowest triplet states. For example, the system benzene + nitric oxide, irradiated within the paramagnetically induced[2] forbidden $T \leftarrow S_0$ band (λ2900–3400 Å.), reacts, the photochemically active radiation being absorbed neither by nitric oxide nor by benzene alone. The effect is considered as the reaction of benzene, excited to the lowest triplet state, with nitric oxide in its ground-state.

The products of reaction were removed from benzene solution by extraction with 0·1 M aqueous sodium hydroxide and identified by chromato-polarographic separation[3], examination of absorption spectra and polarographic curves, as o-nitrophenol and 2,4-dinitrophenol. Hence our previous assumption[1] about the formation of an *iso*nitroso compound was not confirmed. Using the ferrioxalate actinometer[4], we have measured the quantum yield of formation of 2,4-dinitrophenol in monochromatic light of $\lambda = 3130$ Å., finding $\Phi \approx 0{\cdot}012$. o-Nitrophenol is formed simultaneously with comparable efficiency.

The influence of nitric oxide on ultra-violet absorption of benzene is similar to that of oxygen, both being due to paramagnetic properties of nitric oxide or oxygen molecules. It seemed very probable, therefore, that this analogy would also exist in the case of chemical reaction with benzene excited to the triplet state. Pure dried benzene was saturated with oxygen under a pressure of 100 atm. to favour the reaction. The samples were irradiated with ultra-violet light of spectral range λ2900–3600 Å., or with the isolated mercury line λ3130 Å. In both cases the reaction took place. We examined the absorption spectra of products extracted in water or 0·01 M sodium hydroxide solution. The absorption maximum observed in alkaline solution at

285 mμ is similar to that of the phenolate anion. This spectrum reveals also the existence of a second product, probably *o*-benzoquinone. This assumption is supported by the absorption spectrum of neutral aqueous solutions in which a distinct maximum at 277 mμ was observed and by a weak positive reaction with 2,4-dinitrophenylhydrazine. The quantum yield of formation of phenol determined with the ferrioxalate actinometer is $\Phi \approx 0 \cdot 03$. The small values of the quantum yields of both reactions may be ascribed to the low stability of the primary addition products.

Recently, Loeff and Stein[5] irradiated benzene in aqueous buffered solutions and identified phenol and mucondialdehyde as reaction products. They assumed the addition of the hydroxyl radical to the unexcited benzene molecule; alternatively they mentioned the possibility of reaction of the oxygen molecule with an excited hydrocarbon molecule. However, they gave no further details.

In our experiments, the reaction investigated seems to be unambiguously that of benzene excited to the bi-radical triplet state with an oxygen molecule in the ground-state.

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Examination of γ-irradiated Benzene for Optical Activity

IN a recent communication, Starodubtsev, Gurskiy and Sizykh[1] studied optical effects in benzene resulting from its irradiation with γ-rays from a cobalt-60 source with a flux of 3×10^5 r./hr. They report in one short paragraph, which is here directly translated: "Interesting is the fact of rotation of the plane of polarization. Although the rotation is not large (0·7–0·9° at a dosage of 10^7 r. and sample thickness of 10 cm.) it nevertheless indicates the occurrence of asymmetric molecules not possessing a centre or a plane of symmetry".

This observation is potentially of great theoretical significance in that it suggests asymmetric synthesis from a symmetrical chemical reagent and, presumably, symmetrical photons. This could have a bearing on the origin of life as we know it, which is based on asymmetric molecules, and in many other fields. However, since the quoted report runs counter to currently accepted concepts of asymmetric induction and related reaction mechanisms, it was considered important to check the validity and reproducibility of the phenomenon.

For this purpose, specially purified benzene was prepared by taking reagent-grade thiophene-free benzene and subjecting it first to extraction with concentrated sulphuric acid until the washings were colourless, then washing with aqueous sodium carbonate and water, drying over potassium carbonate, fractional distillation from sodium and retaining the middle third cut, two fractional crystallizations and, finally, redistillation from potassium. This product, boiled sharply at 80·5° (uncorr.) at 748 mm., n_D^{25} 1·4981, n_D^{20} 1·5009 ± 0·0001 (compared to n_D^{20} 1·5011 ± 0·0001 reported by Starodubtsev *et al.*[1]). In a polarimeter cell of 40 cm. path length the observed rotation was 0·000° ± 0·002° at 25° for the sodium-*D* line as read on a Rudolph Hi-Precision model 80 polarimeter.

The purified benzene was carefully degassed by alternate freeze-pump-melt cycles and trap-to-trap distillation on a vacuum line. Approximately 30 ml. were distilled into a cylindrical 'Pyrex' ampoule 21 cm. × 2·5 cm. diameter fitted with a break-seal. The sample was sealed under vacuum and irradiated in a 20,000-c. cobalt-60 source of conventional design[2] at a dose-rate of $6 \cdot 0 \times 10^7$ ergs/gm. (c.)/hr.

After irradiation to an integrated dose of $3 \cdot 3 \times 10^7$ r., the sample was removed from the source and again sealed to a vacuum system. The ampoule was opened under vacuum, and an atmosphere of dry helium was admitted to the system. The sample was then opened to the atmosphere and transferred quickly to the proper cells, previously flushed with helium, for examination.

The benzene solution was light yellow in colour and had an unusual not easily describable pungent odour which obscured that of the benzene. In attempts to analyse the solution on a Burrell Kromo-tog gas chromatograph employing an 8-ft. column packed with 'Apiezon *L*' on firebrick, the benzene came off well but the odorous component was retained and could not be removed from the column at room temperature or even at 100°.

The solution after irradiation had a refractive index n_D^{25} 1·4980 ± 0·0001. An ultra-violet absorption difference spectrum was obtained on a Cary model 11*MS* double-beam spectrophotometer with the original purified benzene as the reference solvent. In a 1-cm. cell only four peaks were observed at wave-lengths between the solvent cut-off at 2800 Å. and the instrument limit at 8000 Å. These local maxima and their absorbances (in parentheses) as determined by appropriate dilutions were as follows: 4459 Å. (0·27), 4137 Å. (0·79), 3680 Å. (2·5) and 2767 Å. (38·8).

To check the report of optical activity the irradiated benzene was again examined in the polarimeter in a 40-cm. cell. The observed rotation was 0·000° ± 0·002°, identical with that found for the original unirradiated benzene.

It seems certain, therefore, that although irradiation at the dosage-level described does bring about certain significant effects (colour, spectral change, odour, among others), there is no substantiating evidence from our work that asymmetric genesis of molecules of any optically active material in appreciable amounts has occurred. Since our apparatus was sensitive enough to detect easily 0·005° rotation, this means that for the 40-cm. cell, no effect as great as even 0·2 per cent of that reported by Starodubtsev *et al.* could be found. It seems reasonable, then, to suggest that these workers inadvertently may have had either a contaminated sample or an imperfect polarimeter (in calibration or operation). Their experimental description and apparatus seem simple enough to exclude any unusual irradiation conditions.

We sincerely regret being unable to duplicate the observations of the Soviet workers since the consequences of such validation in the fields of biochemistry, biogenesis, physics, and chemistry would have

been revolutionary and would have revised many of our present concepts of molecular structure, asymmetric induction, electromagnetic interaction, etc.

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CHEMISTRY

Strength of Silica Glass

GRIFFITH[1] extrapolated from his experiments the strength of glass to the order of 1,000 kp./mm.^{2}, which is many times larger than the strength of the best steel. Orowan[2] calculated from mechanical principles a value of the same order. More recent measurements, however, gave a much higher value for several silica-glass fibres, namely, 2,460 kp./mm.^{2} (ref. 3); therefore a calculation based on the atomic structure of glass seems to be important.

Starting from the oxygen ion volume v of glass[4,5], which is in silica glass $22 \cdot 70 \times 10^{-24}$ cm.^{3}, we can calculate the number of oxygen bridges per unit cross-section. The average number of bridging oxygen ions y plus that of the non-bridging oxygen ions x which belong to one silicon ion is 4.

The average number of oxygen ions per net-forming ion (silicon, aluminium, boron, etc.) being R, then:

$$R = \mathrm{O}/(\mathrm{Si} + \mathrm{Al} + \mathrm{B} + \ldots) = x + y/2$$

since the bridging oxygen ion belongs to two net-forming ions at the same time. From the above relations:

$$y/(x + y) = 2 - R/2$$

The plane of the cube containing an oxygen ion being $v^{2/3}$, the number of oxygen ions per cm.^{2} glass cross-section is $1/v^{2/3}$ and that of the bridging oxygen ions:

$$n = \frac{2 - R/2}{v^{2/3}}$$

The strength of any glass is proportional to n if the glass is really a network of tetrahedra connected with bridging oxygen ions. Silica glass has the smallest R value, 2·00, among all silicate glasses (not containing beryllium, boron, aluminium or other network-forming ions of less than four valencies); therefore it has the highest strength, which is in accordance with the experimental facts.

The distance Si—O in silica is $r = 1 \cdot 60 \times 10^{-8}$ cm. and there is a Coulomb attraction $-8e^2/r^2$ between Si^{4+} and O^{2-}. We calculate after Kossel[6] the work necessary for the separation of an oxygen from the SiO_4 tetrahedron (so that an SiO_3 triangle remains) as the difference of formation energy of an SiO_4 ion $-17 \cdot 32e^2/r$ and that of an SiO_3 group $-17 \cdot 08e/r^2$, that is, $0 \cdot 24e^2/r$ per bridging O^{2-} ion or:

$$\frac{0 \cdot 24(4 \cdot 80 \times 10^{-10}\ \text{e.s.u.})^2}{1 \cdot 60 \times 10^{-8}\ \text{cm.}} = -3 \cdot 456 \times 10^{-12}\ \text{erg.}$$

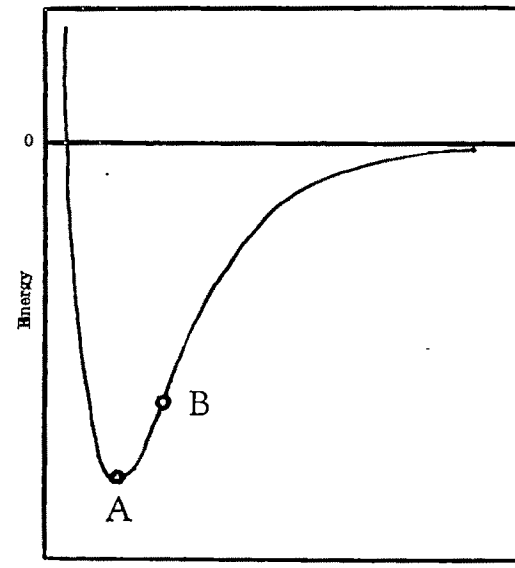

Fig. 1

In the non-periodic network of glass we approximate the potential function of the pseudo-diatomic molecule SiO_3—O by the potential function of a diatomic molecule with the well-known qualitative form of Fig. 1. At the minimum energy (A) there is equilibrium; if a stretching force is applied, the distance grows until the break of the Si—O bond occurs in the point of inflexion (B).

The potential of the pseudo-diatomic molecule SiO_3—O can be taken approximately as the Morse function:

$$U(r - r_e) = D_e\,(1 - e^{-\beta(r - r_e)})^2 \qquad (1)$$

where U denotes the energy, r_e the distance Si—O in the equilibrium, r the actual nuclear distance, D_e the binding energy in the equilibrium and β a constant. Since at the inflexion point $d^2U/dr^2 = 0$, we get from (1):

$$2e^{-\beta(r_i - r_e)} = 1 \qquad (2)$$

where r_i is the nuclear distance in the inflexion point. The force there is:

$$F_i = -\frac{dU}{dr} = [2\beta D_e\,(1 - e^{-\beta(r - r_e)})e^{-\beta(r - r_e)}]_{r = r_i} \qquad (3)$$

The numerical values in this equation are known: $r_e = 1 \cdot 60 \times 10^{-8}$ cm., $D_e = 0 \cdot 24e^2/1 \cdot 60 \times 10^{-8}$ cm. $= 3 \cdot 456 \times 10^{-12}$ erg $= 1 \cdot 74 \times 10^4$ cm.$^{-1}$ hc.; we need calculate only β. This can be done with the aid of the equation[7]:

$$\beta = 1 \cdot 2177 \times 10^7 \omega_e \sqrt{\mu_A/D_e}$$

Here μ_A, the reduced mass, must be expressed in atomic weight units ($\mu_A = 13 \cdot 22$ in the case of the pseudo-diatomic molecule SiO_3—O) and D_e in cm.$^{-1}$; ω_e is the frequency of the fundamental oscillation. On the basis of the relation[8]:

$$D_e = \frac{\omega_e^2}{4\omega_e x_e}$$

and since the anharmonicity factor of the oscillation found for the $^{28}Si^{16}O$ molecule is $4 \cdot 87 \times 10^{-3}$ (ref. 9) and taking this value as an approximation for our case, ω_e can be calculated as 339 cm.$^{-1}$. With

this the value of β becomes $1 \cdot 138 \times 10^8$. Considering (2) we get :

$$F_i = 2.1 \cdot 138 \times 10^8 . 3 \cdot 456 \times 10^{-12} (1 - 0 \cdot 5) . 0 \cdot 5 = 1 \cdot 97 \times 10^{-4} \text{ dyne}$$

for an Si—O bond in the above sense.

The strength of a silica fibre per cm.^{2} is therefore $1/v^{2/3}$ times F_i, that is, $1 \cdot 97 \times 10^{-4}$ dyne/$(22 \cdot 7 \times 10^{-24})^{2/3}$ cm.^{2} = $2\ 42 \times 10^{11}$ dyne cm.$^{-2}$, or 2,472 kp./mm.^{2}. This calculated value is closest to the maximum experimental value, 2,460 kp./mm.^{2}. Apart from the experimental errors we must consider that our calculation is based entirely on the assumption of Coulomb forces although the bond is partly covalent. It seems, therefore, that the errors due to different approximations in our calculation cancel themselves out.

The strength of asbestos fibres[10] and that of industrial glass fibres, although only of the order of 600–700 kp./mm.^{2}, is much higher than the highest strength of thin metal wires, which is about 400 kp./mm.^{2} (for thinnest tungsten wire).

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New Univalent Cobalt Complexes of the $[Co^I dg_2 X_2]$ Type

Dicyano - *bis* - dimethylglyoximato - cobaltate(III) complex, *trans*-$K[Co^{III} dg_2(CN)_2] \cdot 3/2\ H_2O$ (a new compound)[1] ($dg = H_2C \cdot C(NOH) \cdot C(NO) \cdot CH_3$), was found to be reduced at the dropping mercury electrode in one step to a univalent cobalt complex polarographically in 1 *M* potassium chloride supporting electrolyte. The following electrode process was ascertained.

$$\underset{\text{yellow}}{[Co^{III} dg_2(CN)_2]^-} + 2e^- \rightleftarrows \underset{\text{blue}}{[Co^I dg_2(CN)_2]^{3-}}$$

The resulting cobaltate(I) complex, $K_3[Co^I dg_2(CN)_2]$, was isolated from the solution as a blue compound in an atmosphere of nitrogen.

The above electrode reaction is quasi-reversible polarographically. The half-wave potential of the cathodic wave did not agree with that of the anodic one.

On the other hand, *bis*-dimethylglyoximato-cobalt(III) complexes,

$$[Co dg_2(NH_3)_2]Cl \cdot 5H_2O,\ [Co dg_2(NH_2C_2H_5)_2]Cl,\ [Co dg_2 py_2]NO_3\ (py = \text{pyridine}),$$

and so on, were found to undergo the stepwise reduction to a zero-valent cobalt complex irreversibly through cobaltate(I) complexes at the dropping-mercury electrode in the same supporting electrolyte. The main processes of the electrode reaction were concluded to be as follows :

$$[Co^{III} dg_2 X_2]^+ + e^- \longrightarrow [Co^{II} dg_2 X_2] \quad \text{1st wave}$$
$$[Co^{II} dg_2 X_2] + e^- \longrightarrow [Co^I dg_2 X_2]^- \quad \text{2nd wave}$$
$$[Co^I dg_2 X_2]^- + e^- \longrightarrow [Co^0 dg_2]^{2-} + 2X \quad \text{3rd wave}$$

where X denotes a neutral unidentate ligand, such as ammine, ethylamine, or pyridine.

On the contrary, as regards the other complexes of the type, $[Co^{III} dg_2 X_2]$, the ligand of which, X, is a negative radical or ion, only the first wave was obtained in every case, mainly due to the hindrance of a large maximum wave (Table 1).

The diffusion current and the concentration of the complex are linearly related at the concentration in the range of $10^{-3} - 10^{-4}$ *M* with respect to all the complexes.

I wish to thank Prof. R. Tsuchida for helpful discussions.

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A New Synthetic Route to Alkylphosphonous Dichlorides

IT has recently been shown[1] that electron-donating solvents such as diethyl phthalate (DEP) provide a convenient route to the synthesis of alkylphosphonic dichlorides from the complex formed by combination of an alkyl halide, phosphorus trichloride, and aluminium chloride[2]. It has since been found that alkylphosphonous dichlorides may be synthes-

Table 1. HALF-WAVE POTENTIALS OF DIMETHYLGLYOXIMATO COBALT(III) COMPLEXES (25° C.)

Complex compound	$E_{1/2}$	n	Change of valence	$E_{1/2}$	n	Change of valence	$E_{1/2}$	n	Change of valence
$[Co^{III} dg_2(NH_3)_2]Cl\ 5H_2O$	− 0 65	1	$Co^{III} \rightarrow Co^{II}$	$-1 \cdot 04_5$	1	$Co^{II} \rightarrow Co^I$	$-1 \cdot 27_2$	1	$Co^I \rightarrow Co^0$
$[Co dg_2(NH \cdot C_2H_5)_2]Cl$	− 0 66	1	$Co^{III} \rightarrow Co^{II}$	$-1 \cdot 08$	1	$Co^{II} \rightarrow Co^I$	about − 1 25	1	$Co^I \rightarrow Co^0$
$[Co dg_2 py_2]NO_3$	about − 0 22*	1	$Co^{III} \rightarrow Co^{II}$	$-0 \cdot 88$	1	$Co^{II} \rightarrow Co^I$	− 1 18	1	$Co^I \rightarrow Co^0$
$K[Co^{III} dg_2(CN)_2] \cdot 3/2H_2O$				$-1 \cdot 10_7$	2	$Co^{III} \rightarrow Co^I$			
$Na[Co^{III} dg_2(NO_2)_2]$	− 0 35	1	$Co^{III} \rightarrow Co^{II}$						
$H[Co^{III} dg_2 Cl_2]$	+	1	$Co^{III} \rightarrow Co^{II}$						
$[Co^{III} dg_2(NO_2)(OH_2)]$	− 0 15$_5$	1	$Co^{III} \rightarrow Co^{II}$						

Supporting electrolyte, 1 *M* potassium chloride; potential unit, volt versus the saturated calomel electrode; concentration of the complex, 0 005 *M*.

* Small maximum wave (in the absence of maximum suppressor).

ized from similar solutions of the complex by reduction with finely powdered antimony. The reaction scheme is:

$$RCl + PCl_3 + AlCl_3 \longrightarrow [RPCl_3]^+[AlCl_4]^- \overset{DEP}{\rightleftharpoons} RPCl_4 + [AlCl_3][DEP]$$

$$3RPCl_4 + 2Sb \longrightarrow 3RPCl_2 + 2SbCl_3$$

The reactions are exothermic and proceed smoothly in a single flask. Yields of $RPCl_2$ from 90 to 55 per cent have been obtained repeatedly for $R = CH_3$ to $R = C_5H_{11}$. Full details of the method and its application in high-activity synthesis of organophosphorus compounds labelled with radioactive phosphorus will be published elsewhere.

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Use of Spectrophotometric Evidence for Protein-Dye Binding

SHIFTS in the ultra-violet absorption spectra of aqueous organic solutions of some amino-azo dyes on the addition of buffered protein solutions have frequently been interpreted as evidence of complex formation between protein and dye[1-4]. The effect of the buffer itself on the spectrum of the dye has apparently not always been checked, and the fact that this may influence the results is shown by the following experiments.

The powerful carcinogen dimethyl-*p*-aminoazobenzene and its biologically inactive isomer monoethyl-*p*-aminoazobenzene, purified chromatographically on an activated alumina column, were investigated in approximately 10^{-4} molar solutions in 20 per cent dioxane–water mixtures, between 350 and 550 mμ, using a Unicam *SP*500 spectrophotometer. Solutions were thermostatted at 25° C. for 24 hr. to attain equilibrium before measuring the spectra at the same temperature.

The spectra of the azo-dye solutions were determined under the following conditions: (1) With the addition of hydrochloric acid (analytical reagent) to give a range of *p*H 0–5. (2) At *p*H approximately 6 maintained by the use of acetate, phosphate and phthalate buffers, immediately after preparation of the solutions and at intervals of time up to 24 hr. thereafter. (3) In acetate buffered solution at *p*H 6, in the presence of 0·1 per cent gelatin, high grade, edible (Imperial Chemical Industries, Ltd.), and of 0·1 per cent bovine plasma albumin fraction V, and on the addition of 5 ml. of concentrated solution of bovine fibrinogen fraction I, pepsin and trypsin (Armour Biochemicals, Ltd.) per 95 ml. of dye solution. (4) In unbuffered solution in the presence of 0·1 per cent bovine plasma albumin. (5) Before and immediately after shaking for 1 hr. with solid bovine plasma albumin and centrifuging off the solid.

The results of these measurements may be summarized as follows: (1) Plots of extinction coefficient against wave-length for solutions of different *p*H show an isobestic point at 475 mμ for dimethyl-*p*-aminoazobenzene and at 465 mμ for monoethyl-*p*-aminoazobenzene. The peak in the curves for the latter is shifted towards shorter wave-lengths compared with that for the former, which, according to Kubo[2], indicates a lesser ability to release electrons. (2) The spectra of the dye solutions with acetate buffer were unchanged after 24 hr., and those of the dye solutions alone were unchanged after several days, showing that dioxane had not affected the spectra. In the case of the phosphate and phthalate buffers there was a marked and progressive shift with time, up to 24 hr. at least, of the peaks of the curves for both dyes, the changes being most pronounced for solutions of dimethyl-*p*-aminoazobenzene. The shifts are similar to those expected from complex formation, but the nature of any such complex and its slow formation in the present systems seem difficult to explain. The phosphate buffer in addition caused some flattening and lowering of the peaks. This normally indicates the removal of the absorbing compound, although it is impossible to state from the present data the way in which this is occurring here. (3–5) In no case was there any change in the dye spectrum on the addition of protein whether to acetate buffered solutions or to the unbuffered solutions.

The *p*H values of all solutions remained unaltered with time, and observed spectral shifts cannot, therefore, be ascribed to changes in *p*H.

In view of the observed effects of certain buffers on the spectra of the azo-dyes used here, a re-examination of some of the earlier findings seems desirable, together with a more extensive investigation of the effect of these and other buffer solutions on the spectra of such systems.

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BIOCHEMISTRY

Enzymatic Degradation of Deoxyribonucleic Acid into Sub-units

THE generally accepted value for the molecular weight of deoxyribonucleic acid is 6–8 × 10^6 (refs. 1 and 2). In the course of a study of methods of preparation involving extraction with solutions of low ionic strength, it has been found that, under a given set of experimental conditions, preparations from chicken erythrocytes could be obtained which showed reproducibly lower molecular weights (Champagne, M., unpublished work). This finding is reminiscent of some results scattered in the literature[3] and suggestive of some enzymatic activity involving depolymerization of deoxyribonucleic acid. An investigation was therefore undertaken of the action on deoxyribonucleic acid of preparations from chicken erythrocytes.

Two preparations of deoxyribonucleic acid were mainly used in this work: *B1s* from calf thymus

($M_w = 6 \cdot 5 \times 10^6$, $S^0_{20,w.av.} = 20\,S$) and $B2$ from chicken erythrocytes ($M_w = 8 \cdot 0 \times 10^6$; $S^0_{20,w\,av} = 27 \cdot 5\,S$). The crude enzymatic preparations were obtained as follows. Erythrocytes separated by centrifuging one volume of chicken blood, to which half a volume of heparinized 0 15 M sodium chloride – 0·01 M sodium citrate had been added, were lysed with 0·1 per cent saponin in this saline–citrate solvent, then rapidly washed once with distilled water, centrifuged, suspended in distilled water (2 5 vol. per vol. of blood) and shaken overnight in the cold room. The yellowish, viscous, homogeneous suspension was used on the following morning: 1 ml. (containing 3 mgm. nucleoprotein and 3 mgm. protein) was incubated with 30-ml. samples of 0·05 per cent deoxyribonucleic acid in 0·15 M sodium chloride, pH = 5·3.

At the end of digestion, samples were clarified by high-speed centrifugation, then dialysed against M sodium chloride and used for physical measurements and chemical analyses. The final recovery of deoxyribonucleic acid was 80–90 per cent, the losses being accounted for by the co-precipitation of an aliquot of deoxyribonucleic acid with the protein present in the enzymatic preparation.

It was found that very marked changes in the physical properties of deoxyribonucleic acid take place in the first few hours of enzymatic digestion. After 24–48 hr. at 37° C., however, no further significant changes are detectable, even on extending the time of digestion to 120 hr. The molecular weight of the final product was found to be $M_w = 5 \cdot 5 \pm 0 \cdot 5 \times 10^5$. The light-scattering results from it are compatible with a solution of monodisperse rods, having a molecular weight per unit length, M/L, of 200 ± 20/Å., a value which is in very good agreement with the Watson and Crick model for deoxyribonucleic acid[4]. A much higher degree of molecular asymmetry in the final, as compared with the starting, product was also indicated by Couette viscosimetry. The behaviour of the sedimentation constant parallels the drop in molecular weight. The value $S^0_{20,w.av.} = 5 \cdot 8\,S$ finally attained is also indicative of rod-like sedimenting units. Concurrently, the distribution function of sedimentation constants is remarkably narrower in the degraded deoxyribonucleic acid than in the starting preparations.

By using buffers of pH = 4·5–9·0 ($\mu = 0 \cdot 15$) as solvents for the deoxyribonucleic acid, it was observed that the enzymatic activity shows a very pronounced optimum close to 5·5. No degradation of deoxyribonucleic acid was evident at pH 7·0 or higher, in the presence of 0·03 M magnesium chloride (in 0·15 M sodium chloride, pH 5·3), at ionic strength $\mu = 0 \cdot 001$ or $\mu = 1 \cdot 0$ (sodium chloride, pH = 5·3), or when the crude enzymatic preparation had been previously kept 5 min. at 100° C.

It was also possible to show that, during the enzymatic digestion, no dialysable nucleotides were produced, and no significant changes of the absorption coefficient at 260 mμ were detectable. No differences were found between degraded $B1s$ and $B2$, although the degradation of the former was slower than that of the latter.

It is evident from the above results that the fragments obtained by the enzymatic digestion of deoxyribonucleic acid investigated in this work do not originate in a random breakdown All available experimental evidence suggests that they are true sub-units of the larger deoxyribonucleic acid particle, $M_w = 6$–8×10^6. How these sub-units are bound together, what is the nature of their end-groups and whether they possess the same biological properties as the parent molecules are not yet known, and are now being investigated. It is likely, however, that the rod-like sub-units are connected in an end-to-end arrangement by some 'flexible joints' (sites of the enzymatic action) to form the larger deoxyribonucleic acid particle. It has already been shown that the light-scattering data for the latter are compatible with such a model[5].

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Effect of Glucose Concentration on Respiration of Rous Sarcoma and of Chorioallantoic Membrane

CRABTREE'S initial observation that glucose will depress the oxygen consumption of tumour cells has prompted further investigations of this phenomenon, most particularly in Ehrlich ascites cells[1] and in reconstructed systems[2]. It has been recently reported[3] that the virus-induced Rous sarcoma on the chorioallantoic membrane of chicken embryos shows a 'Crabtree effect'. The present communication reports the effect of glucose at various concentrations on the respiration of normal chorioallantoic membrane, and of Rous sarcoma growing on it, and extends the initial observations in this system to other parameters of glucose metabolism.

Standard lot *CT* 842 of Rous sarcoma virus was obtained from Dr. W. Ray Bryan and was stored in a 'dry-ice' chest until used. An inoculum of 0·2 ml. at a dilution of one-tenth of thawed virus in cold sterile saline solution containing 2 per cent inactivated horse-serum was dropped on to the chorioallantoic membranes of chicken embryos 9–10 days old by the false air-sac technique. Incubation at 36° C. during 6–7 days yielded Rous sarcoma. Control chorioallantoic membrane was prepared in the same manner except that virus was not added to the inoculum.

Chorioallantoic membranes used as normal controls were excised aseptically from embryos 16–17 days old. The tissue was cut into small pieces and washed thoroughly in cold saline. Tissue pieces of approximately 1 cm. square were removed from washing solution, blotted briefly on filter paper, and approximately 200 mgm. of wet tissue was added to each Warburg vessel. Rous sarcoma was dissected free of non-tumorous tissue and sliced with a Stadie-Riggs hand microtome. Tissue slices were washed likewise in cold saline and blotted on filter paper.

Tissues were incubated in a final volume of 2 ml. with Hanks's balanced salt solution in the absence of added bicarbonate, and without phenol red indicator. The pH was adjusted to 7·6 with dibasic phosphate ($M/15$). Glucose concentration in the medium was

Table 1. OXYGEN CONSUMPTION OF NORMAL CHORIOALLANTOIC MEMBRANE AND OF ROUS SARCOMA GROWN ON CHORIOALLANTOIC MEMBRANES

All values are expressed as μl of gas per mgm. dry tissue per 4-hr. incubation period. Each value represents the average of duplicate determinations

Initial glucose (μmoles/ml.)	0	2·5	10	50
Chorioallantoic membrane	17·8	22·0	18·8	18·4
	18·0	21·0	16·8	18·4
	17·6	21·0	16·4	17·2
Rous sarcoma	7·2	5·6	7·2	6·0
	9·2	5·2	4·8	3·6
	8·6	4·4	5·2	5·6

varied from 0·5 to 50 mM. Air was the gas used in this manometric work. Initial and final glucose concentrations were determined on aliquots from the reaction vessels.

The manometric results of uninfected chorioallantoic membrane and of chorioallantoic membrane infected with Rous sarcoma virus are summarized in Table 1 and in Fig. 1. While glucose was without effect in depressing the oxygen consumption of chorioallantoic membrane, the respiration of Rous sarcoma was depressed by all concentrations of glucose tested. The results (Fig. 1) are suggestive of an increased depression of oxygen consumption with an increase in glucose concentration from 0·5 to 1·0 mM.

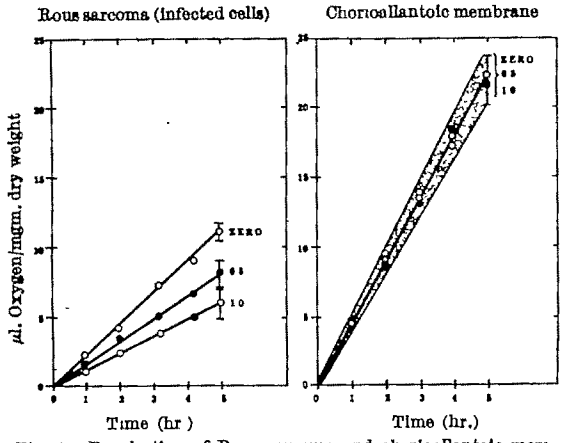

Fig. 1. Respiration of Rous sarcoma and chorioallantoic membrane in the absence and presence of glucose (0·5 and 1·0 μmole/ml.). Each curve represents the mean of three experiments

Respiration of the tissue was linear over a 5-hr. period, and no diminution of the glucose effect was observed with time. No further decrease in oxygen consumption of Rous sarcoma was observed with concentrations of glucose greater than 1 mM.

The utilization of glucose by both the chorioallantoic membrane and the Rous sarcoma was increased with increasing concentrations of medium glucose (Table 2). The Rous sarcoma uses much more glucose than the chorioallantoic membrane. However, the degree of depression of oxygen consumption observed in the Rous sarcoma is not necessarily related to the glucose utilization, that is, an increase in glucose utilization from 0·12 to 1·01 μmoles per mgm. dry tissue per 4 hr. did not result in increased depression of oxygen consumption.

Table 2. EFFECT OF SUBSTRATE CONCENTRATION ON GLUCOSE UPTAKE BY NORMAL CHORIOALLANTOIC MEMBRANE AND ROUS SARCOMA GROWING ON THE CHORIOALLANTOIC MEMBRANE

All values are expressed as μmoles per mgm. dry tissue per 4-hr. incubation period. Each value given is the average of six experiments

Initial glucose (μmoles/ml.)		2·5	10	50
Chorioallantoic membrane		0·08	0·17	0·69
	S.E.	± 0·01	± 0·03	± 0·09
Rous sarcoma		0·12	0·31	1·01
	S.E.	± 0·01	± 0·04	± 0·06

Thus it would appear that the Rous sarcoma virus offers a means of investigating the metabolic events in the induction of neoplastic growth. A comparison of biochemical changes between infected and non-infected cells is expected to reveal differences existing between normal and neoplastic tissues. The Rous sarcoma system offers a means by which sequential metabolic alterations may be observed during tumour development and growth.

The effect of glucose present at various concentrations has been investigated in Ehrlich ascites cells[4,5]. McKee *et al.*[4] have reported that glucose at very low concentrations stimulates oxidative metabolism of these cells and inhibits oxidative metabolism at higher concentrations. Glucose in 5·5 m.moles quantity produces a 'Crabtree effect' in ascites cells during the first hour of incubation, but the depression of oxygen consumption is not observed after this time, during which all the medium glucose was utilized. Block-Frankenthal and Ram[5] have observed no 'Crabtree effect' in ascites cells incubated with 2·5 m.moles of glucose, but a depression of oxygen consumption occurs with 10 m.moles. Further, it has been observed that with 2·5 m.moles of glucose, Ehrlich ascites cells completely utilize all the substrate during the initial equilibrium period[6]. Differences in effective concentrations of substrate in the ascites tumour and the Rous sarcoma may be due in part to the rate with which glucose of the same concentration (2·5 mM.) was utilized. Rous sarcoma uses less than 50 per cent of the added glucose during a 4-hr. incubation period.

Since the Rous sarcoma utilizes appreciably more glucose than the normal chorioallantoic membrane control, the possibility exists that a decreased rate of oxygen consumption by the tumour may be the result of increased glucose utilization.

It has been proposed that increased glycolysis may inhibit oxygen consumption by reducing the intracellular concentrations of inorganic phosphate and adenosine diphosphate[6]. Considering only tumour tissue, it would appear that within certain limits an increase in glucose will cause a further depression of oxygen consumption. However, if the effect of this sugar on the metabolism of normal cells is considered it would appear unlikely that glucose utilization *per se* can depress uptake of oxygen, since increasing the concentration of the substrate in the medium containing normal tissue will increase glucose utilization without changing the respiration.

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Crystalline Dihydropteroylglutamic Acid

THE preparation of dihydropteroylglutamic acid has previously been described by O'Dell *et al.*, who used catalytic hydrogenation of pteroylglutamate[1], and by Futterman, who carried out the reduction with sodium dithionite[2]. The acid prepared by catalytic hydrogenation is unsuitable for many biochemical studies, however, because it contains traces of tetrahydropteroylglutamic acid[3]. The material obtained by the method of Futterman is an amorphous discoloured preparation[2], but was found to be uncontaminated by tetrahydropteroylglutamic acid[3]. No analytical figures have been given for this material. By reducing purified pteroylglutamate with sodium dithionite according to the method of Futterman and twice precipitating the product by slow adjustment of the *p*H between strictly defined values, it has now been found possible to obtain dihydropteroylglutamic acid consistently as a white crystalline product giving analytical results agreeing fairly well with the theoretical values.

The procedure adopted was as follows. Ascorbic acid (1 gm.) was dissolved with mechanical stirring in about 5 ml. of water in a 25-ml. beaker. While stirring continued and continuous readings of the *p*H were made with a glass electrode 1 *N* sodium hydroxide was added slowly until the *p*H rose to 6·0. The volume of the solution was brought to 10 ml. by the addition of water and a solution of 38·2 mgm. of pteroylglutamic acid (purified as previously described[4]) in 1·6 ml. of 0·1 *N* sodium hydroxide added. Mechanical stirring was recommenced and 400 mgm. of solid sodium dithionite added. When all the dithionite had dissolved stirring was continued slowly for 5 min. at room temperature (22–25°). An ice-bath was then placed around the beaker and stirring continued until the temperature had fallen below 5°. Addition of 1 *N* hydrochloric acid from a burette at a rate of approx. 0·1 ml./min. was then commenced while the solution was stirred rapidly at 0–5°. Addition of hydrochloric acid was continued until the *p*H fell to 2·8 (approx. 5 ml. of 1 *N* hydrochloric acid required). After stirring the solution for a further 5 min. to allow complete precipitation, the precipitate was recovered by centrifugation (5 min. at 1,000*g*, temperature 0°) and the supernatant discarded. The precipitate, which was mainly amorphous but contained some crystalline material, was re-suspended in 10 ml. of an ice-cold solution of 10 per cent sodium ascorbate, *p*H 6·0, freshly prepared as previously described. The suspension was returned to a 25-ml. beaker cooled in a nice-bath and mechanical stirring and continuous *p*H measurement recommenced. The bulk of the precipitate redissolved at this stage and the solution was between *p*H 5 and 6. If necessary the solution was adjusted to *p*H 6 by cautious addition of 1 *N* sodium hydroxide, and maintained at this *p*H while being stirred at 0° for a further 5 min. Under these conditions only crystalline material remained undissolved, causing marked birefringence. The dissolved dihydropteroylglutamic acid was crystallized from the solution by slow addition of 1 *N* hydrochloric acid performed exactly as previously. When crystallization was complete (5 min. after reaching *p*H 2·8) the heavy, white, birefringent suspension was centrifuged off as before and washed three times with ice-cold 0·001 *N* hydrochloric acid by suspending and centrifuging. After pipetting off the final supernatant the precipitate was quickly dispersed over the walls of the centrifuge tube, placed in a desiccator over phosphorus pentoxide and potassium hydroxide and the pressure quickly reduced to 0·02 mm. mercury. The solid, which was initially white, was stored in the desiccator in the dark until required. It became discoloured while stored in this way over a period of days, and discoloured even more rapidly when removed from the desiccator. Under the microscope the crystals appeared as fine, very small needles (Fig. 1). After preparation, a sample for analysis was dried for 16 hr. over phosphorus pentoxide (pressure 0·02 mm. mercury) at 25°, rather than at higher temperatures, in order to avoid decomposition. Calculated for $C_{19}H_{21}O_6N_7.2\frac{1}{2}H_2O$: C, 46·72 ; H, 5·37 ; N, 20·08 per cent. Found : C, 47·57 ; H, 5·62 ; N, 19·61

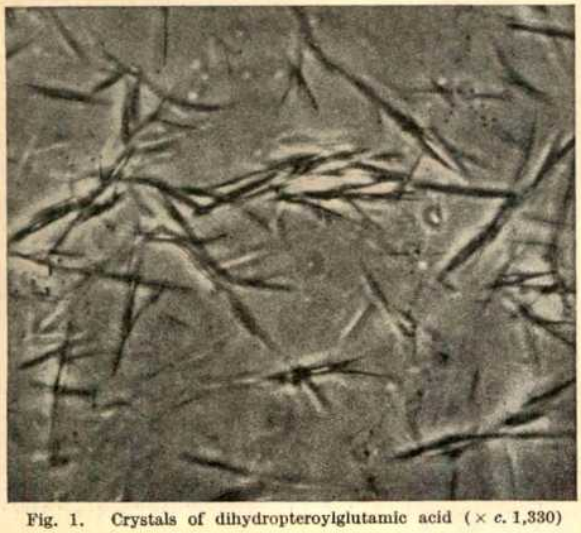

Fig. 1. Crystals of dihydropteroylglutamic acid (× *c.* 1,330)

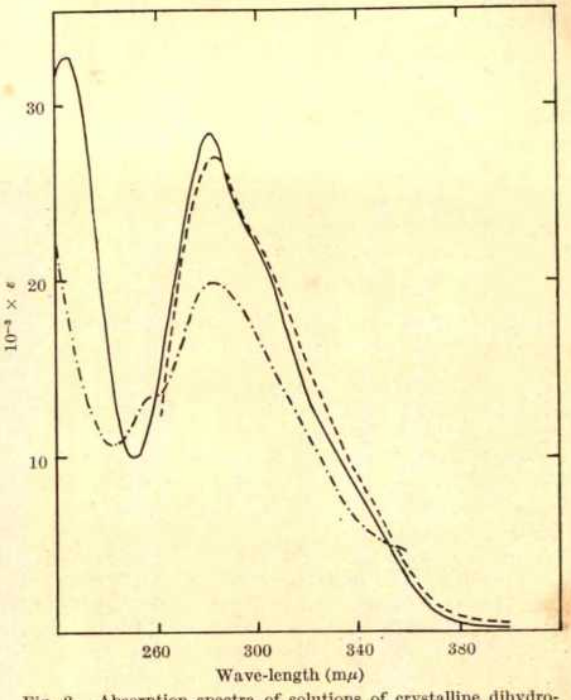

Fig. 2. Absorption spectra of solutions of crystalline dihydropteroylglutamic acid (0·03 m*M*) in 0·1 *M* potassium phosphate buffer (——); in 0·01 *N* sodium hydroxide (– –); and in 0·1 *N* hydrochloric acid (–.–.–)

per cent. Absorption spectra for the crystalline material are shown in Fig. 2.

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Identification of 19-Norandrostenedione in Follicular Fluid

DURING the course of a recent investigation of the steroids present in the follicular fluid of the mare[1], an unidentified $\alpha\beta$-unsaturated 17-ketosteroid was detected, and it seemed possible that this might represent one of the intermediates in the conversion of androst-4-ene-3,17-dione (androstenedione) to œstrone.

Further work on this compound has now established its identity as 19-norandrost-4-ene-3,17-dione (19-norandrostenedione), the evidence being as follows: (1) R_F value of the unknown compound identical with that of authentic 19-norandrostenedione in ligroin/80 per cent methanol and hexane: benzene/formamide paper chromatographic systems; (2) ultra-violet, sulphuric acid and sulphuric acid–ethanol chromogen spectra of the unknown identical with those of authentic 19-norandrostenedione; (3) R_F value of the sodium borohydride reduction product of the unknown identical with the R_F value of 19-nortestosterone in a ligroin/80 per cent methanol chromatographic system; (4) R_F value of the acetate of this reduction product identical with that of 19-nortestosterone acetate in ligroin/80 per cent methanol and hexane/formamide systems; (5) failure of the unknown to be oxidized by chromium trioxide in pyridine, or acetylated by acetic anhydride in pyridine; (6) Zimmermann colour reaction of the unknown identical with that of authentic 19-norandrostenedione; (7) infra-red spectrum of the unknown identical in every respect with that of authentic 19-norandrostenedione.

Since there still remained the possibility that this compound might have been an artefact produced by the action of alkali on 19-hydroxyandrost-4-ene-3,17-dione, 20 μgm. of the latter substance was added to a sample of follicular fluid prior to extraction; however, this did not increase the amount of 19-norandrostenedione present in the final extract.

With the exception of two œstranediols reported by Marker *et al.*[2] in non-pregnant human urine, this is the first time that a non-aromatic 19-nor steroid has been found as a natural product. The mean concentration in eight samples of equine follicular fluid was 20 μgm./100 ml. fluid (range 4–45 μgm./100 ml.), and since it is present in considerable amounts, it is interesting to consider its possible biological significance.

It is now well established that androstenedione serves as a precursor in the biosynthesis of œstrogens, and as a result of *in vitro* studies with a number of endocrine tissues, it was suggested[3] that 19-hydroxyandrostenedione was an intermediate in this conversion. This has now been amply confirmed[4,5], and it has been shown that human placental microsomes *in vitro* can convert androstenedione to œstrone via 19-hydroxyandrostenedione. Since 19-oxoandrostenedione is also readily converted to œstrone, the following biosynthetic sequence has been proposed[6]:

androstenedione → 19-hydroxyandrostenedione → 19-oxoandrostenedione → œstrone

If the results of these *in vitro* experiments with human placental microsomes are an accurate reflexion of the events taking place in the ovary *in vivo*, one might expect to find 19-hydroxyandrostenedione and 19-oxoandrostenedione in follicular fluid. However, this is not the case; repeated attempts to identify 19-hydroxyandrostenedione in large quantities of equine follicular fluid have met with negative results, although recoveries of the pure steroid are satisfactory. Neither is there as yet any evidence to suggest that 19-oxoandrostenedione is present in equine follicular fluid. These negative results could be ascribed to the fact that both intermediates are so rapidly converted to œstrone that they do not accumulate in the ovary. It would be tempting to conclude that in the mare's ovary 19-norandrostenedione serves as an alternative intermediate in the conversion of androstenedione to œstrone. However, it must be remembered that 19-nortestosterone is a relatively inefficient œstrogen precursor *in vitro*[4].

I wish to express my thanks to Dr. R. K. Callow and Mr. Paul Miners for carrying out the infra-red analysis. Reference samples of 19-hydroxyandrostenedione and 19-norandrostenedione were kindly supplied by Dr. Maximilian Ehrenstein (Philadelphia) and the Medical Research Council Steroid Reference Collection (Dr. W. Klyne).

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Isolation of Purified Trichophytin

COMMERCIAL preparations of trichophytin[1] are generally aqueous extracts of the fungal mycelium (for example, *Trichophyton mentagrophytes*) together with a proportion of the culture medium. They thus contain a variety of substances which are not specific to trichophytin sensitivity and which may contribute in a variety of ways to the production of the skin reaction. In order to limit this non-specific response and to define the significance of the trichophytin reaction, an attempt has been made to isolate the antigenic material in a purified form and to obtain preliminary data as to its constitution.

The fungus, *Trichophyton mentagrophytes* (N.T.C. *D*281), was grown in a medium containing glucose (50 gm.), 1 per cent ammonium sulphate (100 ml.), 1 per cent sodium nitrate (100 ml.), 5 per cent acid hydrolysed casein (100 ml.), trace metal ions (1 ml.; ferrous sulphate, 200 mgm.; manganous sulphate, 100 mgm.; zinc sulphate, 100 mgm. in water, 100 ml.) and solutions *A* (540 ml.) and *B* (105 ml.) of

Krebs–Ringer phosphate[2]. After 4–6 weeks, the mycelium was collected, rinsed in distilled water and dried with acetone. Batches of this material were then extracted severally in an 'Ato-mix' with a variety of solvents including *M* sodium chloride, 5 per cent trichloracetic acid and ethylene glycol, filtered through 'Filtercel', dialysed and freeze-dried. All such extracts were antigenically active, but that produced by ethylene glycol extraction ('crude trichophytin') was preferred, since it combined high antigenicity with a low irritant content as determined on sensitized and control guinea pigs. The quantitative yield of 'crude trichophytin' from the acetone-dried mycelium was approximately 10 per cent using two extractions, 80 per cent of this being obtained in the initial extract. Crude trichophytin contained carbohydrate[3] and protein[4] in the ratio 10 : 1 (glucose and crystalline egg albumin as standards). Separation of crude trichophytin by paper electrophoresis in borate buffer *p*H 10 and treatment with the periodate–Schiff's reagent usually showed one major component together with an occasional faint second band moving rather faster towards the anode.

Purification of 'crude trichophytin' was effected by precipitation as a borate–'Cetavlon' complex[5]. Crude trichophytin was dissolved in water (500 mgm./30 ml.) and equal volumes of 'Cetavlon' (B.D.H. 10 per cent) and borate buffer (*p*H 7, 1 per cent) added. *N* sodium hydroxide was then added until precipitation occurred (*p*H 9–10). The precipitate was washed with water, dissociated by solution in 2 *N* acetic acid and poured into ethanol. The resulting precipitate was washed successively with acetic acid–ethanol mixture, ethanol, ether, and dried ('Cetavlon' precipitated fraction). Any borate and 'Cetavlon' ions which remained were removed by passing an aqueous solution down a column of 'Zeokarb 225 (H^+)', dialysing the eluate and recovering the active material by freeze-drying to give purified trichophytin. The non-specific elements of the reaction, indicated by control animals, were almost completely eliminated while the biological response of both 'immediate' and 'delayed' reactions were practically undiminished, in guinea pigs sensitized by the injection of powdered sterile mycelium suspended in Freud's adjuvant (Table 1). Testing solutions could be ampouled and boiled for sterilization, thus avoiding the use of preservatives. Such 'purified trichophytin' showed only one component on paper ionophoresis in borate buffer *p*H 10.

Table 1. PURIFICATION OF TRICHOPHYTIN

Fraction	Guinea pig	Mean delayed reaction diameters ± *S.E.* at concentration of 0·2 mgm./ml.
Ethylene glycol extract (crude trichophytin)	Sensitized	10·8 ± 0·8
	Control	4·5 ± 0·9
'Cetavlon' precipitated fraction	Sensitized	8·6 ± 0·8
	Control	2·4 ± 0·4
Purified trichophytin	Sensitized	9·3 ± 1·5
	Control	0 ± 0

Special care was taken in the removal of the 'Cetavlon' since although the detergent itself appeared innocuous when skin tested in humans at a concentration of 0·1 mgm./ml., its complex with trichophytin produced violent skin reactions. This effect was not apparent when the preparation was first tested in guinea pigs. Passage down 'Zeokarb 225 (H^+)' ensures the complete removal of all the 'Cetavlon' and allows the purified trichophytin to be tested with confidence.

Ultracentrifugal analysis of trichophytin indicates that it has a relatively low molecular weight : 20,000–30,000. Chromatographic analysis of its hydrolysate showed it to contain glucose, mannose and the amino-acids leucine, valine, alanine, glycine, serine, threonine, glutamic acid, aspartic acid and arginine. Evidence from optical rotation ($[\alpha]_D + 88°$ in water) and infra-red spectra (absorption at 838 cm.$^{-1}$) indicated that these sugar residues (equivalent[6,7] to an 80 per cent polysaccharide content) were linked α-glycosidically. The purified trichophytin stained blue ($\lambda_{max.}$ 600 mμ) with iodine. Since this property was destroyed by incubation with α-amylase although antigenic activity was still retained, some at least of the glucose residues were probably present in a mould starch impurity. The ultra-violet absorption spectra of purified trichophytin showed a shallow peak at 270–280 mμ corresponding approximately to a 10 per cent peptide content. Trichophytin contained nitrogen 1·05 per cent (Kjeldahl). Peptide linkages were indicated by infra-red absorption peaks at 1,634 cm.$^{-1}$ (C=O) and 1,510 cm.$^{-1}$ (N—H) since N-acetamido sugars[8] were absent. Purified trichophytin was found to be free from nucleic acid[9,10].

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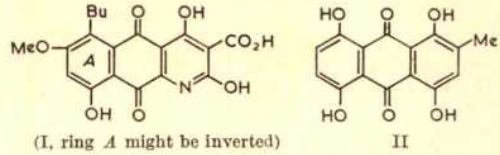
The Pigment of *Phoma terrestris* Hansen

SOME years ago Kögl *et al.*[1] reported the isolation from the fungus *Phoma terrestris* Hansen of a pigment which was named phomazarin. On the basis of degradation studies structure (I) was adopted for this pigment :



(I, ring *A* might be inverted) II

This representation attributed to phomazarin an aza-anthraquinone nucleus which would make it unique among natural products.

Accordingly, we have re-examined a culture of *Phoma terrestris* Hansen, obtained from the Central-

bureau voor Schimmelcultures (Baarn), and grown exactly as described by Kögl. There was isolated from the mycelium, by simple extraction processes, about 1 per cent by weight of cynodontin (II), m.p. 260° (found: C, 63·1; H, 3·9; $C_{15}H_{10}O_6$ requires C, 63·0; H, 3·5 per cent), readily identified as its tetra-acetate, by its infra-red spectrum, and by comparison with an authentic specimen kindly provided by Sir Alexander Todd.

Our experiments suggest the presence of at least one other pigment, but of no compound resembling phomazarin.

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HISTOCHEMISTRY

Enzymes Histochemically Demonstrable in the Earliest Phase of Wound Healing

During my work on local reactions in acutely injured skin, I was attracted by the early appearance of certain enzymes in the healing wound. Most authorities consider that in wound healing there is initially a metabolically inert lag phase of 1–4 days duration. Relatively little is known about the first appearance of enzymes during this phase. Balazs and Holmgren[1] found alkaline phosphatase at the wound margin 24 hr. after the injury. Fell and Danielli[2] and Firket[3] demonstrated during the lag phase that this enzyme was only present in the invading polymorphonuclear leucocytes. Needham[4] considered that acid phosphatase probably plays no part in repair. To the best of my knowledge there has been no previous report of the distribution of leucine aminopeptidase during the lag phase of healing.

I made an experimental study on guinea pigs, cutting circular skin wounds, 5 mm. in diameter, in a closely shaved dorsal area. The skin inside the circle was excised with fine scissors and the wounds were not covered. Groups of animals were killed ½, 1, 2, 4, 8, 16, 32, 64 and 128 hr. after wounding, and a flap of skin containing the circular wound was removed immediately. One-half of each skin flap was fixed overnight in cold neutral 10 per cent formalin. Cryostat sections, 10μ in thickness, of these halves were used for the histochemical demonstration of phosphatases. By means of coupling azo dye techniques, acid phosphatase[5] activity was visualized at *p*H 5·0 and alkaline phosphatase[6] at *p*H 9·2. The other half of the skin flap was frozen fresh and cryostat sections of it were stained for leucine aminopeptidase[7].

Leucine aminopeptidase activity was found to be present as little as 2 hr. after the injury (Fig. 1), gradually increasing up to 32 hr. There was a distinct positive area in the dermis a little beyond the wound edge. In addition to this, the lower layers of the stratum Malpighii showed moderate activity.

A little beyond the edge of the wound a clearly distinguished dermal zone exhibited strong acid phosphatase activity, beginning in a 4-hr. wound (Fig. 2) and increasing up to 16 hr. The uninjured epidermis showed intense activity all through the stratum Malpighii.

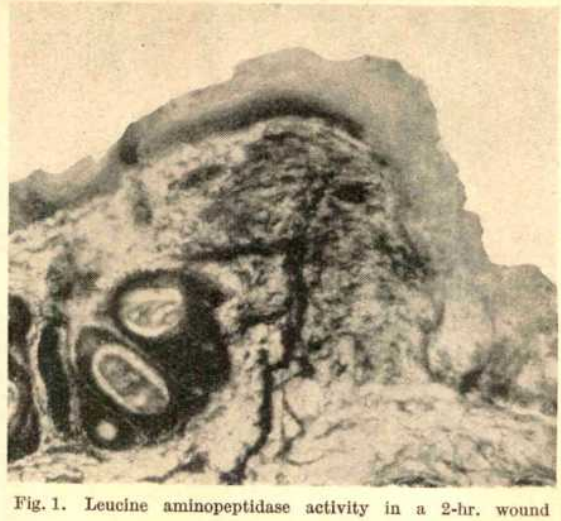

Fig. 1. Leucine aminopeptidase activity in a 2-hr. wound

An active zone in the vicinity of the injured dermis could also be demonstrated in an 8-hr. wound by the technique for alkaline phosphatase (Fig. 3). The activity increased up to 32 hr. None of the epidermal strata nor the hairs showed any demonstrable alkaline phosphatase activity in the uninjured skin.

Except for some solitary invading polymorphonuclears, no distinct leucocytic zone was visible until 16–32 hr. had elapsed. These cells occupied almost the same area as had shown intense activity of enzymes much earlier. Thus leucocytes cannot be

Fig. 2. Acid phosphatase activity in a 4-hr. wound

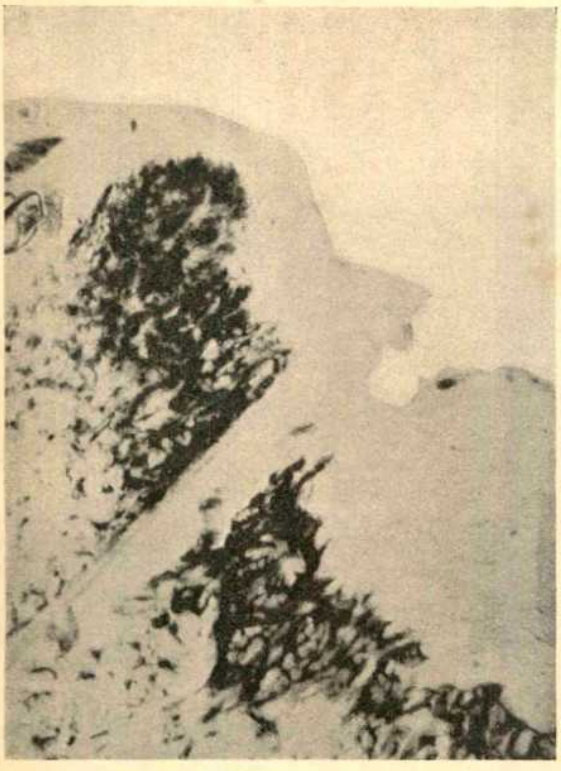

Fig. 3. Alkaline phosphatase activity in an 8-hr. wound

the main source of these enzymes. On the other hand, the most severely injured inner area of the wound showed no demonstrable enzyme activity. Consequently I suppose that the enzymes are not passively released by the seriously damaged cells in the innermost part of the wound. By contrast, in the outer zone the local cells are still able actively to produce enzymes in large amounts. The slight injury to the outer zone might serve as a stimulus activating local defence forces.

Besides functioning as a defence barrier, the enzymes appearing in the outer zone of the wound periphery may play a part in more specific regenerative processes. A synthetic action has been ascribed to leucine aminopeptidase[8], acid phosphatase[9] and alkaline phosphatase[10]. It seems probable, therefore, that the production of these enzymes represents one of the first steps in the repair process starting early in the so-called lag-phase of wound healing.

A more detailed investigation is in progress, the results of which will be published elsewhere.

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PHYSIOLOGY

Argininosuccinase Activity in Brain Tissue

A NEWLY recognized form of mental deficiency, probably caused by an inborn error of metabolism, has been described[1]. The unknown metabolite, now known to be argininosuccinic acid[2], found in this disease was present in the plasma, cerebrospinal fluid and urine. The concentration of this amino-acid was higher in the cerebrospinal fluid than in the plasma, suggesting that the compound is formed in the brain or some other organ in close association with the fluid. Apart from these patients, argininosuccinic acid has never yet been found, even in traces, in plasma, cerebrospinal fluid or urine of man or rats, nor can it be detected in extracts of rat liver, kidney or brain.

The compound was first described by Ratner, Petrack and Rochovansky[3] as an intermediate in the urea-cycle. Ratner and her colleagues described two enzyme activities concerned with metabolism of argininosuccinic acid present in liver and kidney tissue[4,5]. We have found that one of these, argininosuccinase, which catalyses the reaction :

$$\text{argininosuccinic acid} \rightleftharpoons \text{arginine} + \text{fumaric acid}$$

is also present in homogenates of rat brain, spleen and blood cells (but not in plasma) and in ox retina. Walker[6] has also reported argininosuccinase activity in brain, testis, spleen, pancreas, thymus, heart and skeletal muscle of the dog.

Argininosuccinic acid can be separated from other amino-acids by high-voltage electrophoresis on filter paper at *p*H 5 (ref. 7). Using this technique it can be demonstrated that argininosuccinic acid is formed when homogenates of the above tissues are incubated with arginine and fumaric acid at *p*H 7·5 and that ornithine is formed when the homogenates are incubated with argininosuccinic acid in the presence of added arginase.

A method similar to that described by Ratner[8] was used to estimate the argininosuccinase activity in rat brain and liver and also to study its distribution in various regions of the brain. A series of tubes, each containing 50 μM potassium phosphate buffer *p*H 7·5, arginase, at least 6 Van Slyke–Archibald units[9], and 3–15 μM argininosuccinic acid, in 0·5 ml., were prepared and warmed to 37° C. Rat tissue, obtained immediately after the death of the animal, was homogenized in seven volumes of ice-cold water or 0·1 *M* potassium phosphate buffer, *p*H 7·5. The homogenate was brought to 37° C. 1·0 ml. of 20 per cent metaphosphoric acid was added to the first tube followed by 0·5 ml. of homogenate. This tube was used for the zero value. 0·5 ml. homogenate was added to each of the other tubes, which were left to incubate at 37° C. for suitable intervals of time (for brain 20, 40, 60 min. during which time urea production was linear) before the reaction was stopped by the addition of 1·0 ml. of metaphosphoric acid. After centrifuging, urea was estimated in 0·5 ml. of the supernatants using Archibald's method as described by Ratner[8], except that 2·0 ml. acid reagent and 0·1 ml. of a 3 per cent alcoholic α-*iso*nitrosopropiophenone solution were used. Two series of control tubes : (1) as for whole system minus argininosuccinic acid ; (2) as for whole system minus homogenate, were run simultaneously.

Argininosuccinase activity was calculated from the urea formed in the experimental series, minus that of

the controls. From eight estimations, using male rats of the Wistar albino strain weighing 150–180 gm., the average activity of brain tissue was 2·2 μM/hr./gm. wet tissue (standard deviation 0·6) and for liver 200 μM/hr./gm. wet tissue (standard deviation 80). The activity observed in blood is less than 5 per cent of that of the brain of the same animal, so the activity observed for the brain cannot be attributed to included blood.

Using pig brain, all regions, so far as can be determined on a macro-scale, as well as the spinal cord and the meninges have some argininosuccinase activity. The cerebrum has only 40 per cent and the brain stem 70 per cent of the activity of the cerebellum per gram wet tissue (Table 1). An attempt has been made to localize further these activities. No difference could be found in the various regions of the cerebrum; but the white matter always had lower activity than the grey. A similar difference in activity between the white and grey matter of the cerebellum was not observed. The arginase activity of the pig brain homogenates was also determined, and was found to be distributed differently. The cerebrum and cerebellum have approximately the same activity and in both the activity is greater in the grey than in the white matter. This difference is eliminated if the arginase activity is determined in the presence of added manganese.

Table 1. DISTRIBUTION OF ARGININOSUCCINASE AND ARGINASE ACTIVITIES IN PIG BRAIN

Region	Argininosuccinase (μM/hr./gm. wet tissue)	Arginase (μM/hr./gm. wet tissue)
Whole brain	1·5	10·1
Cerebrum, grey	1·3	11·6
white	0·9	8·6
Cerebellum	3·2	11·9
Brain stem	2·3	7·3

The observed distribution of argininosuccinase activity in brain tissue (though it may be due to the distribution of an unrecognized co-factor, or to an inhibitor) is probably a reflexion of the cell densities of the various regions. It seems likely, however, that the activity of some cell types may be greater than others, for the cerebellar activity is only 2·5 times that of the grey cerebrum, whereas Nurnberger and Gordon[10] have shown that the total cell density of the cerebellum is about four times greater than that of the grey cerebrum. Similarly, when considered on a cell basis using the data of Nurnberger and Gordon for total cell density, the activity of the liver per cell is only 45 times as great as that of the brain.

Sporn, Dingman, Defalco and Davies[11,12] have recently shown that urea can be synthesized by rat brain *in vivo*. Argininosuccinase is one of the enzymes of the urea cycle, as modified by Ratner, so it seems likely that some at least of the urea produced by the brain may be formed by a mechanism similar to that of the liver. (Ratner has evidence for the occurrence of argininosuccinase and also of the condensing enzyme responsible for synthesizing argininosuccinic acid from citrulline and aspartic acid in the brains of rats, steers and monkeys—private communication.) It has been suggested that the primary function of the ornithine 'cycle' may be the synthesis of arginine and citrulline[13] rather than of urea. If the complete set of enzymes does exist in the brain, such a function would be particularly interesting.

One of us (S. T.) wishes to thank the Mental Health Fund for a grant which enabled her to carry out this work. She would also like to thank Dr. L. M. Kerly for her advice and constant encouragement.

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An Effect of Insulin on Production of Glucose during Hepatic Glycogenolysis

IN earlier work the effect of a prolonged intravenous infusion of insulin on the utilization and production of circulating glucose was investigated in the trained, unanæsthetized normal dog in the post-absorptive state with the aid of intravenously administered ^{14}C-glucose[1]. The plasma glucose concentration and specific activity were determined at frequent intervals, and from these values were calculated the rates of production of hepatic ^{12}C-glucose and total glucose-uptake by the tissues[2]. It was shown that insulin brought about a hypoglycæmia primarily by increasing the uptake of glucose by the tissues. The rate of production of hepatic ^{12}C-glucose, although temporarily somewhat reduced soon after the insulin infusion was begun, usually rose during the course of the infusion to higher than normal levels, but not sufficiently to restore the plasma glucose concentration to its pre-insulin level. When the insulin infusion was stopped, there was a marked further increase in the production of hepatic ^{12}C-glucose which restored the plasma glucose concentration to its control-level. From these findings it was concluded that, during the period of insulin infusion, the production of ^{12}C-glucose was restrained in spite of severe hypoglycæmia[1].

To elucidate this effect of insulin, experiments have been carried out in which production of hepatic ^{12}C-glucose was raised by treatment with phloridzin or glucagon prior to the infusion of insulin. Phloridzin, injected subcutaneously in normal dogs in the post-absorptive state 2 hr. prior to administration of ^{14}C-glucose, caused a marked glucosuria which continued throughout the experiment. However, the plasma glucose concentration was maintained at near the normal level by a several-fold increase in production of hepatic ^{12}C-glucose. An insulin infusion (0·07–0·14 U./kgm./hr., intravenous) started 4 hr. after the phloridzin injection reduced production of hepatic glucose to about the pre-phloridzin level. When the insulin infusion was stopped, the production of hepatic

glucose rose again to its high pre-insulin level. The plasma glucose concentration was reduced as usual by insulin and rose when the insulin infusion was stopped[3].

In an attempt to eliminate liver glycogen as a source of the ^{12}C-glucose produced by the liver, normal dogs were depleted of liver glycogen by a 2-day fast and continuous phloridzination during the last 24 hr. of the fasting period. These animals exhibited a glucosuria, moderate hypoglycæmia and normal or slightly raised rate of production of hepatic ^{12}C-glucose. The infusion of insulin (0·07–0·14 U./kgm./hr., intravenous) lowered the concentration of plasma glucose, but did not reduce production of hepatic ^{12}C-glucose, in contrast with the effect of insulin in acutely phloridzinized dogs.

In view of these findings, the effect of insulin was studied in normal dogs in the post-absorptive state while hepatic glycogenolysis was being stimulated by glucagon. The infusion of glucagon (4 μgm./kgm./hr., intravenous) markedly increased production of hepatic ^{12}C-glucose and raised the concentration of plasma glucose. An insulin infusion (0·14–0·33 U./kgm./hr., intravenous), superimposed on the glucagon infusion, lowered the elevated rate of production of hepatic ^{12}C-glucose. On termination of the insulin infusion, with continuation of glucagon administration, the rate of production of the hepatic ^{12}C-glucose and the plasma glucose-level increased again.

These observations demonstrate that insulin promptly inhibits production of glucose at times when hepatic glycogenolysis is taking place and fails to do so when liver glycogen has been depleted and when the production of glucose by the liver probably originates by gluconeogenesis (namely, the 2-day fasted, phloridzinized animal). It can be inferred from these observations that insulin should reduce the net breakdown of hepatic glycogen brought about by glycogenolytic agents. Earlier evidence for such an effect of insulin has been reviewed by Cori[4].

The restraining effect of insulin, described earlier, is presumably exerted by a similar mechanism. Thus, when the concentration of blood glucose is lowered by a continuous infusion of insulin, release of physiological glycogenolytic agents is evoked by the hypoglycæmia. So long as the infusion of insulin continues, the ability of these agents to bring about liver glycogenolysis is limited. When the insulin infusion is terminated, this restraint is removed, and the resulting increased glycogenolysis causes a marked increase in the production of ^{12}C-glucose.

The small temporary effect of insulin in reducing production of hepatic ^{12}C-glucose, which we have observed when an insulin infusion is first begun, could be due to a similar effect of insulin on that small portion of the production of glucose which is arising by hepatic glycogenolysis in the normal unanæsthetized dog in the post-absorptive state. It is also conceivable that dogs with initially high blood-sugar-levels due to fright or anæsthesia or dogs having impaired hepatic circulations and maintained on high carbohydrate diets might have larger fractions of their production of hepatic glucose derived from glycogenolysis, and that this might be responsible in some part for the larger initial inhibitory effects of insulin on the production of hepatic glucose which have been reported by others.

The present observations do not permit a definite conclusion as to the mechanism whereby insulin reduces the production of glucose during hepatic glycogenolysis. Interference with phosphorylase action would produce the findings observed; however, stimulation of glycogen synthesis via the uridine diphosphate glucose pathway[5] could also bring about a net decrease in glucose production, but any mechanism of this kind would have to include a special provision to account for the fact that a decrease in production of glucose is observed only during glycogenolysis. Whether insulin exerts an inhibitory effect on production of glucose by acting directly on the liver or by indirect means cannot be stated at the present time.

The present experiments suggest that insulin administered to the intact animal promptly inhibits production of hepatic glucose when glycogenolysis is taking place or is being called for by glycogenolytic factors evoked by hypoglycæmia. This action of insulin would appear to be of physiological significance.

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Production of Free Water in the Mammalian Fœtus

The hypotonicity of the fœtal fluids and urine of many mammalian fœtuses is well known[1], and attempts have been made to explain it in terms of active transport of water or of sodium[2]. In certain conditions, the production of osmotically free water may be the physico-chemical consequence of active anabolism. If the anabolism occurs in a medium isotonic with normal extracellular fluid and is accompanied by little or no catabolism, water will be freed. This situation obtains in the mammalian fœtus which, while showing little catabolic activity, is rapidly synthesizing the large molecules of its cell constituents from small molecules passing through the placenta into its circulation. The osmotic freeing of water by this process is sufficiently great to account for the hypotonicity of the fœtal fluids and urine.

In making a rough calculation one may consider protein synthesis only. On the 23rd day of gestation the rabbit fœtus contains 0·62 gm. protein and on the 27th day, 1·7 gm. protein[3], so in this four-day period it has synthesized 1·08 gm. protein. If one assumes: (*a*) that mean weight of the protein molecules formed is about that of tropomyosin (mol. wt. 80,000; 670 amino-acid residues/mol.), and (*b*) that the amino-acids used in protein synthesis are presented to the fœtal tissues as undissociated molecules in a solution of osmolar concentration 300 milliosmoles/l., one can calculate that during this four-day period of gestation 0·0135 millimole of 'tropomyosin' has been formed from 9·1 millimoles of amino-acids, which would be contained in 30·4 ml. of solution. The 'tropomyosin' thus formed (assuming that the cell contents are isotonic with extracellular fluid) would require only 0·05 ml. water for its solution. The synthesis has therefore set free 30·35 ml. water. Unless the placenta removes this volume of water in excess of solute, some

water will accumulate on the fœtal side of the placenta and dilute the fœtal fluids or urine. Strongly hypotonic allantoic fluid is in fact found in ungulates, the placenta of which is less permeable than that of rabbits[4].

This rough calculation relates not, of course, to the absolute exchange of water between the maternal and fœtal organism, which is known to be very large[5], but simply to the osmotic freeing of water by the conversion of many small molecules into a few large ones. The synthesis of protein will also cause a comparatively small absolute increase in water by release of metabolic water in the formation of peptide bonds.

A similar process in actively growing young plants has been described by Lundgårdh[6]. Wheat seedlings grown in salt-free sugar solutions synthesize protein from the sugar together with nitrates already present in the plant; and during this process the tissue fluid (collected as bleeding sap from the cut end of the stem) becomes hypotonic, as a result of the 'extra water' released by the decrease in the number of molecules present. It is suggested that the hypotonicity of mammalian fœtal fluids and urine may result from an analogous process.

I am indebted to several colleagues for helpful discussions of this point.

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PATHOLOGY

Inhibition of Exogenous and Endogenous Pyrogens by Lysozyme

SINCE lysozyme has been used for therapeutic purposes it has been observed that a rapid fall of temperature may follow its administration. Experiments were, therefore, planned to find out if Fleming's bacteriolysin prevented the rise of temperature caused by exogenous and endogenous pyrogens in rabbits.

Subcutaneous injection of 400 mgm./kgm. of lysozyme were found to reduce to some extent the effects of the intravenous administration of an exogenous pyrogen (pyromen), whereas subcutaneous administration of similar amounts of gelatin did not. Since smaller doses of lysozyme had no effect, it was considered possible that the large doses were producing their effect by interacting with endogenous pyrogen which, as it is well known, is responsible for most of the rise of temperature observed after injecting exogenous pyrogens[1-3].

This assumption has been proved to be correct in experiments carried out by means of Bennet and Beeson's technique[4]. Rabbits were prepared by shaving the abdomen, and 350 c.c. of physiological saline containing 60 units of penicillin and 0·8 mgm. of streptomycin per c.c. was infused into the peritoneal cavity, slowly, so that the infusion was completed in 3 hr. The animals were kept on their backs for 4 hr. after termination of the injection. Then the abdomen was opened and all fluid in the peritoneal cavity was aspirated into sterile Erlenmeyer flasks.

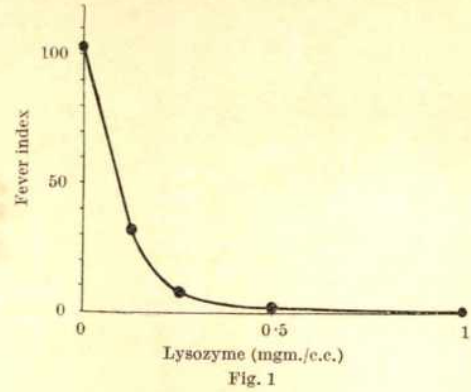

Fig. 1

The peritoneal fluid, which was centrifuged until it was clear, produces the typical hyperthermia due to endogenous pyrogen if it is administered intravenously to rabbits (dose, 10 c.c. per 2-kgm. rabbit). If sterile lysozyme hydrochloride is dissolved in the saline solution to be infused into the abdominal cavity at a concentration of 0·5 mgm./c.c., then peritoneal fluid cleared by centrifugation does not produce hyperthermia, when it is injected intravenously into rabbits (dose, 10 c.c. per 2-kgm. rabbit).

In controls carried out with sterile gelatin, utilizing the same concentrations, the peritoneal fluid cleared by centrifugation can produce the hyperthermia characteristic of an endogenous pyrogen.

Measuring the fever curves with a planimeter, it is possible to determine the 'fever index' utilized by Beeson[5]. The antipyrogenic action of lysozyme is expressed graphically in Fig. 1, in which values of the 'fever index' are plotted as ordinates and values of lysozyme concentration as abscissæ.

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Effects of Hexamethonium Bromide and β-Amino Propionitrile on the Tensile Strength of the Aorta of Mice

Beaven and Murphy[1] suggested that the ganglion-blocking agents, hexamethonium bromide and pentolinium, might weaken the aortic media, because nine of a series of 44 hypertensive patients under treatment with these agents died suddenly from dissecting aneurysm of the aorta. Six of the nine fatal cases had malignant hypertension. Although in a large autopsy service we have observed this association only in one case of malignant hypertension treated with 'Darenthin', we decided to test the hypothesis by comparing the effects of hexamethonium bromide alone and in association with the lathyrous factor β-amino propionitrile on the static tensile strength of the aorta in normal mice. The latter compound is well known to weaken the aortic media in experimental animals by an antimaturant action on collagen[2].

White mice of both sexes aged 3–4 weeks were used in five successive experiments each comprising 60 animals. This age-group was chosen because Ponseti and Shepard[3] found that the most marked aortic lesions were produced in the rat when treatment with a lathyrous diet was begun before the age of 4 weeks. Further, Gillman and Hathorn[4] suggest that animals immediately after weaning should be used to assess the aortic effects of β-amino propionitrile because at this time aortic growth and remodelling are maximal.

In each experiment the 60 mice were divided at random into four groups of 15 animals. Each experiment lasted 3 weeks. Animals in group 1 received a single daily subcutaneous dose of 5 mgm. of β-amino propionitrile. Those in group 2 were given two doses daily each of 0·5 mgm. of hexamethonium bromide. This dose was determined after preliminary trials, which showed that a single dose of 1·5 mgm. caused rapid convulsive death and that 0·5 mgm. was the maximum dose which could be given over a period of 3 weeks without causing significant mortality. Group 3 received each day the combined regime of a single dose of 5 mgm. of β-amino propionitrile and two daily doses of 0·5 mgm. hexamethonium bromide. The β-amino propionitrile and the first dose of hexamethonium were given close together each morning and the second dose of hexamethonium each afternoon. Group 4 animals were uninjected controls.

At the end of the experimental period of 3 weeks the mice were killed in random order over a period of 3 days, during which no drugs were given. The thoracic aorta was carefully dissected free from fascia, suspended between clamps and weights added to the lower clamp until the aorta broke.

The breaking strain was found to vary considerably between animals treated alike. Results are shown in Table 1.

Table 1. Breaking Strain (gm.) of Aortic Media

	Control	β-Amino propionitrile alone	Hexamethonium alone	β-Amino propionitrile + hexamethonium	Experiment mean
Experiment 1	44·2	38·8	48·0	36·6	42·1
Experiment 2	47·6	44·7	42·7	35·8	42·8
Experiment 3	47·2	39·3	47·6	40·3	43·5
Experiment 4	44·3	37·3	38·4	38·3	39·5
Experiment 5	44·7	32·5	40·3	34·8	38·1
Treatment mean	45·7	38·7	43·4	37·2	40·5

The standard errors of the difference between individual treatment means was 1·94. It was therefore apparent that β-amino propionitrile produced a significant weakening of the aortic media, but that treatment with hexamethonium bromide did not do so, nor did it potentiate the weakening effect of β-amino propionitrile.

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BIOLOGY

De novo Origin of the Nuclear Membrane

The behaviour of the nuclear membrane in prophase and telophase is indeed one of the most attractive features of mitosis for the electron microscopist and cytologist[1]. This was recently emphasized by Porter and Machado[2] in their review of the literature preceding their own electron microscope observations of mitotic onion root cells. In summary, the nuclear membrane or envelope is formed either by a coalescence of vesicles derived from the endoplasmic reticulum at the chromosome surface, or, as in the case of the onion cells, by slender lamellar units of the endoplasmic reticulum draping themselves around the chromosomes at the poles in telophase. Not one of these studies shed any light on the intriguing question posed by Bernhard[3] regarding the possibility of a *de novo* origin for the nuclear membrane.

In a problem like this, the selection of proper research material is perhaps more important than formulation of the original proposition. In such material, the number of cells undergoing mitosis should be unusually high, and the cells should not contain much endoplasmic reticulum and relatively few mitochondria. Electron microscope studies for an entirely different problem revealed that fœtal liver (human and rat) is an excellent tissue for a number of cytological problems[4]. At certain stages of development, the actively proliferating erythroblastic cells may outnumber the hepatic cells and even deform them by encroachment. In the youngest erythroblasts, fixed with buffered osmic acid, the sparse slender profiles of endoplasmic reticulum disappear gradually by fragmentation into small vesicles. Basophilic erythroblasts (normoblasts), which are characterized by an abundance of ribonucleoprotein particles and a small volume of endoplasmic reticulum or an involution of it[5,6], are mitotically quite active.

During prophase the nuclear membrane leaves the surface of the contracting chromatin, fragments and migrates towards the cell periphery. It is apparently metabolized after further fragmentation into vesicles. Although this lamellar structure may persist into the telophase stage, it is not related to the reconstitution of the new nuclear membrane.

Reconstitution of the nuclear membrane occurs first, multicentrically, around the periphery of the daughter cell chromosomal mass farthest away from the interzonal spindle fibres (Fig. 1). Examples of aberrant chromosomal masses and differential mitosis further emphasize that remnants of lamellar endoplasmic reticulum are not required for the formation of the nuclear membrane in erythroblasts.

This evidence for the *de novo* origin of the nuclear membrane assigns to the chromosomal mass a much more important role in its formation than has been possible in previous electron microscope studies because basophilic erythroblasts are remarkably free from lamellar and vesicular endoplasmic reticulum. This interpretation is in keeping with light microscope studies showing that the nuclear membrane is first formed in telophase by the coalescence of membranes from the cytoplasmic surface of each of the chromosomal vesicles[7]. Hence, the nuclear membrane stands in a direct genetic relation to the chromosomal parts[8],

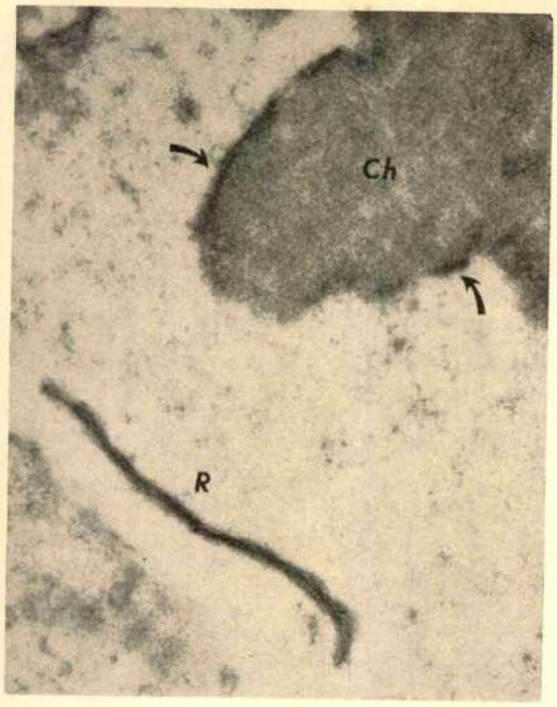

Fig. 1. Electron micrograph of a portion of the chromosomal (*Ch*) mass in telophase of an erythroblast from a 15-day rat fœtal liver. Arrows indicate the reconstitution of the nuclear membrane. A remnant of the nuclear membrane from the preceding prophase nucleus is shown at *R*. A portion of a mitochondrion is in the upper left corner. (× 16,666)

and in the case of basophilic erythroblasts, it would be actively involved in the nucleo-cytoplasmic exchange of basophilic material.

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Auxin Control of Protein-Levels in Detached Autumn Leaves

IT is well established that when mature leaves are detached from the plant the protein-level in the blade falls[1]. It has also been demonstrated by both Vickery, Pucher, Wakeman and Leavenworth[2] and Mothes and Engelbrecht[3] that an external supply of carbohydrate or of nitrogenous substances such as nitrates, ammonium salts or urea, will only slow down the rate of the protein degradation. If detached leaves are maintained in nitrogen, however, the fall in protein can be considerably retarded without the addition of metabolites[4], while the reduction in protein-level can be entirely suppressed under normal aerobic conditions once root initials have been formed on the petiole[3]. The retention of protein in detached but rooted leaves caused Chibnall[5] to propose that a root factor, possibly hormonal in nature, is essential for the synthesis of protein in leaf tissue. In this connexion the findings of Richmond and Lang[6] and Person, Samborski and Forsyth[7] are of considerable interest. The former workers showed that when detached unrooted leaves of *Xanthium* were kept with their petioles in 5 or 10 mgm./l. kinetin the loss of protein was retarded, and the chlorophyll and green colour of the blade were maintained. Person *et al.*[7] reported similar effects on detached wheat leaves floated on solutions of benzimidazole. Later, Mothes, Engelbrecht and Kulajewa[8] elegantly demonstrated that when solutions of kinetin were applied locally to the surface of mature tobacco leaves the original levels of protein and chlorophyll were maintained in the treated areas; furthermore, nitrogenous compounds applied to other parts of the leaf moved towards the parts treated with kinetin. In a recent communication[9], one of us directed attention to the importance of auxins in the control of physiological changes occurring during the autumn senescence of both attached and detached leaves. Local applications of the *n*-butyl ester of chlorinated phenoxyacetic acids to the surface of green autumnal leaves of cherry resulted in a retention of photosynthetically active chlorophyll and the conservation of alcohol-insoluble nitrogen in the treated areas. In contrast, untreated parts and control leaves became completely yellow and showed a greater reduction in the protein-level. These investigations have now been extended, and more detailed work has revealed that the total protein-levels in the auxin-treated areas of the leaf may be wholly maintained for periods of more than two weeks, during which time the total protein in control leaves and untreated parts of the treated leaf may fall to half the original values.

Fully green leaves were removed from trees of *Prunus serrulata* in late October. A drop (1·9 μl.) of an ethanol solution of the *n*-butyl ester of 2,4-dichlorophenoxyacetic acid was applied to the upper surface of the lamina, on each side of the main vein, to give a total dose of 25 μgm./spot (acid equivalent). Control leaves were treated with ethanol. The leaves were maintained in high humidity in an unheated greenhouse in normal day-length. The cut ends of the petioles dipped into beakers containing distilled water which was changed daily.

Within 6 days, control leaves and the untreated areas of the treated leaves began visibly to lose chlorophyll and turn yellow, and by the eleventh day, the areas treated with 2,4-dichlorophenoxyacetic acid remained as green islands of tissue in an otherwise yellow leaf. At appropriate intervals the levels of different nitrogen fractions were determined in disks of tissue, 1·5 cm. in diameter, cut from control leaves and from treated and untreated parts of the treated leaves. Determinations of total, 80 per cent ethanol-insoluble and 80 per cent ethanol-soluble fractions of nitrogen from duplicate samples of tissue were carried out by the usual micro-Kjeldahl techniques. After correcting for the small changes that occurred in the fresh weight of the leaf and hence in the leaf area it could be shown that there was no change in the total nitrogen value for the different areas of the blade. Results are therefore expressed as the ratio of 80 per cent ethanol-insoluble nitrogen

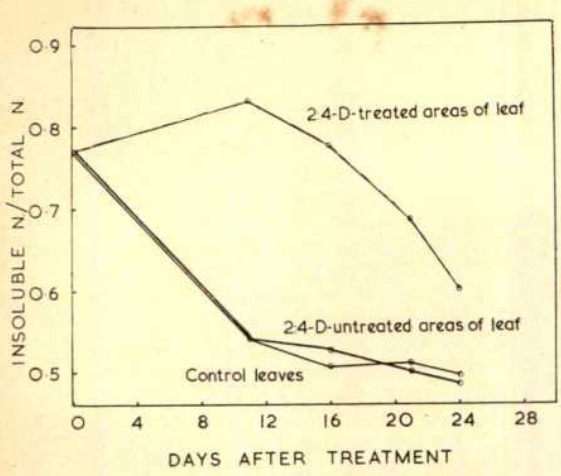

Fig. 1. Ratio of 80 per cent ethanol-insoluble nitrogen/total nitrogen in control leaves and in areas treated and untreated with 2,4-dichlorophenoxyacetic acid in blades of detached autumn leaves of *Prunus serrulata*. The departure from the mean for each individual point varies from 0–6·5 per cent

to total nitrogen. This measure of protein nitrogen within the tissues at different times after treatment is shown in Fig. 1. It is clear that while nearly 50 per cent of the protein is degraded in control and untreated areas the protein-level is maintained in the tissues treated with 2,4-dichlorophenoxyacetic acid. Further estimations have shown that in the control and untreated tissue, there is an increase in α-amino, amide and ammonia nitrogen corresponding to the decrease in protein.

Treatment of detached cherry leaves with 2,4-dichlorophenoxyacetic-ester labelled with carbon-14 in the carboxyl group, followed by detection of carbon-14 by autoradiography, showed that the labelled carbon is retained entirely within the areas of tissue which remain green. It was also found that neither the continuous supply to the petioles of an aqueous solution of kinetin at 25 mgm./l. nor a local daily aqueous spray of kinetin at 100 mgm./l. was effective in delaying protein degradation or preventing yellowing of the blade. Indole-3-acetic acid was equally ineffective, but spot applications of indole-3-aceto-nitrile produced visible responses similar to those described for 2,4-dichlorophenoxyacetic acid.

Respiratory measurements on leaf disks from control leaves or from untreated areas of leaves treated with 2,4-dichlorophenoxyacetic acid revealed a similar and continuing increase in oxygen-uptake starting after detachment from the tree and reaching a peak some ten days later. Concomitant with this increase in oxygen consumption there was a rapid fall in protein-level and a loss of chlorophyll. This phase was followed by a continuous decline in oxygen consumption corresponding to the further slow decrease in protein-level. In the areas treated with 2,4-dichlorophenoxyacetic acid the period of increasing oxygen consumption was postponed by some twenty days from the time of detachment and treatment, and, as with the control and untreated areas, the peak of oxygen-uptake again corresponded with the period of rapid protein degradation. By the end of the experiment (24 days) the tissues in the treated areas were still light green and capable of fixing labelled carbon dioxide in the light. At no stage was there any visible indication that root formation, cell division or other morphological change had occurred in the treated leaves.

Since the areas which remain green are the only ones in which carbon-14 can be detected after treatment with carbon-14 labelled 2,4-dichlorophenoxyacetic acid, and since the retention of chlorophyll and protein is restricted to these areas, it must be concluded that these effects on chlorophyll and protein are due to a direct effect of treatment with 2,4-dichlorophenoxyacetic acid. In both the yellowing control leaves and the untreated parts of the treated leaves it is clear that degradation of protein must exceed synthesis.

A number of postulates can be advanced to explain the ways in which 2,4-dichlorophenoxyacetic acid may control the protein-levels in these senescing leaves.

(1) The retention of actively photosynthetic chlorophyll might lead to a sparing of protein by increasing the supply of carbohydrates. However, Vickery, Pucher, Wakeman and Leavenworth[10] have shown that active photosynthesis and even accumulation of carbohydrate in mature detached tobacco leaves does not, in fact, retard protein breakdown. It is improbable, therefore, that the effect of 2,4-dichlorophenoxyacetic acid can be accounted for in terms of increased carbon substrates.

(2) Racusen and Aronoff[11] showed that in soya bean leaves the incorporation of labelled carbon dioxide into the amino-acids of protein decreased with increasing time after detachment from the plant. It may be, therefore, that 2,4-dichlorophenoxyacetic acid acts by preventing a decline in the rate of incorporation of amino-acids.

(3) It is also possible that protein turnover is completely blocked by treatment with 2,4-dichlorophenoxyacetic acid, so that neither synthesis nor degradation occurs.

Many metabolic processes have now been shown to be correlated with the hormone status of the plant. The evidence presented here suggests that auxins are controlling factors in certain pathways of protein metabolism.

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Influence of Light from an Infra-red Bulb on the Mutagenic Effect of Colchicine on *Sorghum*

TRUE-BREEDING diploid mutants have been found to arise from colchicine-treated *Sorghum* seedlings of the true-breeding lines, Experimental 1 and Experimental 3[1-5]. Their true-breeding nature is similar to that obtained after many generations of selfing so that they appear to be immediately homozygous for the new characteristics. Some non-true-breeding mutants also occur. It was proposed that the true-breeding condition might arise by a somatic reductional division of the chromosomes, similar to that observed by Huskins[6], with subsequent restoration to the diploid number, and that the mutant condition might arise through concentration of chromatin from one of the original ancestors from which Experimental 3 had been derived. However, from cytogenetic studies of hybrids between true-breeding mutants and their untreated full sibs, the genetic changes appear to be due to gene mutations[4,7-9]. Tests of the somatic reduction hypothesis using chromosome markers (recessive genes and reciprocal translocations) in the heterozygous condition in sorghum and other materials have not been decisive[1,7,10] except for one case in flax (gene markers) which indicated its seeming validity[11].

The definition of a laboratory method for the production of true-breeding mutants after colchicine treatment has been found to be of paramount importance from the point of view of testing the hypothesis of somatic reduction since variable success results under greenhouse conditions. For this purpose the influences of environmental factors on the induction of mutants are being determined. Recent investigations involving more than 1,000 colchicine-treated seedlings have been carried out using aseptic cultures kept under light and temperature conditions with various degrees of control[12]. Only four mutated plants, none true-breeding, were obtained. The problem, therefore, was to identify the particular factors responsible for the difference in results between sand jars in the greenhouse, which had given as high as 42 per cent true-breeding mutants[2], and aseptic cultures under light and temperature conditions controlled to varying degrees, which gave very few mutants, none true-breeding. Light was a possible factor since most of the seedlings in aseptic culture were grown in a box with artificial light, or in the laboratory, or under shades in the greenhouse, while those in sand jars were grown in the greenhouse without shades. Infra-red light was investigated since these rays penetrate glass, have been found to modify chromatin re-arrangements induced in *Drosophila*[13] and in *Tradescantia*[14], and have been shown to play an active part in the control of many aspects of growth and differentiation[15].

In experiments in Table 1, untreated and treated seedlings of line Experimental 3 were grown in glass-covered jars on sand with tap-water and in test-tubes on agar both with full nutrient and with distilled water. Treatment consisted of application of 0·5 per cent colchicine in lanolin to the coleoptiles immediately after germination. Comparisons were made between shaded and unshaded conditions in the greenhouse and continuous illumination from a 'Heat Ray' bulb (infra-red, 250 W.) at approximately 78° F. for seven days immediately after treatment. Progeny tests were made of surviving plants from these experiments.

Light conditions and medium influenced both survival of treated seedlings and induction of mutants. Infra-red light cannot be considered the only factor precipitating the appearance of true-breeding mutants since changing the culture from sand to agar prevented their induction. It may be of importance that mutants appeared only under conditions which gave high mortality. This observation agrees with previous findings that although agar with or without nutrients increased survival of treated seedlings over that in sand jars, the number of mutants induced by colchicine treatment is decreased by this and other improved growing conditions[12]. The high rate of mortality associated with the induction of true-breeding diploid mutants suggests that the balance between stress conditions causing death and those causing origin of a mutated shoot, which displaces

Table 1. INCIDENCE OF TRUE-BREEDING DIPLOID MUTANTS AND POLYPLOID PLANTS, AS INDICATED BY PHENOTYPE AND VERIFIED BY PROGENY TESTS, FROM UNTREATED AND COLCHICINE-TREATED SORGHUM SEEDLINGS (LINE EXPERIMENTAL 3) WITH DIFFERENT ILLUMINATION AND MEDIA

Medium	Greenhouse				Infra-red bulb (7 days)	
	Shaded		Unshaded			
	Untreated	Treated	Untreated	Treated	Untreated	Treated
1957 Experiment						
Sand, tap-water						
Original number	20	20	—	—	20	60
Survivors	19	7	—	—	13	9
Polyploids	0	0	—	—	0	0
True-breeding diploid mutants	0	0	—	—	0	4
1958 Experiments						
Sand, tap-water						
Original number	20	60	10	20	30	80
Survivors	19	33	10	5	27	6
Polyploids	0	0	0	1	0	0
True-breeding diploid mutants	0	0	0	0	0	1
Agar, full-nutrient*						
Original number	—	—	10	20	10	20
Survivors	—	—	10	20	10	15
Polyploids	—	—	0	2	0	4
True-breeding diploid mutants	—	—	0	0	0	0
Agar, distilled-water						
Original number	—	—	10	20	10	20
Survivors	—	—	10	20	5	13
Polyploids	—	—	0	1	0	0
True-breeding diploid mutants	—	—	0	0	0	0

* 5 × major minerals, 1 × minor elements, 2 per cent sucrose and 0·05 p.p.m. indole-3-acetic acid (ref. 12).

original tissues, is delicate and subject to many factors difficult to control.

The true-breeding diploid mutants which arose after infra-red illumination were similar to those obtained previously from treated seedlings grown in an unshaded greenhouse. Both groups exhibited obvious changes in height, leaf, midrib, panicle, glumes, awns and seed colour, and bred true immediately. These results provide a clue to the variability in occurrence of mutants in greenhouse experiments since light conditions change with the amount of sunshine. They are particularly significant since it is indicated that the phenomenon of the induction of true-breeding mutants can be produced under laboratory conditions. There are therefore external conditions such as light, medium and temperature which determine the occurrence of this phenomenon as well as internal conditions determined by the genotype as indicated by Atkinson *et al.*[2].

Induction of true-breeding mutant types by colchicine treatment of germinating seedlings in the greenhouse has been used with great success in the sorghum-breeding programme at South Dakota State College both to secure new variability and to obtain fixed genotypes immediately. The significance of this phenomenon for currently held theories regarding the behaviour of chromosomes within somatic tissues would seem to be far-reaching, particularly in our understanding of growth processes and, perhaps, of the origin of abnormal growths such as cancer.

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Changes in Amounts of Organic Acids in Citrus Leaves during Periods of Cold Storage

STORAGE of certain plant products at temperatures below 15° C. but above freezing can cause severe injury to their tissues. As one mechanism to explain this, it has been suggested that cold temperatures could cause changes in the rates of metabolic reactions which would result in an increase or decrease in amounts of metabolic intermediates[1]. Such changes, when excessive, could directly or indirectly damage the plant cells.

Storage at cold temperatures has been shown to cause increases in the respiratory rate of citrus fruit[2], leaves (Eaks, Irving L., personal communication, 1960), and other plant materials[3,4] both before and after the breaking point for the onset of injury. The earliest measured response of sweet potatoes to the chilling temperatures was an accelerated respiratory rate[4], even though at this time no injury had resulted.

Biochemical studies on sweet potatoes indicated that changes in mitochondrial activity could not explain the increased respiratory rate of tissues which had been stored at low temperatures[5]. There is a possibility that changes in amounts of organic acids caused by the periods of cold storage could explain such respiratory increases. The amounts of a number of organic acids in citrus leaves were determined, therefore, to see if any changes occurred and if these changes were associated with cold injury.

Three lemon plants (Lisbon variety, 3 months old) were placed in a darkened chamber at 1° C. An identical number of plants were introduced into darkened chambers at 10° C. and 20° C. A continuous stream of air, saturated with water vapour, was passed through each chamber so that one exchange of air occurred approximately every 15 min. After a predetermined storage period the plants were removed. The third fully expanded leaf from the growing point was removed from each plant. The plants were then placed in a greenhouse, and after 48 hr. the leaf damage resulting from the cold-temperature storage on the unexcised leaves was recorded. Each leaf which was removed was weighed and ground in a pestle and mortar with quartz sand and 3·0 ml. of distilled water. After centrifugation, one aliquot of this solution was titrated to a phenolphthalein end-point with standard sodium hydroxide. The results obtained from this titration were used to determine the total acidity present. Another measured aliquot (usually 1·5 ml.) was mixed with 0·05 ml. of 36 *N* sulphuric acid and 1·5 gm. of silicic acid. The free-flowing powder was quantitatively transferred to a previously prepared silica-gel column. The method of Bulen *et al.*[6] was used for the determination of the acids present. Each determination, therefore, gave the acids present in a single leaf. This procedure was repeated on identical groups of plants stored for varying periods of time at the different temperatures.

The results in Table 1 indicate that cold storage caused as much as a 140 per cent increase in amount

Table 1. CHANGES RESULTING FROM COLD TEMPERATURE STORAGE IN AMOUNTS OF ORGANIC ACIDS IN CITRUS LEAVES*

Organic acid	Normal level	Change due to cold storage	
	2 weeks at 20° C. μ equiv./gm. of leaf	2 weeks at 1° C. $\Delta\mu$ equiv./gm.	2 weeks at 10° C. $\Delta\mu$ equiv./gm.
Unknown	23	− 3	− 3
Acetic	4	− 2	0
Fumaric and formic	48	− 7	− 7
Succinic	5	+ 4	+ 6
Malonic	6	+ 1	+ 2
Oxalic	81	−13	−17
Glycolic	82	−25†	−19
Malic	59	+62†	+83†
Citric	280	−88†	−98†
Isocitric	73	+14	+ 8

* Each value is the average obtained from six different leaves. Gain of acid over 20° control is indicated by plus values, loss by negative values.

† Significantly different from the amount of the same acid found in the 20° C. sample at the 5 per cent probability-level.

of malic acid in the leaf tissue and a 35 per cent decrease in amount of citric acid. In one case not shown there was a 170 per cent increase in malic acid and a 77 per cent decrease in citric acid. Similar results were obtained in all the experiments conducted. It should be noted that the greatest part of the changes produced by the cold storage occurred between 20° C. and 10° C.

A comparison of the total free acids present in the leaf tissue stored at the lower temperature with those at 20° C. revealed that essentially no significant change had occurred even though malic acid and possibly *iso*citric acid were accumulated.

These results suggest that the ratio of the individual acids to each other was important in the development of cold injury. It is not inconceivable that the accumulation of malic acid and loss of citric acid was in some direct way related to the stimulation of respiration which has been reported and perhaps to the primary damaging reactions producing the injury.

In this type of work it is important to differentiate between those changes which are the result of the death of the cells and those primary changes which cause the death of the cells. Since a redistribution of organic acids occurred both before and after the breaking point for the onset of leaf injury, the organic acid changes reported here could have been closely associated with the primary cause of cold-temperature injury.

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Morphological Reactions of Germinating Seeds as Criteria for the Plant Growth Regulating Activity of Auxin-Type Chemicals

STUDYING the plant growth regulating effects of more than one hundred chemicals, we directed our attention to the following problems, closely related to the mode of action of auxins: (1) Is there only one, common, basic (auxin-) reaction, underlying the diversity of 'auxin-like' growth effects? (2) Do higher plant species differ with regard to their relative sensitivity towards different auxins? (3) Is the physiological activity of potential auxin precursors to be simply explained by the conversion of the inactive precursor to the active auxin? (4) How far can species differences in the enzymatic conversion of auxin precursor to auxin explain the differences between their sensitivity to the application of auxin precursors? None of these questions has been so far answered[1–6].

With the above considerations in mind, our attention was directed to the wide range of different abnormalities in seedling development, caused by treating germinating seeds with 2,4-dichlorophenoxy acetic acid. The gross morphological effects of this compound were found to consist mainly of inhibition of growth in length on one hand, and stimulation of growth by abnormal cell proliferation

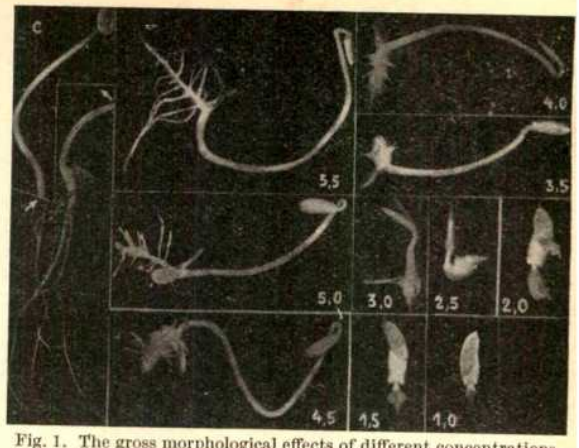

Fig. 1. The gross morphological effects of different concentrations of 2,4-dichlorophenoxy acetic acid on 6-days-old cucumber seedlings. *C*, untreated control, 5·5 to 1·0; the negative logarithm of the 2,4-dichlorophenoxy acetic acid concentration, with 1·0 equal to 1,000 p.p.m.

on the other hand, in the different tissues of the seedlings. The development of the diverse growth effects has shown strikingly high correlation. By comparing the gross morphological effects on cucumber seedlings of an unknown concentration of 2,4-dichlorophenoxy acetic acid to a series of reference standards, the logarithm of the concentration in the experimental Petri dish was found to be determinable within the concentration-range 0·03–1,000 p.p.m. with an accuracy of $\pm$ 0·25 (Fig. 1). Determination of concentrations of 2,4-dichlorophenoxy acetic acid was found to be possible using the same method with seedlings of any other species, although the great sensitivity obtained with cucumber seedlings could be achieved with other species generally only in a narrower range of concentrations of 2,4-dichlorophenoxy acetic acid.

The method, as applied by us in typical experiments, might briefly be described as follows: Three disks of filter paper were placed in Petri dishes and moistened with aqueous solutions of 0·1, 1, 10, 100, and 1,000 p.p.m., respectively, of the substance to be studied. Dry seeds of 23 species of crop plants were placed in a series of dishes (20 seeds of one species per dish, giving the above series of concentrations with every species), and incubated at 24° C. in the dark. The effects were evaluated on the sixth day, by comparing the morphological effects of every concentration with photographs (supplemented by detailed morphological descriptions) of the effects of a comparable series of concentrations of the reference substance(s) on the same species. Activity of a given concentration was expressed by that concentration of the reference substance which proved to be equally effective. In case the equal effectivity at any concentration of the reference substance seemed to be doubtful (due, for example, to a changed correlation between some of the observed growth effects) the disagreement with the reference substance was described and the seedlings photographed. Experiments were repeated at least three times; the results were found to be highly reproducible, in different seasons, and with seeds harvested in different years.

Our test as described above is opposed to the accepted auxin tests, in which statistically evaluated exact measurements of but one aspect (preferably growth in length) of the observable effects are involved while the others are neglected. The overall morphological effect is considered by us as a whole instead,

and used for the determination of equal effectivity with the standards. Fig. 1, nevertheless, illustrates convincingly that the evaluation of the results of the described 'phototest', within the limits of sensitivity given above, is free of subjective errors, and that the sensitivity of the method is comparable to any other biological auxin test. The visually perceptible great sensitivity of germinating seeds to different concentrations of the same auxin-type chemical is caused by strict correlations existing among a great variety of induced growth phenomena which, as a whole, are unmistakably characteristic for a narrow range of concentrations of the substance given. Differences, on the other hand, in the correlations between the observed growth effects, induced by different auxin-type substances, might yield much useful information about problems 1 and 3. In addition, the method presented is a laboratory test, highly reproducible, and reducing the importance of such secondary factors as uptake and transport, for studying possible differences in the sensitivity of different species to auxins as well as to auxin precursors. These characteristics of the method enabled us to draw some tentative conclusions concerning the problems summarized in the introduction, to be described in detail in further communications under preparation.

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Transduction in Actinomycetes

GENETIC transduction has been demonstrated in a limited number of bacterial species, such as *Salmonella*, *Escherichia coli*, *Shigella* and *Pseudomonas aeruginosa*[1–4].

As regards Actinomycetes, we[5] have shown that the donor culture on which the actinophage developed determined the pattern of the recipient variation, induced by this actinophage. The ability of actinophage to transfer the prototrophic property from the wind-type strain to the auxotrophic one was also shown. Later, we attempted to obtain prototrophic colonies from an auxotrophic strain, treated with an actinophage, grown on another auxotrophic strain. In this case it was necessary that the donor auxotroph should differ in its nutrient requirements from the recipient auxotroph.

In our experiments, auxotrophic strains No. 2 (Cys^-His^+), No. 74 (Met^-His^+), and No. 80 (Met^+His^-), obtained after the treatment of *Act. olivaceus* strain *N*-6 with X-rays, were used. The transduction was carried out with a temperate phage No. 1. Three different combinations of the above auxotrophs were used. In the first combination, strain His^+Met^- (74) was used as the donor and strain His^-Met^+ (80) as the recipient. Strain His^-Met^+ (80), treated with a phage, grown on the same strain, and the culture of strain His^-Met^+ (80), not treated with phage, were used as the controls.

In the second combination, strain His^-Met^+ (80) was used as the donor and strain Met^-His^+ (74) as the recipient.

In the third combination strain Cys^+His^- (80) was used as the donor and strain Cys^-His^+ (2) as the recipient. The controls in the second and the third combinations was carried out in the same manner as in the first combination.

When corresponding phagolysates were plated on the minimal medium, it was observed that combinations His^+Met^- (74) × His^-Met^+ (80), His^-Met^+ (80) × His^+Met^- (74) and His^-Cys^+ (80) × His^+Cys^- (2) very rarely produced prototrophic colonies similar to the wild-type colony (approximately 0·1 per cent). At the same time many small, compact and asporogenic colonies were detected on the Petri dishes. Such colonies were studied by transferring single isolates to the minimal agarized medium in tubes. The majority of them appeared to be auxotrophic with nutrient deficiency of the recipient. In addition, prototrophic colonies, characterized by distinct sporulation when grown on the minimal medium, were observed among them.

In the control combinations His^-Met^+ (80) × His^-Met^+ (80), His^+Met^- (74) × His^+Met^- (74), and His^+Cys^- (2) × His^+Cys^- (2) small asporogenic

Table 1. EMERGENCE OF PROTOTROPHS FROM AUXOTROPHS, TREATED WITH ACTINOPHAGE, GROWN ON AUXOTROPHS DIFFERING BY THEIR NUTRIENT REQUIREMENTS FROM THE RECIPIENT

		Donor	Recipient	No. of colonies studied	Prototrophs isolated	
					Absolute No.	Per cent
Combination No. 1	Experiment	His^+Met^- (74)	His^-Met^+ (80)	388	31	8·0
	Control No. 1	His^-Met^+ (80)	His^-Met^+ (80)	365	0	0·0
	Control No. 2	No donor	His^-Met^+ (80)	583,000	0	0·0
Combination No. 2	Experiment	His^-Met^+ (80)	His^+Met^- (74)	292	18	6·1
	Control No. 1	His^+Met^- (74)	His^+Met^- (74)	290	0	0·0
	Control No. 2	No donor	His^+Met^- (74)	345,000	0	0·0
Combination No. 3	Experiment	Cys^+His^- (80)	Cys^-His^+ (2)	212	12	5·6
	Control No. 1	Cys^-His^+ (2)	Cys^-His^+ (2)	188	0	0·0
	Control No. 2	No donor	Cys^-His^+ (2)	143,000	0	0·0

Table 2. PLATINGS OF PROTOTROPHIC COLONIES, GROWN AS A RESULT OF TRANSDUCTION

Plating of prototrophic colonies grown from the following combinations	Colony type (per cent)			
	Prototrophic colonies	Recipient type colonies	Donor type colonies	Colonies with double nutrient deficiency
His^+Met^- (74) × His^-Met^+ (80)	21·4	42·8	23·8	11·9
His^-Met^+ (80) × His^+Met^- (74)	4·0	14·0	66·0	16·0
Cys^+His^- (80) × Cys^-His^+ (2)	18·9	20·7	46·6	13·8

colonies were also observed. The analysis of these colonies did not reveal any prototroph among them. All these colonies appeared to be auxotrophs of the recipient type. No prototrophic colonies were detected among the many colonies obtained from auxotrophs No. 2, No. 74 and No. 80, not treated with actinophage.

The results of these experiments are presented in Table 1.

Two types of prototrophic colonies were shown to emerge from the platings of phagolysates. The first type, observed in all three combinations, formed only prototrophic colonies. Examination of the subsequent generations of these prototrophs showed the stability of the prototrophic property. The second type of the prototrophs, also observed in all the combinations studied, segregated out four colony types, that is, prototrophic colonies, auxotrophic colonies with nutrient deficiency of the donor, auxotrophic colonies of the recipient type and auxotrophic colonies with double nutrient deficiency, that is, with nutrient deficiency of both the donor and the recipient (Table 2). The subsequent generations of the four variant types isolated from the platings of the prototrophic colonies were studied. Some variants continued to segregate out colonies of the four types, others segregated out only two or one type of the colonies. However, after one or two transfers, non-segregating and stable lines of all four types were obtained.

How can we explain the segregation of all these forms out of prototrophic colonies, obtained as a result of transduction? If the prototrophs obtained are considered as hybrids, then the segregation of auxotrophs with nutrient requirements of the recipient is the segregation of the parent forms, while the segregation of auxotrophs belonging to the donor type, auxotrophs with double nutrient requirements, and prototrophs appearing stable through further generations are the result of recombinations similar to those induced by transduction in bacteria[6–8]. As for Actinomycetes, it is likely that a definite region of the chromosome appears to be in the 'diploid' state. The fact that on subsequent transfers the variants studied continue to segregate colonies with different nutrient deficiencies may be explained either by presence of different nuclei in the spores, or persistence of the nuclear 'diploid' state through several cell generations. It should also be pointed out that segregation of the donor-type auxotrophs and auxotrophs with double nutrient deficiency out of the prototrophic colonies may be the result of simultaneous transference by the actinophage of two factors, the normal allele of the biochemical deficiency of the recipient and the gene of the biochemical deficiency of the donor.

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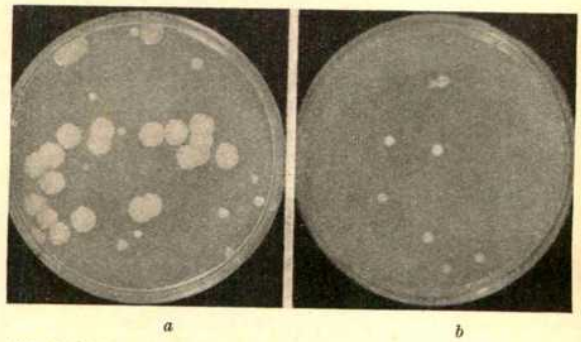
Transformation of a Strain of *Rhizobium lupini*

Transfer of Cysteine-independence. Strain *H*–13, which is a cysteine-dependent mutant of the prototroph *Rhizobium lupini* strain *H*, developed cysteine-independent colonies on treatment with the deoxyribonucleic acid of strain *H* (Fig. 1).



a *b*

Fig. 1. (*a*) Transformed cysteine-independent colonies on minimal agar; (*b*) untreated control.

The small colonies are altered small-step reversions to prototrophy. 10^7 plated cells

The deoxyribonucleic acid was prepared by lysis with sodium deoxycholate (1 per cent) at 55° C. for 10–15 min., followed by deproteinization by Sevag's method and precipitation by 3 vol. ethanol. The transformation was accomplished in a basal salt medium containing cysteine and glucose, on cells pre-incubated for 24 hr.

Fig. 2 shows a typical experiment. In general, I varied the time of addition and action of deoxyribonucleic acid, its concentration, and also the concentration of the cells and the growth-limit, the latter by decreasing the concentration of cysteine.

The following observations were made concerning the mechanism of transformation: (1) at least three

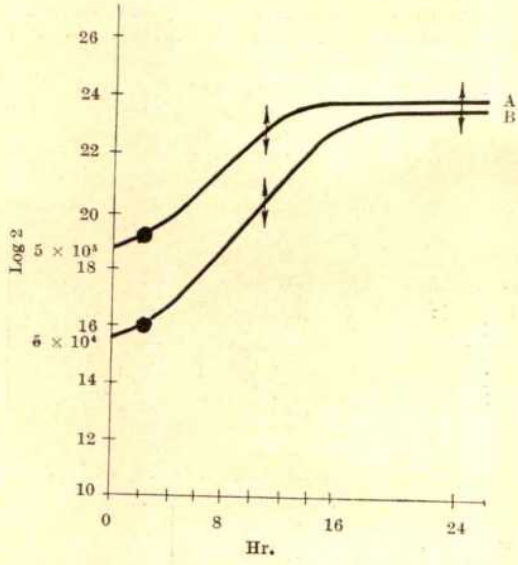


Fig. 2. ●, Time of addition of deoxyribonucleic acid (0·15 μgm./ml.); ↕, time of plating on minimal agar.

Number of transformed colonies: (*A*) plating after 10 hr., 23; 24 hr., 86. (*B*) plating after 10 hr., 15; 24 hr., 24

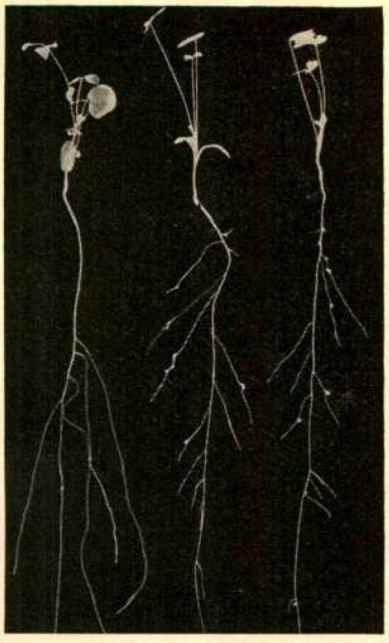


Fig. 3. From left to right: nodule formation of H–13 after one transformation; H–13 after two transformations; M–32 (control). Plants 4 weeks old

cell divisions are necessary to bring about transformation; (2) the phenotypic expression of transformed cells is preceded by a long transformational lag, during which there is apparently no need for cell division and the transformed character is not yet multiplying.

In consequence of the rather low frequency of transformants—generally the numbers attained did not exceed those given in Fig. 2—the system was not appropriate for more detailed investigations of the mechanism. Probably it is the mucous consistency of strain H–13 which opposes the penetration of deoxyribonucleic acid; although it is possible that the medium employed may not have been optimal. Experiments now in progress with rough strains rather point to the first assumption.

Change of Host-specificity. It was proved by Nutman[1] that the relation of *Rhizobium* to the host plant is genetically determined by the plant. On the other hand, interspecific transformations carried out with several species of *Rhizobium*[2] show that the host specificity also is genetically controlled by the bacteria.

In the following experiments the cysteine-dependent *Rh. lupini* (strain H–13) was transformed by the deoxyribonucleic acid of an *Rh. meliloti* strain (M–32). Lucerne plants inoculated *in vitro* with M_{32} form root-nodules on 95–100 per cent of the plants, whereas lucerne plants inoculated with H–13 form no nodules at all.

Preparation of M_{32} deoxyribonucleic acid and transformation of strain H–13 were carried out as described above.

In a series of plants inoculated with deoxyribonucleic acid-treated H–13, out of 120 plants 14 (11·7 per cent) formed nodules. Generally these were atypical structures developing late; only three plants formed rather typical nodules of greater size. Nitrogen fixation did not occur anywhere. In some series inoculated with single colonies isolated from these nodules, a somewhat higher number of mostly belated ineffective nodules were formed. The percentage yield did not change when cells of isolated colonies were newly transformed with the deoxyribonucleic acid of M_{32}; however, one part of the nodules formed developed at the same time as in the controls inoculated with M_{32} and proved to be typical and later to be effective (see Fig. 3).

These observations suggest that two or more successive distinct transformation types are needed to produce the new host-specificity.

H–13 exhibited in an intraspecific system a low transformation frequency (see above), so in this interspecific combination we suppose the frequency to be essentially lower still, and the changed character as being detected only by the strong selective power of nodule formation.

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CYTOLOGY

Mammalian Cell Chromosome Counts: a Simple Method for making Preparations

For those who work with small mammals, it is sometimes desirable to determine the chromosome complement in cells of particular individuals. Until recently, the most reliable technique for chromosome number determinations depended on the reasonably high mitotic rate and other desirable properties of the seminiferous tubules (for example, Matthey[1]). The difficulty with those techniques is that they do not permit the assessment of chromosome numbers in females, or in males apart from during the breeding season. Beatty[2] described a method of preparing corneal epithelial cells for chromosome counts, which overcame the shortcomings of relying on testicular cells, but many of the metaphase plates were not adequately spread. As a consequence, chromosome counts of only 20 cells from a total of 445 could be listed as exact counts. More recently, Ford *et al.*[3], and many other workers, have described very elegant techniques for mammalian chromosome counts, employing short-time culture of cells from a variety of tissues, primarily bone marrow. The primary difficulty with these techniques is the fact that very few laboratories have the equipment or personnel necessary for the carrying out of tissue culture. Another difficulty is the apparently large number of cells which possess chromosome numbers different from the diploid number. One cannot be sure if this heteroploidy is present in the tissue in the live animals or arises as a result of the extensive preparatory technique. This communication sets forth a relatively simple method for preparing corneal epithelium cells for reliable chromosome counts.

The animal, the cells of which are to be examined, is injected intraperitoneally with 0·01 ml. of 0·04 per cent aqueous colchicine solution/gm. of body-weight. After 3–4 hr. the animal is killed, the eyes are cut out and placed in 0·3 per cent sodium chloride at 37° C. for ½ hr. Fixation takes place in aceto-carmine overnight. Pieces of the epithelial layer are

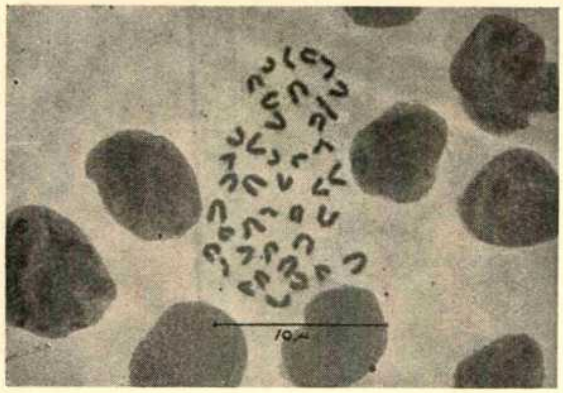

Fig. 1. Metaphase chromosomes of male *Mus musculus*

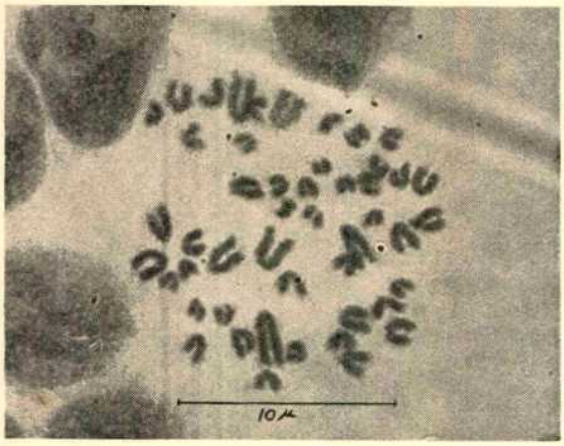

Fig. 2. Metaphase chromosomes of *Apodemus sylvaticus*

scraped from the cornea into a drop of aceto-carmine on an albuminized slide. The drop is then covered with a piece of 'Cellophane', a $\frac{7}{8}$-in. square cover-slip and filter paper, and the tissue is squashed in a press, delivering a pressure of about 40 kgm./sq. cm. of cover-slip (see Beatty[2] for details of the press). The 'Cellophane' is removed by letting the slide stand in tap water for about 5 min. Slides are then stained by the standard Feulgen procedure. Hydrolysis is for 10 min. in *N* hydrochloric acid at 60° C.

Preparations made this way from *Mus musculus*, *Apodemus sylvaticus*, and *Clethrionomys* sp. have invariably yielded many clear, well-spread metaphase plates, excellently suited to chromosome counting. As many as 30 metaphase plates suitable for counting are available from the epithelium of one mouse cornea. Typical plates are shown in Fig. 1 for the mouse and Fig. 2 for *Apodemus*.

In order to assess the efficacy of this method, the chromosomes of 5 cells from each of 10 male and 10 female mice were counted. The first 5 cells to appear suitable during examination with a low-power microscope objective were counted. The results are shown in Table 1. Of the 100 cells counted, an exact count was possible in 77, that is, there was no overlapping or crowding of the chromosomes so that no doubt existed about the precision of the count. Of these 77 cells, all but one contained 40 chromosomes. This one contained only 36. In 23 cells there were one or two places where mistakes might have occurred in counting, and these were therefore

Table 1. NUMBERS OF CELLS CONTAINING VARIOUS CHROMOSOME NUMBERS

	Chromosome count					
	36	40	40 ± 1	40 ± 2	44 ± 2	
Males		35	11	4		
Females	1	41	5	2	1	
Total	1	76	16	6	1	100

not scored as exact counts. Nevertheless, in 22 of these 23 cells, the 'most likely' number of chromosomes was 40. In one cell the 'most likely' number was 44. If one combines the exact counts and the 'most likely number' counts, it is seen that 98 of 100 cells have chromosome numbers compatible with the number 40. This confirms the observation of Beatty that the corneal epithelium exhibits extremely high constancy in regard to chromosome number. The apparent advantage of the method described here over that described by Beatty is in the much greater proportion of cells the chromosome number of which could be exactly determined. When compared to the techniques involving tissue culture, my method enjoys the advantages of simplicity and constancy of chromosome number, but suffers the disadvantage that the animal must be killed. Because the corneal epithelium is a surface tissue and because both chromatids of each chromosome are clearly visible in the cells prepared by this technique, it would appear that this might be an excellent means of ascertaining the extent of chromosome breakage in the living animals which is caused by ionizing radiation or other agents.

This work was done during the tenure of a Nato postdoctoral fellowship. I would like to express gratitude to Prof. C. H. Waddington for permission to work at the Institute of Animal Genetics and for providing space and facilities ; to Dr. J. G. Campbell for taking the photographs ; and to Dr. R. A. Beatty for continual helpful advice, and for collecting the wild rodents.

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Structural Changes in Mitochondria of *Acanthamoeba* at Encystation

FOR some time now the mitochondria have been ascribed a role in cellular respiration and more recently changes in intracellular ion concentration and tonicity have been shown to have marked effects on both mitochondrial volume and respiratory activity[1]. This communication reports changes in the structure of the mitochondria of a small amœba occurring at a time in the life-cycle when the intracellular environment is undergoing profound changes and respiratory activity is reduced to a minimum, namely, at encystation.

A clone strain of a soil amœba, *Acanthamoeba* sp., was isolated in this laboratory and maintained in monoxenic culture with *Aerobacter aerogenes* on 0·2 per cent peptone agar plates. The organisms were washed off the plates with distilled water before

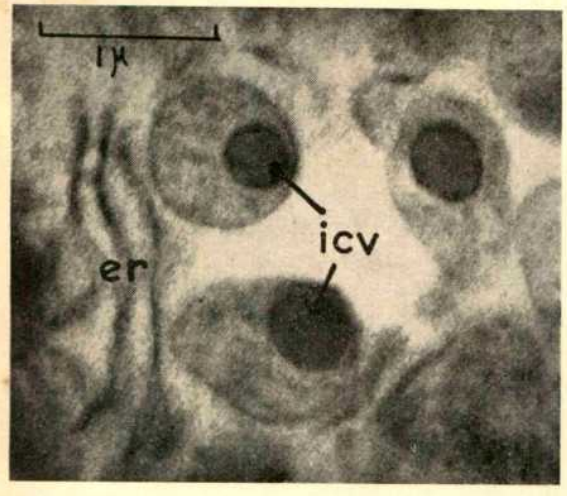

Fig. 1. Part of section of cyst showing three mitochondria with intra-cristal vesicles (*icv*), also tubules of endoplasmic reticulum (*er*)

fixing in permanganate[2] at *p*H 7·2 for 2 hr. at 4° C. Dehydration was in ethanol, 'staining' in 1 per cent phosphotungstic acid in absolute ethanol and embedding in 'Araldite'. Silver or gold sections were cut on the Porter-Blum microtome, mounted on carbon films and examined in the Siemen's Elmiscope 1*b* electron microscope.

The mitochondria of trophic amœbæ are usually oval in shape and measure 0·5–1·5μ × 0·5–1·0μ, but the shape is variable, and cup-shaped and even branched mitochondria have been seen in sections. Their internal structure resembles that of other free-living Protozoa. Each is surrounded by a double membrane: from the inner membrane tubular cristæ project into the mitochondrial lumen and in some cases they can be seen to traverse it. Often small spherical inclusions can be seen inside the cristæ. These have a diameter of 500–1000 Å. and if not completely electron-dense have a thick electron-dense cortex. More than one of these intra-cristal inclusions has never been observed in a mitochondrion.

In the mitochondria of the cyst the intra-cristal inclusions take the form of larger vesicular structures. They have a diameter of 3000–5000 Å. (0·3–0·5μ) and they are more opaque to the electron beam than is the surrounding mitochondrial matrix (Fig. 1). Electron-dense granules, irregular in size (50–300 Å.) and shape, lie immediately beneath the bounding membrane of the vesicle. The mitochondria of the cyst are usually spherical, 0·5–1·0μ in diameter. In some sections of cysts the outer membrane of a mitochondrion appears to be continuous with the membrane of a tubule of the endoplasmic reticulum.

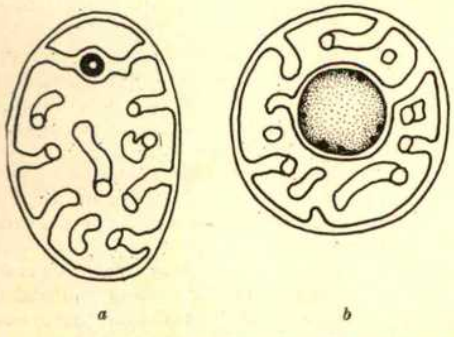

Fig. 2. Diagrams of mitochondria of amœba (*a*) and cyst (*b*) seen in section to show intra-cristal inclusions

It appears that at encystation in *Acanthamoeba* the intra-cristal bodies of the mitochondria swell to become vesicles which occupy a considerable part of the mitochondrial lumen. This change is represented in diagrammatic form in Fig. 2. One effect of this swelling is presumably to reduce the volume of the mitochondrial lumen. In a recent experimental study of the osmotic properties of isolated *Acanthamoeba* mitochondria, Klein and Neff[1] found that respiratory-rate was proportional to mitochondrial volume and that both were decreased by raising the tonicity of the surrounding medium. They suggested, however, that mitochondrial volume changes were under most conditions not primarily due to osmotic effects but rather to colloid swelling and shrinking phenomena. The effects of experimental changes in tonicity on the intra-cristal inclusions of *Acanthamoeba* have not yet been studied. A fuller report of work on the fine structure of this and other *limax* amœbæ will be published elsewhere.

I wish to thank Prof. J. Z. Young for facilities in his electron microscope laboratory and Dr. J. D. Robertson for his interest and advice.

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BACTERIOLOGY

Heterogeneity of Cultures of *Escherichia coli B/r*

A LARGE amount of the recent literature in radiation bacteriology and allied fields is concerned with the detailed behaviour of cultures labelled *Escherichia coli B* and *Escherichia coli B/r*. *E. coli B* is a bacterial strain that has been maintained for many years, mainly in laboratories concerned with bacteriophage synthesis and behaviour. It is characterized by its unusual sensitivity to several deleterious agents, including the *T* series of *coli* bacteriophages. *E. coli B/r* is one of a large group of mutants selected from *E. coli B* after irradiation with ultra-violet light. Witkin carefully defined *B/r* and distinguished it from *B* and other ultra-violet-selected mutants of *B*[1,2]. *E. coli B/r* was characterized by, among other things, its enhanced resistance to ultra-violet light, X-rays, penicillin, and sodium sulphathiazole. Furthermore, the snake-like forms found with very high frequency in *B* cultures irradiated with ultra-violet were found only occasionally in *B/r*.

A survey of the literature and our own experimental experience suggest that the various cultures labelled *E. coli B/r* are not identical. For example, Morse and Carter[3] claimed that *B/r* had 3–4 times more deoxyribonucleic acid per cell than *B*, whereas Harold and Ziporin[4] claimed that there was no difference. Preliminary results obtained in this Laboratory suggested that the viable cell titres and X-ray sensitivities of two *B/r* cultures being used routinely were not identical. The experiments

reported here were designed to compare, under standardized conditions, various aspects of *B/r* cultures obtained from different sources.

E. coli B ORNL and *E. coli B/r ORNL* were obtained from the Carnegie Institution, Cold Spring Harbor, about 12 years ago, and have been stocked on refrigerated agar-slants at Oak Ridge National Laboratory since then. They have been transferred at approximately 6-month intervals. These are the cultures most frequently used for work reported from this Laboratory. *E. coli B CSH* and *E. coli B/r CSH* were received from the Carnegie Institution about 3 years ago and have been stocked on refrigerated nutrient-agar. *E. coli B/r* Cornell University, *E. coli B* Institut du Radium, and *E. coli B/r* Institut du Radium were received from the institutions indicated and were refrigerated on arrival. All the cultures were transferred, by mass inoculum, at the beginning of this series of experiments to a medium (total volume, 1 l.) composed of 10 gm. of 'Bacto-Peptone', 1 gm. of dextrose, 1 gm. of yeast extract, 7·6 gm. of dipotassium hydrogen phosphate, 4·5 gm. of potassium dihydrogen phosphate, and 20 gm. of agar. These slants were used as inocula for all experiments.

Preparation of cells and irradiation techniques with X-rays and ultra-violet light are described elsewhere[5]. Determinations of snake-formation and penicillin sensitivity were carried out essentially as described by Witkin[2]. Optical density was determined with a 'Lumetron' colorimeter with a 650-mμ filter.

Fig. 1 shows that the *B/r* cultures are heterogeneous with regard to X-ray sensitivity. Three of them

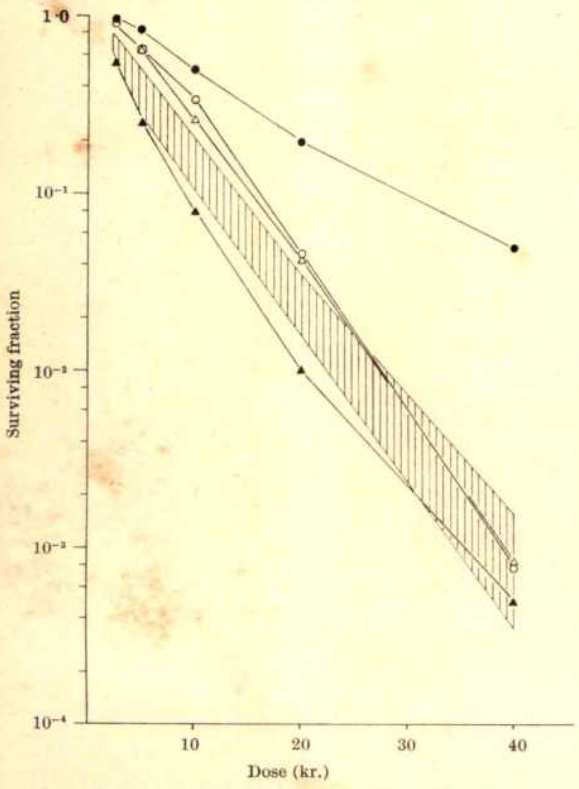

Fig. 1. Sensitivity of four *B/r* cultures to 250 kV. X-rays. Lined area represents range of results obtained with three *B* cultures. ●, *B/r ORNL*; ■, *B/r* Institut du Radium; △, *B/r* Cornell University; and ▲, *B/r CSH*

Table 1. CHARACTERISTICS OF *B* AND *B/r* CULTURES

Culture	'Snake' formation after 50 ergs of ultra-violet radiation	Final optical density*	Units of penicillin '*G*' required for 100 per cent inhibition
B ORNL	+	0·309 ± 0·017	40
B CSH	+	0·303 ± 0·023	40
B Institut du Radium	+	0·297 ± 0·016	40
B/r ORNL	−	0·332 ± 0·034	60
B/r CSH	−	0·243 ± 0·035	120
B/r Institut du Radium	−	0·218 ± 0·030	120
B/r Cornell University	−	0·179 ± 0·025	60

* Based on six determinations per value. One *S.E.* is indicated.

are not strikingly different in sensitivity from the group of three *B* cultures, which form a relatively homogeneous group. To test whether these three *B/r* cultures had 'reverted' to *B*, several criteria were used. Table 1 shows that none of the *B/r* cultures forms 'snakes' after exposure to low doses of ultra-violet light, whereas all the true *B* cultures do. It also shows that the *B/r* cultures are a heterogeneous group with respect to final optical density and that optical density is not correlated with radiation sensitivity. Table 1 also shows the concentration of penicillin required to achieve 100 per cent inhibition of growth as determined by final optical density.

We attempted to determine the sensitivity to ultra-violet radiation of the *B* and *B/r ORNL* and *B* and *B/r CSH* pairs. The results are confounded by a disturbing amount of variation observed in absolute sensitivities from experiment to experiment, even though elaborate precautions were taken to avoid photoreactivation, heat restoration, and other known variables. Nevertheless, it is fair to make certain conclusions based on six independent experiments done for each pair of cultures. Both the *ORNL B/r* and the *CSH B/r* cultures show sigmoid survival curves to ultra-violet radiation. They are each somewhat more resistant than the corresponding *B* cultures, which show more nearly exponential survival. The difference in sensitivity in any one experiment between a *B* and its corresponding *B/r* is never as large as that reported by Witkin[2].

The results reported here support the contention that cultures labelled *E. coli B/r* being used in different laboratories form a genotypically and phenotypically heterogeneous group. *E. coli B* cultures are relatively homogeneous.

Cultures of the strain *B/r* differ from each other in their response to X-irradiation, and their physiological capabilities under standardized conditions. Three of the four cultures have an X-ray sensitivity characteristic of *B* cultures, but cannot be classified as 'revertants' since they do not form the 'snakes' characteristic of *B* cultures. Two of these three, although they have strikingly similar X-ray sensitivities, can usually be distinguished from each other on the basis of final optical density and sensitivity to penicillin.

The results obtained with ultra-violet irradiation (2537 Å.), although variable and not done under conditions identical to those used by Witkin[2], suggest that none of the *B/r* cultures is as strikingly resistant to ultra-violet light as the original *B/r*.

Since the current trend in much radiation bacteriology research is to relate radiation sensitivity to the detailed metabolic mechanisms of cells and to

generalize results from one laboratory to another, our results indicated the need for a note of caution. This is particularly true if one also considers that any one of these cultures may show several forms of sensitivities to X-rays and ultra-violet light, depending on the growth medium and other factors[5]. The cultures used in this work were not pre-selected for heterogeneity. They were chosen because they were readily available. It is likely that other groups of *B/r* cultures from other laboratories would be equally heterogeneous. Greater attention to the techniques of maintaining cultures and periodic checking of culture characteristics may allow a more meaningful correlation of the results obtained in different laboratories. We suggest that the designation *E. coli B/r* be reserved only for cultures having all the characteristics originally observed by Witkin.

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Chitin Breakdown of Rhizosphere Bacteria

BENECKE[1] was the first to isolate chitinovorous bacteria from Kiel harbour. Since then much work has been done on microbiological breakdown of chitin. Micro-organisms producing chitinase have been observed in fresh and salt waters, in various kinds of soils, in plants and animal bodies, both living and decomposing. It has been reported that pathogenic micro-organisms also break down chitin.

I have studied whether bacteria living in the rhizosphere of superior plants are capable of attacking chitin.

For this purpose chitin has been prepared from the wing-cases of *Melolontha melolontha* L. with the Zechmeister procedure applied also by Gehring[2]. The native chitin obtained in this way was suspended in medium according to Bucherer[3]. The chitin was present in the medium as the sole source of carbon and nitrogen in amounts of 0·1, 0·25, and 0·5 per cent. Dipotassium hydrogen phosphate and magnesium sulphate (0·03 or 0·1 per cent) were added. The solid medium contained 2 per cent washed agar. In all cases the *p*H was 7.

Bacteria were isolated on chitin agar and meat agar plates from the rhizospheres of winter wheat (*Triticum vulgare*), sugar-beet (*Beta vulgaris saccharifera*), and false acacia (*Robinia pseudoacacia*) with Tepper's[4] successive washing method (from the dilution of washed and triturated root). About 20 per cent of the bacterial colonies grown on meat agar, tested on both solid and liquid media, proved to be chitinivorous.

The bacterial colonies grown on chitin agar did not show a great variety of types, but the number of individuals was rather high. Their total reached several hundred thousands per 1 gm. of washed root.

From the chitinivorous rhizosphere bacteria of winter wheat and false acacia a rod-shaped, most frequently occurring, active chitinivorous organism—one from each—was selected. These retained their capacity of breaking down chitin for rather a long time. These bacteria were subjected to detailed examination. In addition to them the capacity of breaking down the chitin of rhizosphere bacteria isolated on non-chitinous media by other workers was also studied: none of the five *Pseudomonas* strains belonging to various serological groups, grown from the rhizosphere of flax by Lovrekovich[5], tested with the method described above, was found to decompose chitin. Out of the sixteen *Bacterium* strains grown from sugar-beet, Gyurkó[6] subjected to detailed physiological examination five strains proved to be chitinivorous and the strains kept on meat agar have preserved this property for more than two years.

I wish to thank my colleagues, L. Lovrekovich and P. Gyurkó, for the strains examined.

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VIROLOGY

Influenza Virus Sialidase

THE sialidase of influenza virus has been investigated quantitatively using the method recently described by Warren[1] for determining free sialic acid in the presence of the compound bound to mucoprotein substrates. For this work, the substrate used was a mucoid derived from the nest-cementing substance of the swiftlet (*Collocalia* sp.). The crude material, available as Chinese 'edible birds' nest', was extracted with water at 60–65° to yield a product which contained 10 per cent acid-hydrolysable sialic acid and which in high titre inhibited the agglutination of chicken erythrocytes by 'indicator' virus. Active virus was sedimented from freshly gathered chorioallantoic fluid by centrifugation at 35,000*g* for 90 min. The virus pellet was re-suspended in water to a volume 1/50–1/100 that of the original fluid, effecting thereby a corresponding increment in haemagglutinin titre as well as separation of virus from interfering chromogens present in chorioallantoic fluid.

Aliquots of virus (*A*2/Japan/305/57) representing a six-fold concentration of infective chorioallantoic fluid were mixed with substrate in phosphate (*M*/15) buffers, *p*H 4·0–7·8, at 37°, in the proportion 10 μgm. viral nitrogen to 1·4 mgm. substrate. Samples were removed at 10-min. intervals from 0 to 50 min., and were immediately heated to 75° for 10 min., a temperature found to inactivate the virus completely. All samples were either stored frozen or at 4° prior to being analysed simultaneously for sialic acid. Virus alone and solutions of substrate at each *p*H, after incubation and heating to 75° for 10 min., showed no free sialic acid. The most rapid evolution of chromophore due to enzyme occurred at *p*H 5·3 and 6·1. These values probably encompassed the *p*H optimum for this strain, as the enzymatic release of sialic acid at *p*H 4·0, 7·0 and 7·8 was significantly slower (Fig. 1*A*). Closely similar results were obtained with three other strains of virus (*NWS*, *FM*1 and *PR*301) and are therefore not given in

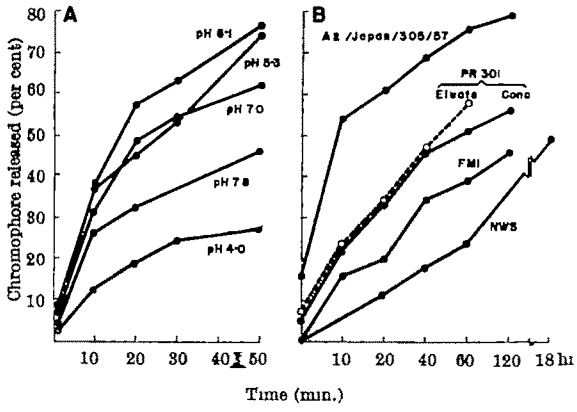

Fig. 1. *A*, Liberation of sialic acid (expressed as percentage of total acid-hydrolysable thiobarbituric acid chromophore) in relation to time, at 37°, *p*H 4·0–7·8. (*A*2/Japan/305/57 concentrated six-fold from chorioallantoic fluid.) *B*, Relative enzymatic potency, at *p*H 5·5, 37°, of four strains (*A*2/Japan/305/57, *PR*301, *FM*1, *NWS*) after concentration and adjustment to the same turbidity

detail. At each *p*H the per cent sialic acid released, expressed as a fraction of total acid-hydrolysable chromophore, approached the same maximum (greater than 80 per cent) after incubation at 37° for more than 2 hr. In acetate buffer (*M*/100) at *p*H 5·5, the sialidase of the *A*2 strain of virus was inhibited by copper (*M*/800), but not by nickel, zinc, magnesium or manganese, was fully active in the presence of versene (0·02 per cent), and more active at 37° than at 26°. Specific enzymatic activity was proportional to virus concentration. Receptors in *Collocalia* mucin for several indicator strains of influenza virus were inactivated by treatment with concentrated active virus. N-acetylneuraminic acid was identified chromatographically as the only chromogenic substance liberated by viral enzyme from this substrate.

The activity of *A*2/Japan/305/57 virus was compared with that of *FM*1, *PR*301 and *NWS* viruses. The concentrated viral suspensions were adjusted to the same optical density as measured on a Coleman nephelometer, and assayed at *p*H 5·5 as described above. Under these conditions, the *A*2 strain was far more active than either of the other three (Fig. 1*B*), releasing more than 50 per cent of the chromogen in 10 min. As also shown in Fig. 1*B*, the same preparation of concentrated *PR*301 virus was adsorbed to and eluted from chicken erythrocytes with no loss of enzymatic activity.

The *A*2 strain of virus was grown in monkey kidney monolayers in 2-oz. prescription bottles. Prior to inoculation, the growth medium was removed, the cells washed and 5 ml. serum-free maintenance solution added (2 parts mixture 199 and 1 part Earle's balanced salt solution). Hæmagglutinin appeared in 3–5 days, followed by gross cytopathic changes. 10 ml. of culture fluid from two bottles of the fourth passage were centrifuged at 40,000*g* for 90 min., the pellets resuspended in 0·1–0·2 ml. water, and assayed for enzyme. More than 80 per cent of the bound sialic acid in samples of *Collocalia* mucin was liberated by this virus preparation after incubation at 37° for 16 hr. Normal culture fluid had no enzymatic activity.

The sialidase activity of an *A*2 strain of influenza (Japan/305/57) appeared to be far greater than that of the other strains tested. Even the few seconds necessary to mix virus with substrate was sufficient to permit the liberation of 15 per cent of the thiobarbituric acid chromophore. These results are in general agreement with the findings of Seto *et al.*[2], who concluded that *A*2 strains showed greater sialidase activity than any other strains previously studied. These authors state that their *NWS* strain of influenza *A* had no sialidase activity, whereas the *NWS* strain used in the present work showed pronounced enzymatic activity, albeit less than that of the *A*1 strains. The reasons for this discrepancy are not apparent and deserve further investigation.

Reliance on turbidity measurements alone as a quantitative measure of virus particle concentration, and therefore as a basis of comparison, is subject to obvious error because of the possible inclusion of varying amounts of chicken tissue particles in each concentrated virus sediment. It is unlikely, however, that either the extent or variation of tissue contamination from one virus preparation to another was great enough to account for the major differences in enzymatic activity between the *A*2 strain on one hand and the *A* and *A*1 strains on the other. Further comparative investigations are planned with enzyme purified from both egg-grown virus and that produced in monkey kidney cell cultures which appears to be enzymatically just as active.

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A Plaque Technique for the Primary Isolation of Arthropod-borne Viruses

THE demonstration that a wide range of different arthropod-borne viruses could produce plaques in monolayer cultures of chick embryo cells[1] raised the possibility that this technique could be used for the primary isolation of viruses in this group. This point was investigated first by the examination in London of material submitted from Uganda, and later during a visit of one of us to the Virus Research Institute, Entebbe.

During an epidemic of O'nyong-nyong fever in Uganda a number of strains of a virus which was classified as a member of the group *A* arthropod-borne viruses[2] was isolated from sera collected from persons during the acute stage of the illness[3]. One such serum, which had yielded virus by the intracerebral inoculation of one-day-old mice, was forwarded to London packed in ice at 0° C. When dilutions of this serum were tested by the plaque technique, approximately 50 plaques were produced in plates inoculated with 0·5 ml. of a 1 : 10 dilution, and 3 and 4 plaques developed in plates infected with serum diluted 1 : 100. The same results were

obtained in a second experiment carried out in London with the same serum sample. Since O'nyong-nyong virus requires a number of serial passages in one-day-old mice before it kills these regularly, the advantages of a direct tissue culture system are obvious.

When this experiment was repeated at Entebbe with another sample from the same batch of serum, once again plaques were produced. However, six other sera collected in the course of the same epidemic which had previously been shown to contain virus failed to produce plaques, although simultaneous tests carried out in one-day-old mice showed that virus was still detectable in four of them by this method. Since these sera had been stored for several months at approximately −60° C. it was felt that fresh material might provide a more useful basis for the comparison of the two techniques. Unfortunately, no fresh material was available from O'nyong-nyong fever patients, but a small outbreak of Rift Valley fever in the vicinity of Entebbe[4] was investigated by both methods.

One acute phase human serum produced more than 100 plaques per 0·5 ml. of a 1 : 10 serum dilution, and 22 plaques per 0·5 ml. of a 1 : 100 dilution. Rift Valley fever virus was isolated from this serum sample by the inoculation of one-day-old mice, the virus titre being $10^{2.5}$ per 0·1 ml. A second human serum also yielded virus by both methods. A mosquito pool suspension from which Rift Valley fever virus had been isolated in mice was retested by both methods after 8 days storage at −20° C. On this occasion no virus was isolated in mice, but one plaque developed in a plate infected with 0·5 ml. of a 1 : 10 dilution of the mosquito suspension. When material from this plaque was inoculated into mice, Rift Valley fever virus was again recovered. The identity of the virus was established by the inhibition of plaques produced by infected mouse brain suspension around a bead containing a known Rift Valley fever immune serum.

These preliminary experiments indicate that virus isolations may be accomplished by the direct use of the plaque technique, but that the method is probably less sensitive than the use of one-day-old mice, though a much larger series would be required to give a better assessment of the comparative sensitivities of the two methods. The single occasion when virus was recovered in tissue culture and not in mice may be explained in terms of the considerably greater volume of material used in the former system; had an equivalent volume of mosquito suspension been inoculated into further mice, it is probable that virus would have been recovered by that process also.

Although this has not yet been accomplished in practice, a combination of primary isolation in tissue culture, together with plaque inhibition around beads dipped in specific antisera, offers the possibility of virus isolation and identification in a single process.

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Entebbe.

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[2] Porterfield, J. S., *Bull. World Health Org.* (in the press).
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SOIL SCIENCE

Negative and Positive Adsorption of Chloride by Kaolinite

Schofield and Samson[1] have indicated that the edge face of kaolinite crystals should, under acid conditions, adsorb one chloride ion for each 33 Å.^{2}. They obtained results which showed that on the acid side of neutrality the positive edge charge of a potassium kaolinite was such that it exceeded the negative adsorption of chloride ions resulting from the repulsion of these ions from the negative cleavage face. Further, these authors noted that for conditions more alkaline than about *p*H 6·5 in 0·005 *M* sodium chloride the clay exhibited a negative adsorption. When Schofield's[2] theory was applied to these results, a surface area of 25 m.^{2}/gm. was obtained and this was lower than the 39 m.^{2}/gm. obtained by low-temperature nitrogen adsorption. The constant negative adsorption for alkaline conditions was interpreted as being due to the disappearance of positive edge charges. Work reported here, however, shows a positive adsorption dependent on concentration under conditions as alkaline as *p*H 10. When allowance is made for this positive adsorption the correct value is obtained for the surface area.

The results reported here were obtained for a kaolinite obtained from the pallid zone of a laterite at Rocky Gully in Western Australia. It is the same material designated as kaolin *S* by Samson and Schofield. The clay (less than 2μ) was washed with *M* potassium chloride containing 10^{-3} hydrochloric acid; then with water until the chloride ion concentration was less than 10^{-3} *M*. The required amount of base and electrolyte was added. The clay suspension was centrifuged at low speeds and chloride was determined by an electrometric method in the centrifuged clay and the supernatant liquid.

In Fig. 1 the negative adsorption of a potassium kaolinite at *p*H 9 can be seen to be considerably less than that expected on the basis of Schofield's theory. It is interesting to note that the value obtained at 0·01 *M* potassium chloride is in agreement with that obtained by Schofield and Samson. Although the *p*H of the suspension was 9, it was suspected that the low

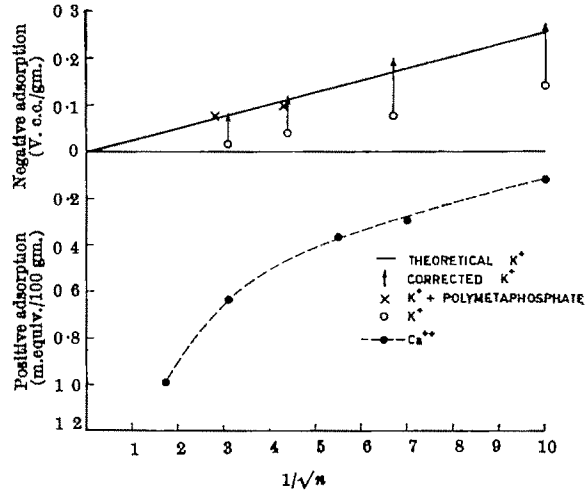

Fig. 1. The negative and positive adsorption of chloride by potassium and calcium kaolinite at *p*H 9. *n*, Concentration in m.equiv. per ml.

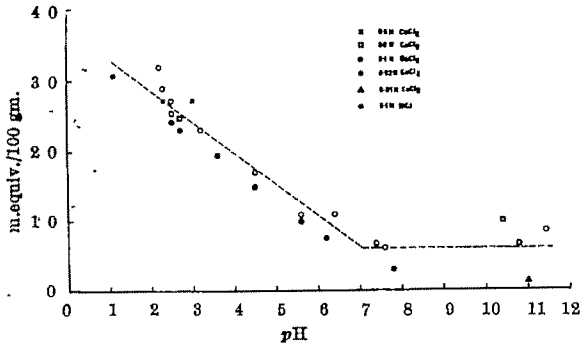

Fig. 2. Effect of pH on the positive adsorption of chloride by calcium kaolinite

values for the negative adsorption were caused by a concomitant positive adsorption. The kaolinite was treated with sodium polymetaphosphate (6 m.equiv./100 gm. adsorbed) and the results obtained by the negative adsorption of chloride then agreed with the theoretical expectation. Since this was considered only circumstantial evidence for the existence of chloride uptake at pH 9, more direct proof was sought. Since the negative adsorption of chloride for a clay saturated with a divalent cation is considerably less than for a monovalent ion, the kaolinite was saturated with calcium and it was found that positive adsorption predominated and also that the chloride adsorption was dependent on concentration. When the potassium kaolinite results were corrected for the amount of positive adsorption for the calcium kaolinite, the arrows in Fig. 1 indicate that the cleavage face is in fact repelling chloride ions in the expected fashion. It is pointed out that since there would be some negative adsorption of the calcium kaolinite this procedure would under-estimate the positive charge and hence the corrections applied to the potassium kaolinite would be slight under-estimates.

In Fig. 2 the effect of pH and electrolyte concentration on the adsorption of chloride by a calcium kaolinite is shown. At about pH 7 in 0·1 M calcium chloride there is a transition from concentration-dependent to concentration-independent chloride adsorption.

The ceiling value of 3 m.equiv./100 gm. attained at about pH 3 represents an edge surface area of 6 m.^{2}/gm. and this is 14 per cent of the B.E.T. area for the material. Cashen has reported edge areas of 11 and 19 per cent for Mercks and Peerless kaolin. These were measured by titration of the kaolins with cetyl trimethyl ammonium bromide before and after treatment with pyrophosphate or oxalic acid, both of which would render the edge face negative.

As noted by Schofield and Samson this kaolinite contains a small quantity of iron oxide (< 2 per cent goethite) as impurity but this would only affect the results to a minor extent.

These investigations are continuing and work on the importance of edge faces as the site of phosphate fixation are in progress.

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MATHEMATICS

William Stroud and Quantity Calculus

THE convention of representing physical quantities, rather than their measures, by letters is said to have been "devised in the eighties of last century by that versatile genius Prof. William Stroud, of Leeds University"[1]. A succession of teachers of applied mechanics at the Royal Naval College, Greenwich (J. B. Henderson, B. P. Haigh, J. G. Docherty, F. W. Thorne and A. C. Walshaw), and other teachers have always referred to this convention as the 'Stroud system'[2]. It is the main purpose of this communication to present some reasons why this attribution is unsatisfactory and why it would be better to replace it by the term 'quantity calculus' used by E. A. Guggenheim and others[3].

There is no written evidence that William Stroud ever used the conventions of quantity calculus. The following question from one of his examination papers shows that he did not use it in his teaching: "The thermo-electric power of Cu—Pb = $0{\cdot}0124\,(67 + t)$ and for Fe—Pb = $0{\cdot}042\,(357 - t)$. Find the E.M.F. in a Cu—Fe circuit whose junctions are at 100° C. and 200° C."[4].

There is evidence that others were advocating and using quantity calculus before or at the time that William Stroud is said to have been teaching it. Following the publication of J. B. Henderson's account of the 'Stroud system'[1], E. H. Neville[5] immediately pointed out that J. D. Everett[6] had certainly used quantity calculus in 1879, though, I would add, not always in a consistent manner. It is of interest to note that William Stroud was certainly acquainted with J. D. Everett's text-books, because one of the recommended books for the first-year course in physics at the Yorkshire College was Deschanel's "Natural Philosophy", Vol. 1, thirteenth edition, which was translated and edited by J. D. Everett[7]. The first clear expression of the principles of quantity calculus is undoubtedly A. Lodge's very concise presentation of its conventions under the significant title: "The Multiplication and Division of Concrete Quantities"[8].

In view of these historical difficulties, it would appear to be best to speak of 'quantity calculus' rather than of the 'Stroud system'.

I wish to acknowledge the help I have received from Miss D. M. Leak, of the Brotherton Library, University of Leeds; the Directors of Barr and Stroud, Ltd., Glasgow; and Prof. F. W. Thorne, Dr. A. C. Walshaw and Dr. J. G. Docherty.

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17 Calderstones Avenue,
Liverpool 18.

[1] Henderson, J. B., *Math. Gaz.*, **12**, 99 (1924).

[2] Grundy, R. H., "Symbols for Students" (George Reed, Liverpool, 1943). Jeffreys, H., "Scientific Inference", second ed., 87 (Cambridge Univ. Press, 1957). Thorne, F. W., and Walshaw, A. C., "Engineering Units and the Stroud Convention" (Blackie and Son, London, 1954). Walshaw, A. C., *Bull. Mech. Eng. Educ.*, **15**, 28, 79 (1959).

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[7] "The Yorkshire College Leeds Calendar", 1895–6, p. 95.

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FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, October 17

UNIVERSITY OF LONDON (at Senate House, London, W.C 1), at 5 15 p m.—Prof. J. Piaget (International Bureau of Education, Geneva): "The Thinking of Young Children".*

UNIVERSITY OF LONDON (at Queen Elizabeth College, 61–67 Campden Hill Road, London, W.8), at 5.30 p m.—Prof. A. J. Ayer: "Contemporary British Philosophy".*

INSTITUTE OF METALS, LONDON LOCAL SECTION (joint meeting with the INSTITUTE OF METAL FINISHING, at the Northampton Polytechnic, St. John Street, London, E.C.1), at 6.15 p.m.—Mr. C. Williams: "Electroplating Processes and Effect on Fatigue Strength and Embrittlement of the Substrate".

INSTITUTE OF NAVIGATION (at the Royal Geographical Society 1 Kensington Gore, London, S.W.7), at 8.30 p.m.—Dr. Eric Axelson, "Henry the Navigator and the Sea Route to India" (First Eva G R Taylor Lecture).

Tuesday, October 18

UNIVERSITY COLLEGE (in the Anatomy Theatre, Gower Street, London, W.C.1), at 1.15 p.m.—Dr. H. Kalmus: "The Biology of Fighting".*

UNIVERSITY OF LONDON (in the Great Hall, Queen Mary College, Mile End Road, London, E.1), at 1 30 p.m.—Sir Vivian Fuchs: "Antarctica Today".*

UNIVERSITY OF LONDON (at King's College, Strand, London, W.C.2), at 5.30 p.m.—Prof. F. Hirzebruch (University of Bonn): "The Rôle of Characteristic Classes in Algebraic Topology".* (Further lectures on October 19 and 20.)

BRITISH ORNITHOLOGISTS' UNION (joint meeting with the BRITISH ORNITHOLOGISTS' CLUB, in the new Lecture Hall of the British Museum (Natural History), Cromwell Road, London, S W.7), at 6 p.m.—Annual Scientific Meeting. Dr. A. J. Cain: "Tropical Forest and Bird Ecology" (illustrated with slides and a film).

OIL AND COLOUR CHEMISTS' ASSOCIATION, LONDON SECTION (at Manson House, 26 Portland Place, London, W.1), at 7 p.m.—Mr. R. D. Griminski and Mr. F. M. P. Meredith "The Lacquering of Aluminum–Magnesium Alloys".

Wednesday, October 19

UNIVERSITY OF LONDON (at the Postgraduate Medical School of London, Ducane Road, London, W 12), at 2 p.m.—Dr. K. Lowe: "Tests of Renal Function".*

GEOLOGICAL SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Dr. J. E. Prentice: "The Stratigraphy of the Upper Carboniferous Rocks of the Bideford Region, North Devon"; Dr. D C. Knill and Dr. J. L. Knill: "Time Relations Between Folding, Metamorphism and the Emplacement of Granite in Roseguill, Co. Donegal".

ROYAL METEOROLOGICAL SOCIETY (at 49 Cromwell Road, London, S.W.7), at 5 p.m —Scientific Papers.

INSTITUTE OF FUEL (at the Institution of Civil Engineers, Great George Street, London, S.W.1), at 5.30 p.m.—Discussion on "Pulverized Fuel Flames", led by Mr. G. G. Thurlow.*

INSTITUTION OF ELECTRICAL ENGINEERS, SUPPLY SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. J. E. L. Robinson. "The Developing Engineer" (Chairman's Address).

ROYAL MICROSCOPICAL SOCIETY (at Tavistock House South, Tavistock Square, London, W.C.1), at 5.30 p.m.—Prof. R. Ruggles Gates F.R.S: "The Histology of Skin Pigmentation".

CEMENT AND CONCRETE ASSOCIATION (at the Institution of Structural Engineers, 11 Upper Belgrave Street, London, S.W.1), at 6 p.m.—Mr. F. R. Belson: "Lift Slab Design and Construction."

SOCIETY OF CHEMICAL INDUSTRY, CORROSION GROUP (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Mr. C. Edeleanu and Mr. J. B. Cotton: "Anodic Protection". (*A*) "Principles". (*B*) "Practical Application".

BRITISH INSTITUTION OF RADIO ENGINEERS, MEDICAL AND BIOLOGICAL ELECTRONICS AND COMPUTER GROUPS (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6.30 p.m.—Symposium on "The Use of Computers in Biological Waveform Analysis".

Thursday, October 20

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C 1), at 1.15 p.m.—Dr. J. H. Callomon: "The Danish East Greenland Expeditions, 1957–58".*

INSTITUTION OF MINING AND METALLURGY (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 5 p.m.—October General Meeting.

UNIVERSITY OF LONDON (in the Physiology Theatre, University College, Gower Street, London, W C.1), at 5 p.m.—Dr. V. P. Whittaker: "The Subcellular Localisation of Neurohormonal Agents".* (Further lecture on October 27)

UNIVERSITY OF LONDON INSTITUTE OF EDUCATION (in the Great Hall, Goldsmiths' College, New Cross, London, S.E.14), at 5 p.m.—Mr. A. B. Clegg: "An Extra Year".* (Fifth of a series of lectures on "The Future of Education".)

UNIVERSITY OF LONDON (at Senate House, London, W.C.1), at 5.30 p.m.—Prof. C. H. Waddington, F.R S.: "The Significance of Developmental Biology".* (First of fifteen lectures on "The Scientific Basis of Medicine", organized by the British Postgraduate Medical Federation.)

SOCIETY OF CHEMICAL INDUSTRY, ROAD AND BUILDING MATERIALS GROUP (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Mr. L. E. Akers: "The Manufacture and Properties of Wood Chipboards".

ROYAL INSTITUTE OF CHEMISTRY, LONDON SECTION (joint meeting with the SOUTH-EAST ESSEX TECHNICAL COLLEGE SCIENTIFIC SOCIETY, at the South-East Essex Technical College, Longbridge Road, Dagenham, Essex), at 7 p.m.—Dr. G. I. P. Levenson: "Some Chemical Aspects of Colour Photography".

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE (at Manson House, 26 Portland Place, London, W 1), at 7.30 p.m —Opening Meeting of the 54th Session. Dr. Telford Work will show a film entitled "Kyasanur Forest Disease in India".

BRITISH INSTITUTE OF RADIOLOGY (in the Reid-Knox Hall, 32 Welbeck Street, London, W.1), at 8 p m.—Mr. J. W. D. Bull "The History of Neuroradiology" (Presidential Address).

UNIVERSITY OF LONDON (at Wye College, Wye, Ashford, Kent), at 8 p.m.—Sir Eric Ashby: "Reflections on Soviet Education".*

Friday, October 21

PHOTOELECTRIC SPECTROMETRY GROUP (in the Department of Chemistry, Imperial College of Science and Technology, London, S W.7), at 2 p.m.—Meeting on "Recording Ultraviolet Spectrophotometers".

ROYAL INSTITUTION (at 21 Albemarle Street, London, W 1), at 9 p.m.—Mr. S. H. Clarke: "Fire Research".

Saturday, October 22

BIOCHEMICAL SOCIETY (at the National Institute for Medical Research, The Ridgeway, Mill Hill, London, N.W.7), at 10.25 a.m.—Scientific Papers.

WORKERS' EDUCATIONAL ASSOCIATION (at Mullard House, Torrington Place, London, W.C.1), at 2 p.m.—Meeting on "Science and the Arts".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the date mentioned:

HEAD (graduate, with good industrial and teaching experience) OF THE ENGINEERING DEPARTMENT (Civil, Electrical and Mechanical Engineering)—The Acting-Principal, Dudley and Staffordshire Technical College, Dudley (October 21).

SENIOR LECTURER/LECTURER (preferably in possession of a medical qualification and also a higher degree) IN PHYSIOLOGY—The Secretary, London Hospital Medical College (University of London), Turner Street, London, E.1 (October 21).

SENIOR LECTURER (with high qualifications and wide experience) IN PHYSICS to teach to honours degree level; and an ASSISTANT, Grade B, IN PHYSICS—The Clerk to the Governors, Woolwich Polytechnic, London, S.E.18 (October 21).

LECTURER IN STATISTICS—The Registrar, University College of North Staffordshire, Keele, Staffs. (October 24).

RESEARCH FELLOW IN ORGANIC CHEMISTRY to work on the study of factors affecting polymerization of compounds containing boron–nitrogen bonds—The Registrar, The University, Nottingham (October 29).

SCIENTIFIC OFFICER (with a first- or second-class honours degree with physical or inorganic chemistry as the principal subject) IN THE DEPARTMENT OF PEDOLOGY, for work which will involve investigations upon soil formational processes with a physico-chemical bias—The Secretary, The Macaulay Institute for Soil Research, Craigiebuckler, Aberdeen (October 29)

ASSISTANT LECTURER OR DEMONSTRATOR IN PATHOLOGY—The Registrar, The University, Manchester (October 31).

CHAIR OF MATHEMATICS—The Registrar, The University, Hull (October 31).

LECTURER IN THE UNIVERSITY COMPUTING LABORATORY, Newcastle upon Tyne—The Registrar, University of Durham, 46 North Bailey, Durham (October 31).

LECTURER OR ASSISTANT LECTURER (qualified in pure or applied mathematics) IN MATHEMATICS—The Registrar, University College of North Staffordshire, Keele, Staffs. (October 31).

FELLOW (with field and laboratory experience in virology and the epidemiology of insect-transmitted viral diseases) IN THE DEPARTMENT OF MICROBIOLOGY, John Curtin School of Medical Research, Australian National University, to work on the epidemiology of arthropod-borne virus infections in Australia and the islands to the north of Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, November 4).

LECTURER (with qualifications in pure mathematics) IN MATHEMATICS—The Secretary, The University, 38 North Bailey, Durham (November 12).

RESEARCH DEMONSTRATOR (preferably with experience and interest in field and soil mycology) IN MYCOLOGY IN THE DEPARTMENT OF BOTANY—The Registrar, University College of North Wales, Bangor, North Wales (November 14).

SENIOR ASSISTANT LIBRARIAN (preferably aged 25 to 35 with a good knowledge of chemical literature and experience in an industrial or other special library)—The General Secretary, The Chemical Society, Burlington House, Piccadilly, London, W.1 (November 14).

CHAIR OF CHEMISTRY, and a READER IN PHYSICAL CHEMISTRY AT THE UNIVERSITY OF KHARTOUM—The Registrar, University of Khartoum, c/o Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (November 15).

LECTURER (with an honours degree in zoology) IN ZOOLOGY AT THE UNIVERSITY OF CANTERBURY, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand and London, November 15).

READER or SENIOR LECTURER or LECTURER IN AGRICULTURAL BIOCHEMISTRY; and a READER or SENIOR LECTURER or LECTURER IN ENTOMOLOGY IN THE FACULTY OF AGRICULTURE, University of Khartoum—The Registrar, University of Khartoum, c/o Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (November 15).

ASSISTANT LECTURERS (2) IN THE DEPARTMENT OF BIOCHEMISTRY—The Registrar, University College of South Wales and Monmouthshire, Cathays Park, Cardiff (November 19).

CHAIR OF GEOGRAPHY AT THE LONDON SCHOOL OF ECONOMICS—The Academic Registrar, University of London, Senate House, London, W.C.1 (November 21).

CHAIR OF PSYCHOLOGY—The Registrar, University College of South Wales and Monmouthshire, Cathays Park, Cardiff (November 26)

LECTURER/SENIOR LECTURER and a LECTURER (with research and teaching experience in some branch of pharmaceutical chemistry) IN PHARMACY at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, November 26).

CHAIR OF PHILOSOPHY—The Registrar, The University, Hull (November 30).

LECTURER IN PSYCHOLOGY at the University of Tasmania, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C 1 (Australia and London, November 30).

LECTURER (preferably with special qualifications in physiology or genetics) IN BOTANY at the University of Tasmania—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, November 30).

ASSISTANT LECTURER, Grade "B" (with a good honours degree or equivalent with some teaching and/or industrial experience, and an interest in research) IN CHEMISTRY, to specialize in inorganic or physical chemistry to Grad.R.I.C. and B.Sc. General standard—The Clerk to the Governors, South-East Essex Technical College and School of Art, Longbridge Road, Dagenham.

BIOLOGIST (with a good degree in physiology or zoology and considerable research experience, preferably with spermatozoa) to join a small research team investigating cervical mucus, with particular reference to problems of fertility—The Secretary, National Institute for Research in Dairying (University of Reading), Shinfield, Reading, quoting Ref. 60/13.

GEOLOGISTS (with a degree of a recognized university with either first- or upper second-class honours in geology, two years approved postgraduate experience, and preferably some specialization in mining geology) IN THE GEOLOGICAL SURVEYS DEPARTMENT, Federation of Malaya—The Recruitment and Personnel Division, Malaya House, 57 Trafalgar Square, London, W.C.2.

HEAD (medical graduate or science graduate with a higher degree) OF THE DIVISION OF VIROLOGY, for duties which include the supervision of diagnostic services and the carrying out of special investigations on and research into virus diseases—The Director, Institute of Medical and Veterinary Science, P.O. Box 14, Rundle Street, Adelaide, South Australia.

MICROBIOLOGIST (previous medical experience not essential) IN THE BACTERIOLOGY LABORATORY OF THE DEPARTMENT OF CLINICAL PATHOLOGY—The Administrator and Secretary, University College Hospital, Gower Street, London, W.C.1.

POSTDOCTORATE FELLOWS IN BIOCHEMISTRY, CHEMISTRY, ENGINEERING AND METALLURGY, PARASITOLOGY, PHYSIOGRAPHY, PHYSICS or TEXTILES—The Personnel Officer, Ontario Research Foundation, 43 Queen's Park Crescent, Toronto, Ontario, Canada.

PROFESSORS (preferably with Ph.D. or M.Sc.) OF PHYSICS, CHEMISTRY, and BIOLOGY at the Medical College, Mosul, Iraq—The Director, Recruitment Department, British Council, 65 Davies Street, London, W.1, quoting N.14.N(60).

RESEARCH ASSISTANT (graduate in biochemistry, chemistry or physiology) for research on metabolic disturbances in neurosurgical patients—Dr. H. M. B. Buckell, Department of Pathology, Atkinson Morley's Hospital, Copse Hill, Wimbledon, London, S.W.20.

RESEARCH FELLOWS IN PHYSICS for research on optical and electronic instrumentation for high energy physics in connexion with the experimental programme of the 7 GeV. Synchrotron at the Rutherford Laboratory, Harwell—Prof. G. W. Hutchinson, Department of Physics, The University, Highfield, Southampton.

TECHNICIAN to cut and stain histological sections in connexion with a research programme IN THE DEPARTMENT OF PHYSIOLOGICAL CHEMISTRY—The Assistant Bursar, The University, Reading.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Planning, Vol. 26, No. 442 (June 1960): Division in Europe. By Miriam Camps. Pp. 137–204. (London: Political and Economic Planning, 1960.) 6*s*. [197

Department of Scientific and Industrial Research. Report of the National Chemical Laboratory 1959: Report of the Steering Committee for the period 1st October 1958 to 31st December 1959, and Report of the Director of the National Chemical Laboratory for 1959. Pp. iv+72. (London: H.M Stationery Office, 1960.) 4*s*. 6*d*. net. [197

Scientific Council for Africa South of the Sahara. Publication No. 35: Mental Disorders and Mental Health in Africa South of the Sahara—CCTA/CSA—WFMH—WHO Meeting of Specialists on Mental Health, Bukavu, 1958. Pp. 269. (London: Joint Secretariat, Scientific Council for Africa South of the Sahara, 1960.) [267

Planning, Vol. 26, No. 443 (25 July 1960): Government by Appointment. Pp. 205–228. (London: Political and Economic Planning, 1960.) 3*s*. 6*d*. [267

Department of Scientific and Industrial Research: Geological Survey and Museum. British Regional Geology. Scotland: The Northern Highlands. By Dr. J. Phemister. Pp. vii+104+8 plates. (Edinburgh and London: H.M. Stationery Office, 1960.) 5*s*. net. [267

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EDUCATION FOR AN INDUSTRIAL SOCIETY

SO many conferences of a self-duplicating nature are arranged by educationists in industry that the question often arises as to what the organizers do when they are not taking in each other's washing. As recent reports show, the British Association for Commercial and Industrial Education has not been entirely free from the criticism that some of the many conferences it arranges are but repetitions of previous ones and attended by the same round of converted disciples[1]. It is gratifying, therefore, to direct attention to the Association's annual conference which was held at Cambridge during September 22–24, 1960[2]. This was the kind of conference which could not fail to stimulate those attending; there was a co-ordinating theme which was readily apparent and the active participants were there because they—nearly all—had something to say, and said it with conviction. In addition, the organizers had prepared advance copies of each paper containing, as introduction, a summary of a recent Government report which the speaker had been invited to consider. As a result conference members were presented with the opportunity to examine the whole broad front of educational advance and the way it could affect young people in our industrial society.

The Albemarle, Crowther, McMeeking, Carr, Anderson, and Willis Jackson Reports were all considered, as were the work of the Industrial Training Council and the Government's new proposals for management studies. With one exception, each speaker was not only able to present a review from intimate knowledge of a report but also was able to illuminate passages which had hitherto been dark.

The Albemarle Report, for example, was considered by M. J. W. Clapham, a director of Imperial Chemical Industries, Ltd., who showed how a sceptic came to support the ten-year development programme for young people put forward by an enthusiastic committee. The approach itself is one which should commend itself to all who are appointed to important national committees and may well explain why the Minister of Education was able to announce his acceptance of the committee's proposals on the same day that the Report was published.

It was unfortunate that a Report which has been far less favourably received—and especially by industry—should not have been presented in a similar manner. Instead, Miss M. G. Green, a member of the Central Advisory Council for Education (England), which produced the Crowther Report, chose simply to summarize its main recommendations for those who cannot or will not read. So much controversy has arisen over the priorities and timings of the Committee's main recommendations that those who support them should not throw away opportunities to gain public sympathy; many industrialists believe that the Crowther Committee has mixed up its priorities and has produced a Report lacking urgency and conviction.

The Carr Report on apprenticeship training was considered particularly in relation to its foster-child, the Industrial Training Council. While Lord McCorquodale, chairman of the Industrial Training Council, strove loyally to extol the work of his gently moving organization, the revelations of the Minister of Labour, the Right Hon. John Hare, showed that industry has failed lamentably to accept the Government and Industrial Training Council exhortations to provide greater facilities whereby school-leavers can systematically learn the skills of a craft. From the Minister's address it became apparent that the short-sightedness and remissness of employers could, inside a generation, starve the country of the skilled and adaptable workers who are essential to an economy based on science and technology. The Government has already intervened by providing places for three hundred apprenticeships, and the portents are that, with the failure of industry, massive Government intervention is inevitable.

Reviewing the Report which bore his name, Sir Colin Anderson did not hesitate to speak "between the lines", and made it clear why the majority of his Committee believes that the way to the university should no longer be controlled by the means or wishes of the parents. Further education should be something which the student can secure for himself by the use of his own brains, initiative and energy, even if his parents are uninterested.

The danger confronting the universities, and especially the older foundations, in becoming public trustees for the higher education of the nation—which implies much of its financial as well as other resources—was also examined by Sir Colin, who showed that the universities need lose none of their spiritual autonomy in a free, industrialized society.

The sponsors of the conference may have combined joint consideration of the McMeeking Report with the new scheme for management studies for their own good reasons. Despite the garnishing, the dismal failure of efforts to build up the National Certificates in Commerce since the publication of the McMeeking Report some eighteen months ago has led to considerable speculation about the Government's rejection of a Working Party's recommendations to develop an Intermediate Certificate in Management Studies and its virtual substitution by the new Higher National Certificate in Business Studies. Many members of the conference felt that the Ministry of Education

had placed administrative convenience before the genuine needs of management students and was determined to push the latter into courses in business studies. This, no doubt, will shore up the precarious courses in business studies by providing enough students and teachers to make classes worth running. Mr. J. C. W. Stead, a director of Batchelor Peas, who was a member of the Working Party appointed to examine the Scheme of Management Studies, was right to insist that a fundamental mistake had been made by the Ministry in trying "to combine a course which purports to help people to an understanding of management principles with a course which sets out to attract young people, in some cases straight from school, at an age of 18, for the purpose of studying certain commercial subjects". Before proceeding with this irreconcilable union, the Ministry should seek the advice of the Committee set up under the chairmanship of Sir Keith Joseph to consider the establishment of courses in management studies at one or more universities. The Ministry is revealing the same attitude to management studies as it did to science education some forty to fifty years ago. It should encourage part-time students who come up the hard way to extend their knowledge with studies of management principles and practice; such students bring qualities to industry which are not always present in management trainees recruited from graduates.

Sir Willis Jackson dealt in an exemplary manner with his own Report on the Supply and Training of Teachers for Technical Colleges. He described separately the proposals contained in the Report and action taken afterwards. The pay of full-time technical teachers, for example, was raised by the Burnham Committee in 1959 and has been followed by appreciable increases in the scales of part-time teachers. Consultancy work is beginning to develop in the advanced colleges, and more teachers are following courses of study leading to higher qualifications. The supply of part-time lecturers of standing to such day students is slowly increasing but the disparity in salaries is proving a considerable barrier to the transfer of senior scientific Civil Servants. The short courses for training serving teachers to teach better have been extended, and a new teachers' training college is being developed at Wolverhampton. Enough money has been raised to establish the Staff College for technical teachers and the location of the College and appointment of the director of studies should shortly be made. Sir Willis also described the arrangements for increasing the total number of teachers for technical institutions and deserves considerable praise for the part he is playing in this.

The conference was one which the British Association for Commercial and Industrial Education can feel proud to have organized. Those attending should now see that the weighty matters discussed are not allowed to be forgotten in their local activities.

[1] Education for Survival. Report of the Ninth Annual Conference of the British Association for Commercial and Industrial Education, East Midlands Group. The Implications of the Crowther Report. Report of the B.A.C.I.E. Spring Conference.

[2] Policy in Perspective. Annual Conference of the B.A.C.I.E., 1960.

LIFE IN THE SOIL

Living Earth

By Peter Farb. Pp. ix+178+8 plates. (London: Constable and Co., Ltd., 1960.) 21*s*. net.

ON learning, from the inside flap of the dust-jacket, that the author of this book "was formerly a Feature Editor of *Argosy* magazine", and further, from the author's own preface, that his "approach has been that of the science reporter", the intending reader might feel (as I did) some slight apprehension lest he should be in for a piece of journalistic pot-boiling. But he would be quite wrong. This is a soberly, sanely and attractively written work, presenting a comprehensive and often entertaining picture of what is at present known of the teeming inhabitants of the soil, and of their varied conditions of life. Even for many readers with a broad knowledge of natural history it will certainly provide an introduction to an entirely new world; and for once—*mirabile dictu*—a reviewer may be permitted to agree with a publisher's blurb, when it uses such enthusiastic expressions of approval as the "fascination" and "excitement" of the book.

Mr. Farb is an American, living in the State of New York (he was formerly secretary of the New York Entomological Society), and his book has naturally a New World emphasis. He discusses the life of the soil under the three main headings of "Forests", "Grasslands", and "Deserts", with an introductory section on "The Living Soil", and a concluding section on "Mutual Survival". A four-and-a-half page descriptive bibliography and a (not entirely adequate) index complete the work.

One is tempted to quote liberally from a book that is so full of good things. A feature that especially commends itself is the author's emphasis on the interdependence of all forms of life, their intimate mutual relationships, and their complex interactions with their environment, forming with it one indivisible whole. Of certain 'wayfarers from the soil' he writes: "We can but divine their rôles in the intricate web of grassland life; for no creature of the soil stands alone—all are interwoven, their pasts and their futures, in the economy of a piece of earth" (p. 130) "The dividing line between animals and plants is often a slim and artificial one . . . The line between living and non-living forms is not so sharp as [was] once supposed" (p. 15).

The author has the valuable gift, in the midst of his factual reporting, of lifting his eyes to wider horizons and pointing out some of the implications of the facts he records. In the course of his remarks on the soil-dwelling social insects, to which he devotes much space, he says of the termites: "Termites are a very ancient form of insect life . . . going back well over 250 million years . . . In their great age, termites question one of the popular beliefs about evolution—that all living things on the planet are progressing toward more perfect organisms Termites reached their full structural and social development, including their very complicated system of castes, in the Tertiary period, many million years ago. Since then, they have neither advanced nor fallen by the wayside, but now populate the earth in their age-old pattern" (p. 83). "Many experimenters have looked upon the termite nest as actually a superorganism in which each of the castes functions as a part of a single, larger organism . . . The superorganism theory . . . has many biological obstacles

to meet . . . yet in the hot termite mounds may lie an answer to one of the most perplexing questions about life itself" (p. 91). How faithfully certain aspects of human activity are sometimes mirrored in the lives of creatures allegedly 'lower' in the scale! One of Mr. Farb's most dramatic and vivid passages is that in which he describes the seasonal sequence of events in a wasps' nest (pp. 91–94). Towards the end of the summer, after the departure of the new queens and kings, "a madness begins to eat away at the very foundations of the city . . . workers take to devouring the larvæ; but still unsated, they abuse, then torture, the young. An orgy has begun that will end only with the death of the city . . . They rush through the combs looting and destroying. The queen is assassinated, and every worker becomes a queen. It is democracy in its most horrible form."

The interesting and important part played by root secretions, or 'diffusates' (this word, incidentally, is missing from the index), is touched upon in many places. While their primary function is no doubt to provide some kind of benefit to the owner of the root—for example, the encouragement of the growth of symbiotic or otherwise beneficial fungi and bacteria in its immediate vicinity, or the prevention of the growth of certain other plant competitors within a certain radius—it is evident that many other organisms have 'cashed in' on this secretory activity of root-systems for their own ends. It is found, for example, that root diffusates exercise a positive attraction to wireworms, the larvæ of click-beetles (Elateridae), which use the roots as food; that they act as a stimulant to the awakening of encysted nematodes, which then enter the root and commence their work of destruction; and that they also provide the stimulus for the germination of the seeds of certain pernicious root-parasites, such as *Striga* (Scrophulariaceae). It is clear that these chemical substances are one of the most vital factors in the complex interactions of organisms in the soil.

A few points call for criticism. The photographs are, on the whole, very good, but the text-figures are often poor. No list, either of plates or of text-figures, is supplied. Misprints are commendably few—curiously enough consisting almost entirely either of singulars for plural, or the reverse: the fractions on p. 67 ("1/100ths", etc.) are very odd. Some startlingly untrue statements are clearly slips: "the most obvious part of the fungus . . . is its vegetative organ, the toadstool" (p. 66); "this animal [the Mycetozoan swarm-spore] divides a few times by simple fusion" (p. 71). Some may have been due to misunderstanding of informants: "most orchids have little or no chlorophyll" (p. 63). Certain remarks betray carelessness of phraseology or looseness of thought: "Alfred R. Wallace . . . co-discoverer with Darwin of the theory of evolution" (p. 75) (How does one 'discover' a 'theory'?); "Linnaeus, the Swedish botanist who invented the modern method of classifying living things into various categories" (p. 83). But there are one or two remarks over which I am still scratching my head. "This mold [the Mycetozoa] may well be 'the slime of the earth' of the Book of Genesis" (p. 70). Has Mr. Farb had access to a new and shattering Hebrew manuscript? Or has he merely got a bit mixed between Genesis ii, 7 and xi, 3? "On a beastly summer day in South Africa . . ." (p. 84). Never having been in South Africa, I have no idea whether its summer can be really as unpleasant as the author seems to imply; but his scathing epithet seems to rise from the page with the impact of a blow to the solar plexus, leaving one slightly winded. Finally: "Dr. Livingstone, before being hounded by the intrepid Stanley, was an enthusiastic naturalist" (p. 84). Poor, meek, weak-minded Livingstone! Poor, splendid, overbearing Stanley! Do they really deserve these aspersions?

But it is not necessary to end on a frivolous note. Mr. Farb has written a most interesting, thought-provoking and worthwhile book.

H. K. Airy Shaw

THE STRUCTURE OF BACTERIA

The Bacteria

A Treatise on Structure and Function. Edited by I. C. Gunsalus and Roger Y. Stanier. Vol. 1: Structure. Pp. xiv+513. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1960.) 13 dollars.

"HERETOFORE, there has been no comprehensive source of information about modern knowledge of the general biological properties of bacteria." This statement of the editors is the clue to this volume and, presumably, to the four others projected which will cover the fields of metabolism, biosynthesis, growth and heredity, and will be welcomed by the growing legion of bacteriologists whose interests lie primarily in the bacteria themselves and not in the immediate medical or industrial applications of bacterial properties.

There are ten chapters, each contributed by an internationally distinguished worker, which bear the following headings: "The Bacterial Protoplasm—Composition and Organization"; "The Internal Structure of the Cell"; "Surface Layers of the Bacterial Cell"; "Movement"; "Morphology of Bacterial Spores, Their Development and Germination"; "Bacterial Protoplasts"; "*L*-Forms of Bacteria"; "Bacterial Viruses—Structure and Function"; "Antigenic Analysis of Cell Structure"; and "Localization of Enzymes in Bacteria". Chapter 1 is a general introductory survey.

As might be expected in a treatise by many authors total co-ordination was difficult, but it is perhaps a feature of strength rather than weakness that some overlapping occurs. Occasionally, seeming contradictions have crept in, as: "Even the processes involved in all forms of motion of living organisms seem to share a common basic metabolism; stimulation of contractile protein with ATPase activity by the common substrate adenosine triphosphate" (p. 4), while the same author on p. 26 states, "No report of ATPase activity in flagellar protein has been made". The enigma is partially solved in the section on movement (p. 173), "Not very much is known about the energy supply of active flagella. . . . De Robertis and Franchi claim that bacterial flagella contract in the presence of ATP. De Robertis and Peluffo have found that ATP enhances the motility of *Proteus vulgaris*. On the other hand, Barlow and Blum found no ATPase activity in flagella preparations". Such conflict is the seed of science, and as the text is generously impregnated with references (more than 1,500) the reader can easily discover the sources of the claims made and judge them for himself.

The authors have refrained from dogmatism, and long-standing disputes such as the nature of bacterial

nuclear material, the method of its division and whether flagellar movement is the cause or the result of the movement of the organism, are treated impartially. The chapter on bacterial viruses appears short when viewed against the activity and interest in this field—less than twenty pages excluding illustrations. Many of the illustrations included in the volume are outstanding examples of the advances made in technique, especially with the electron microscope.

The various topics are clearly sub-headed and used in conjunction with the detailed contents, and author and subject indexes make this a very accessible reference work and augurs well that the completed treatise will be the most significant addition to bacteriological literature for some years. It will also be expensive.

L. B. QUESNEL

GENES AND PROTEINS

The Molecular Basis of Evolution

By Christian B. Anfinsen. Pp. xiii+228. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1959.) 56*s*. net.

AT first glance, some features of this book are likely to seem a bit disconcerting. At the present time there are three fields of inquiry which have considerable claims to be considered, both particularly active and peculiarly important for general biology: one is the evolutionary process; the other two, which are closely connected, are the sub-structure of genes, and the configuration of the protein molecule. Dr. Anfinsen seems to be claiming to have gathered all three together into the confines of a comparatively small book. Its dust-cover states that he "regards the evolutionary process as the integrated form of genetics and protein chemistry". Unless the word 'genetics', which is a notoriously elastic one, is here taken to include such matters as natural selection, mutation, species divergence and so on, this way of regarding evolution would certainly seem to be a bad case of Hamlet without the Prince of Denmark.

However, it would be a pity to take these first impressions too seriously. Apart from reproducing a few well-known figures from a book by G. G. Simpson in the first chapter, and giving a short outline of elementary genetics in the second, the author in fact pays little attention to the subject of evolution. What he has actually produced is a summary of recent work on the relation between the sub-structure of the genes and the proteins which they specify. Most of this account follows the lines which are already becoming recognized as orthodox. For example, in the description of studies of the mechanism of chromosome duplication with the aid of radioactive labels, Anfinsen describes the work of Taylor and his associates, in which the chromosomes did what they had been expected to do, but does not mention that of Plaut and Mazia, who came to different conclusions, although he does add a footnote concerning the results of La Cour and Pelc, which also differed from those of Taylor.

The writing in this part of the book is rather slapdash and not very accurate. For example, in discussing Taylor's work on chromosome duplication on page 59 the author writes: "In an occasional 'second generation' pair of chromosomes, individual sister chromatids were labelled for only part of their length . . . and in such cases the corresponding portion of the other chromatid showed radioactivity. This behaviour is to be expected for crossing-over and resembles the cytological observations that have been made for the chromosomes of other species (e.g. the giant salivary gland chromosomes of *Drosophila*)". Actually the situation is that when crossing-over occurred in Taylor's chromosomes, and a chromatid was found to be labelled for only part of its length, the corresponding part of the sister chromatid did *not* show radioactivity. Moreover, no phenomena comparable to crossing-over occur in the giant salivary gland chromosomes of *Drosophila*. Again, to give another example, on p. 88 Anfinsen writes: "As we discussed in connection with the 'lozenge' genes of *Drosophila* (Chapter 2), three closely linked genetic loci all appear to be part of the same functional unit since crosses between double heterozygotes bearing both mutant loci on the *same* strand of the chromosome duplex (i.e. in the *cis* arrangement) produced wild-type recombinants, whereas crosses between double heterozygotes in the *trans* arrangement did not". This sentence suggests a state of complete confusion. In the first place the phrase 'chromosome duplex' is normally used to refer to the two helically twisted strands which together make up the deoxyribonucleic acid molecule; and the point at issue is not whether the mutant loci are on the same or different strands in such a duplex, but whether they are on the same or different chromosomes. Then the well-known '*cis-trans* criterion', to which Anfinsen is referring, does not turn on the nature of the recombinants which may be produced by crossing the double heterozygotes, but on the simple fact whether the double heterozygote itself shows the mutant character or not. Anfinsen actually describes this quite correctly in Chapter 2. Presumably the confusion that has arisen in the passage quoted was due simply to some lapse of attention.

It is when we pass from the more genetical parts of the book to the more chemical sections that its true value begins to emerge. Anfinsen is himself a protein chemist, and his handling of the chemical aspects of his subject is much more confident than that of the genetical material and, at least to a genetical reader, carries much more conviction. He provides an admirably clear account of recent work on the analysis of the sequence of amino-acids in various proteins, and of attempts to unravel their secondary and tertiary structures. This is illustrated with a large number of very clear diagrams. It will undoubtedly be extremely useful and suggestive to many biologists who are interested in this topic without being expert in it. Thus, in spite of certain inadequacies, therefore, his book has very real value.

C. H. WADDINGTON

GENETIC ANTHROPOLOGY

The Mothers

By Robert Briffault. Abridged, with an Introduction by Gordon Rattray Taylor. Pp. 451. (London: George Allen and Unwin, Ltd., 1959.) 36*s*. net.

THE re-publication of "The Mothers", reduced from more than two thousand pages to less than five hundred, is intended to make it available to "the maximum possible public". It is doubtful, however, whether any great interest in it will be aroused among social scientists, except as an example of a

phase in the development of anthropology. There is a fundamental difference between an attempt such as Briffault's to reconstruct the hypothetical course of the development of the institution of the family over the ages, and modern anthropology, *pace* Prof. Gordon Childe and Dr. Freud. Indeed, genetic anthropology is, in Prof. Evans-Pritchard's phrase, now generally regarded as an "attempt to explain what we know something about by what we know next to nothing about"; the reaction against it occurred at the beginning of the present century, and developments since then have been along quite different lines.

On the other hand, the controversy between Briffault and Westermarck, which was waged with such bitterness a generation ago, still has a direct interest for us to-day. The immediate issue at stake is no longer a live one; it centred round the problem whether the origin of the family is to be found in a primitive matriarchy (as Briffault thought), or in the activity of masculine jealousy and possessiveness and therefore, as Westermarck held, a patriarchy. The significance of the conflict for the contemporary social scientist is in the manner in which the conclusions of each of the protagonists was built into his work by his primary assumptions; this also determined the selection of the evidence which was discussed as well as the interpretation placed on it.

"The Mothers" may thus be regarded as a brilliant piece of special pleading, and may well live in the literature of the social sciences as the classic example of illustrative or interpretative, rather than truly analytic, work. It may also serve a very valuable purpose indeed as proof of the fact that a text in the social sciences can be written with brilliance, and captivate the interest of the reader. Information collected from the four corners of the earth must be used for scientific purposes with the greatest caution, but it does give the thesis it illustrates liveliness and colour for all that. By no means the least of the merits of this abbreviation of the text is the extent to which it preserves the literary qualities of the original work.

T. S. SIMEY

PROGRESS IN THE STUDY OF VISION

Physiology of the Retina and the Visual Pathway

By G. S. Brindley. (Monographs of the Physiological Society, No. 6.) Pp. xi+298. (London: Edward Arnold (Publishers), Ltd., 1960.) 35*s*. net.

THIS thoughtful and provocative book provides a critical synthesis of the present state of a wide range of visual physiology and biochemistry. Its primary interest is with human vision. Though written by one of the younger workers in the field, it is in large part concerned with matters with which he has already established direct experimental contact; for since 1952, when his first papers appeared, Dr. Brindley has made important contributions in many areas of visual investigation

A special characteristic of the present volume is its attempt to formulate explicitly the logical structure that underlies areas of sensory investigation in which most previous workers, with notable exceptions, have been content to muddle through to whatever solutions seemed reasonable to them at the time. This is a noteworthy and laudable effort, bound to have an effect, however time deals with the specific arguments. Indeed Brindley makes no attempt to create an illusion of finality. He is anxious to expose whatever argument he makes in all its strengths and weaknesses, frequently stressing the latter. The field of vision is now developing rapidly, and the present volume maintains a continuous impression of work in progress. Again and again Brindley leads the reader into some present puzzle, and ends with the reassurance that, judging by the present rate of progress, more clarity may be expected shortly.

Perhaps I have already conveyed the impression that this is a highly individual view of the subject. It is perhaps the most wide-ranging attempt to produce order in this field, by a consistent exercise of logical rigour tempered with good sense, since Helmholtz. Indeed my few complaints in reading the book came from the occasional sense of being shut out. Brindley now and then, though rarely, announces some awareness that the reader is presumed to share, since no attempt is made to explain it, but which the person whose work is under discussion apparently missed. A good example occurs on p. 199, where Newton is said to have "published a diagram for predicting the results of colour mixture which, if it were exactly valid (which it clearly is not), would imply trichromacy . . . Newton . . . did not point out its implications". What sticks here is the "would imply trichromacy". Newton's diagram had seven components, to simulate the seven tones of the musical scale. Brindley sees an implication of three primaries, probably with good reason, but does not stop to explain.

Another such passage strikes closer to home. On p. 184 Brindley says: "A mechanism which would achieve something like a suitable relation was suggested by Wald (1954): a rod might consist of many compartments, each inactivated by the photolysis of any one of the molecules of rhodopsin in it. In its original form, this suggestion is contradicted by the very data that Wald used to support it". I should certainly like now to change some parts of my original presentation of this theory; yet I do not know what contradiction Brindley has in mind, and he does not say.

The book opens with what is, on the whole, an expert and searching review of retinal chemistry. This chapter, and Chapter 3 on the central pathways of vision, represent areas with which Brindley has had least direct contact; yet here as elsewhere in the book he presents a valuable critical synthesis of the data. Chapter 2 discusses the electrical activity of the retina. Its main points are the acceptance of Brown and Wiesel's identification of Bruch's membrane as the high-resistance structure across which the electro-retinographic potential is built up, replacing Brindley's earlier idea that this is the external limiting membrane; and Brindley's present conviction that the bipolar cells of the retina are the dominant source of the electroretinogram.

Chapter 4 introduces the discussion of the sensory experiments that occupy the remainder of the book, with an analysis of the logical structure underlying such experiments. All such observations involving reports by experimental subjects contain psychological as well as physical components, which must be connected, implicitly if not explicitly, by what Brindley calls "psychophysical linking hypotheses". He distinguishes class *A* observations, which involve only statements of equality or non-equality of sensations, from class *B* observations, in which a sensory judgment must be made, demanding some

special evaluation, interpretation, or abstraction from the total experience. Brindley discusses the limits of usefulness of class *B* observations, and ways of improving their status. He then applies this logical apparatus to the analysis of a variety of entoptic phenomena, after-images, contrast phenomena and electric phosphenes (Chapter 5); functions involving visual thresholds and adaptation (Chapter 6); and colour vision (Chapter 7).

Brindley characterizes this volume in his preface as "a tightly written book, very full of information and for this reason not easy to read from end to end consecutively". This is fair enough, though I should add that it repays handsomely whatever trouble one takes with the reading. A few typographical errors at times make special trouble: in Fig. 2·4 (p. 50), the legend says 155μ when it means 255μ; and in Fig. 2·14, the legend should read "In *a*, taken at 140μ from the outer ends of the receptors, a large response is recorded from the *inner* pipette, but almost none from the *outer*".

GEORGE WALD

THE SEPARATION OF ISOTOPES

Electromagnetic Isotope Separators and Applications of Electromagnetically Enriched Isotopes

By J. Koch, R. H. V. M. Dawton, M. L. Smith and W. Walcher. Pp. xi+314. (Amsterdam: North-Holland Publishing Company, 1958.) 26.50 guilders.

THE separation of isotopes on a large scale was achieved by several methods during the Second World War as a necessary stage in the manufacture of the atom bomb. Of the various methods employed the electromagnetic separator (calutron), based directly on the mass spectrograph principle, was able to be brought to the production stage earliest. The uranium-235 for both the Alamogordo test explosion and the Hiroshima bomb came from the electromagnetic separators. After the War the far more economical gaseous diffusion process was brought into large-scale production so that the calutron process became redundant for the production of uranium-235.

Nevertheless, the many uses for comparatively small amounts of separated stable isotopes of a wide variety of elements which can be obtained most conveniently from electromagnetic separators has kept an interest in the subject alive, so that many laboratories all over the world have acquired such separators in recent years. The availability of samples of almost pure individual isotopes greatly facilitates the work of the nuclear physicist in working out the details of nuclear interactions, in assigning activities to particular isotopes, and in the investigation of the validity of different nuclear models. It is of importance in spectroscopy where it has enabled the elucidation of the finer details of spectra previously masked by the presence of several isotopes, and where it has made possible the achievement of greatly improved wave-length standards. Such separated isotopes have also been used in solid state physics and in biological studies.

The present work consists mainly of a survey of the construction of such practical separators and of the physical principles of their operation. It also includes a very brief discussion of some of the applications of the enriched isotopes produced by the method It confines its attention to the calutron type of apparatus so that it is not comprehensive in the discussion of all types, even of electromagnetic separators. There is no discussion, for example, of the omegatron. It is divided into three parts, each of about equal length. The first part, written by J. Koch, is devoted mainly, but not exclusively, to separators developed largely independently of the American experience gained during the Second World War. These were mainly developed after the War, but since the American experience was not declassified until the early 'fifties, independent development was necessary.

The second part, by R. H. V. M. Dawton and M. L. Smith, is mainly devoted to the description of the Harwell separators which were constructed in full knowledge of the American war-time experience. The method of treatment necessarily entails a considerable overlap between these two articles. They are both concerned mainly with technical constructional details rather than physical principles and will therefore have a rather restricted appeal.

The physical principles of the ion-optical systems employed, the high-current sources and the fascinating problems raised by the space-charge neutralization of ion beams are discussed by W. Walcher in the third section, which will be of more general interest. The book should prove of great use for those interested in designing isotope separators while the third section will be of interest to wider circles of physicists.

E. H. S. BURHOP

EDUCATING YOUNG NATIONS

Educating Young Nations

By W. E. F. Ward. Pp. 194. (London: George Allen and Unwin, Ltd., 1959.) 15*s*. net.

A MAN who took Beethoven's Fifth Symphony to the Gold Coast thirty-five years ago, and made that music understood, and who to-day writes of the necessity to foster, through education, common nationhoods, which yet respect cultural diversities, has within him a Greek sense of balance and a Christian humanity. These qualities make Mr. Ward's book memorable, kindly and historical. It will be of political and professional value to administrators and educationists working in the newly independent countries of Africa and Asia which have grown up overnight.

Mr. Ward wrote this book in 1959. It is now past history which will interest the newcomers to the field of public service. To those who shared the experience it will provide nostalgic delight. The validity of the thesis that education, particularly the education of a reserve of good teachers, "everyone of whom will be needed when the day of expansion comes", has already been proved. The plea for European technicians to stand by, while the new nations find their feet, is already the theme of the speeches of the more balanced politicians. The proposal that money for education should be looked upon by governments as aid to development rather than to welfare projects, commanding assistance "as if it were a scheme for irrigating the Sahara" is likely to gain the sympathy of the new Ministries of Finance.

Mr. Ward is probably the last author to write contemporarily of "the Colonies" and of "expansion" as a synonym for "independence". His catholic experience of teaching and administrating in places as dispersed as the old Gold Coast and Mauritius, his representation of the interests of those countries in the

United Nations, his work as a senior adviser on education to the Secretary of State for the Colonies, give him an authority which will be a reassurance to those still serving that nothing is too difficult for courage and that good human relationships are still more important than politics or race.

The major educational issues with which the book deals—poverty, syllabuses, language, the education of women, selection for secondary work, multi-racialism and teacher-training—will continue to find their various experimental solutions; but the need of humanity for humanity is timeless. There is a charming parable of interdependence in the story of the student offering his notes for a school practice lesson on "The Elephant, a Pachyderm". The apparatus listed was "one elephant, one pin", the latter to prove the toughness of the elephant hide. "Have you your pin?". "Yes Sir, here it is". "And your elephant?" "Sir, as for that, I thought that you could help me".

Mr. Ward points out, soberly enough, that the enormous growth in demand for education, off-set by lessened recruitment from the United Kingdom, is likely to result in a temporary loss of standards in schools. He records the political and social implications of so-called education by teachers who are "mainly chalk and talk" and stresses that, so far as possible, quality should be maintained at the top. One is left guessing at the contents of the unwritten chapter on the influence of the new leadership on education and the length of time during which, with genuine trust and expectation, those who are achieving independence will continue to look to an older order for the production of the elephant.

MIRIAM JANISCH

A HISTORY OF METALS

A History of Metals

By Leslie Aitchison. Vol. 1: Pp. xxi+1–304 (figures 1–127). Vol. 2: Pp. xvii+305–647 (figures 128–262). (London: Macdonald and Evans, Ltd., 1960.) 168*s*. the two volumes.

"A HISTORY OF METALS" differs from many others on a similar theme, first in that it has been written by one who is a metallurgist of wide experience and high reputation, qualifications not found in all writers on the subject. In the second place, the author has painted his picture against a background of the history of civilization itself, which both provided the conditions in which metallurgy could develop and which, on the other hand, were themselves fundamentally modified by those very developments. The appeal of these volumes should, therefore, be not only to the metallurgist but also to the archæologist and social historian.

In the author's treatment there emerges little which is essentially novel; in his own words the book is "a fractional distillation" of the work of others. His duty has been to collect facts already known, to sift the wheat from the chaff, and then to present a reasoned, critical account of his harvest. It follows, therefore, that he has inevitably been dependent on others for his original data Cross-linkages, however, are not infrequently possible which strengthen the main structure and give it a stability in so far as the chief features are concerned. Details, at times even important ones, particularly those relating to the earlier stages of development, are still uncertain, and not everyone will agree with the author in all particulars. This is perhaps especially true, as he makes abundantly clear, in connexion with any attempt to provide more than an approximation to actual dates.

These volumes cover a period of some six or seven thousand years of which Volume 1 carries the story down to about 1000 A.D. and deals with the seven metals gold, copper, silver, lead, tin, iron and mercury together with their alloys bronze, brass, pewter, steel and amalgams. "Broadly, the several metals and alloys were used for much the same purposes at the end of this long period as at its beginning the evidence of development appearing more in the variety of articles made . . . than in novel applications. As the centuries passed, technological improvements in metallurgical processes were effected and greater weights of material were handled, but during the whole of the . . . years dealt with . . . metals were won and worked by manual power. . . . Appropriately, therefore, Volume 2 opens at the time when power that has not been generated by human muscles was first applied to metallurgical operations", in any event on a substantial scale. The processes by which the metals were extracted from their ores, however, remained essentially unchanged for another two or three centuries at least. As Dr. Aitchison points out, "when the thirteenth century opened, iron—in most parts of Europe and certainly in England—was still being extracted by almost exactly the methods that had been used three millenia earlier" and much the same is true of the other metals.

In the author's view a metallurgical medievalism then occurred which lasted until the beginning of the eighteenth century, though these five hundred years were by no means static. From a craft an industry was relatively rapidly evolved, a medieval industrial revolution. It may well be that Dr. Aitchison's main contribution is to be found in the three chapters which, starting with the Crusades and followed by the discovery of the American Continent, deal with this period.

It is not surprising that an author, most of whose life has been spent in industry, should turn his readers' attention to commerce as well as to technology. His chapter on "Traders from Troy" draws a picture of the commerce of the third millennium B.C. of particular importance from his point of view in its profound influence on the resulting dispersion of knowledge of the technologies in general.

The predominating importance of the metals in moulding and stimulating scientific thought in all ages is reflected in three chapters concerned with this aspect of his history, first in antiquity, then during the birth of modern science and finally in the present era of nuclear transformations. Although the later parts will be well known to scientific readers, Dr. Aitchison justifiably stresses the part played by technological processes and products in the evolution of our scientific and philosophical ideas.

No review of these volumes would be adequate which did not emphasize the author's easy presentation of his material and his skilful avoidance of technicalities. The excellent illustrations have been well chosen, and many, in any event, will be new to most readers: there are a list, comprehensive but not exhausting, of sources for further reference and a good index. The price is high, but those who are able to acquire this book will have a treatise well worth possessing.

F. C. THOMPSON

Sedum of the Trans-Mexican Volcanic Belt

An Exposition of Taxonomic Methods. By Robert T. Clausen. Pp. x+380. (Ithaca, N.Y.: Comstock Publishing Associates, Cornell University Press; London: Constable and Co., Ltd., 1959.) 65*s*. net.

THIS very thorough investigation of 28 species of *Sedum* growing in the Trans-Mexican Volcanic Belt should be noted by all those interested in modern taxonomic methods entailing population studies in the field and experimental garden as well as the examination of herbarium specimens and literature. The author's conclusions, in his own words, are based primarily on gross morphology and ecology: only limited data about chromosomes, anatomy, embryology, etc., were available. "Such data, when used to overrule conclusions based primarily on details of gross morphology and ecology, should be based on samples sufficiently large to be of statistical significance." His own approach to the problem of sampling and the study of environmental modifications should be read by everyone working on revisions of critical north temperate plants, and his comparison (Chapter 8) of his own work on *Sedum* with that of his predecessors, Berger and Fröderstrom, is revealing *Sedum* was a good genus to choose for attack by modern taxonomic methods: material is easy to propagate for cultural experiments, and "dried specimens of *Sedum* in herbaria are not reliable for descriptive data, regardless of how valuable they may be for indicating the distribution of species".

N. Y. SANDWITH

Heredity of the Blood Groups

By Prof. Alexander S. Wiener and Irving B. Wexler. Pp. x+150. (New York and London: Grune and Stratton, 1958.) n.p.

DURING the past fifteen years, as the authors point out, knowledge of the blood groups has progressed with great rapidity, and blood grouping has become a fundamental pathological science, knowledge of which is important in many fields. The heredity of the blood groups should be clearly understood, and the authors in this book set out their conception of this; but the book is not solely a study of the inheritance of the blood groups—it contains a good deal of serological information as well, and concludes with chapters on medico-legal applications and anthropological studies.

There is an introduction and then sections on the ABO, MNS, P, Rh and other blood-group systems. The main chapter in the book, however, concerns the Rh-blood group system, and of the 146 pages in the book, about 40 are devoted to this chapter. In it are described the details of the Rh–Hr system of notation and its various applications; anyone who is not familiar with Dr. Wiener's views on this subject will find them clearly set out in this chapter. Some of the other blood-group systems are rather sketchily dealt with, for example, the Lutheran, Duffy and Kidd systems occupying only 1–2 pages each, but in certain instances useful information is given in a condensed form; the Kell system is a good example of this. One of the less-pleasant features of the book is the use of bold-face type for certain of the blood group symbols; it would be better if this were discontinued. In certain of the rarer blood group systems, the authors substitute a notation of their own for that which is more widely and generally accepted by other workers. This, for example, is done in the Duffy and Kidd blood group systems; it is unfortunate that they have decided to do this.

This is a book summarizing many aspects of work on blood groups and will be of greater interest to those primarily concerned with blood groups than to the general reader.

F. STRATTON

A Text-Book of Metallurgy

By Dr. A. R. Bailey. Second edition. Pp. x+561. (London: Macmillan and Co., Ltd.; New York: St. Martin's Press, Inc., 1960.) 30*s*. net.

THE first edition of this book, published in 1954, was very favourably received because it provided an elementary account embracing almost the whole field of metallurgy, from ore-dressing to the physical behaviour of metals, written in a concise and accurate manner. The general form of this book is retained in the new edition, but the author has made many additions referring to modern developments and has provided an adequate number of up-to-date references. The coverage of the book is so large that inevitably most subjects do not receive great depth of treatment and the level is that of first-year metallurgy at a university or the equivalent stages of a technical college course. It is a good preparation for the more specialized texts which must be used at a later stage. In any technological subject, a balance must be struck between basic theory and practice, and indeed the author of the present book succeeds in blending these two aspects to form a harmonious whole. For example, the student can find in one chapter a simple treatment of dislocations, while in another he can read an admirable account of the various mechanical working processes used in industry. The book is, in the reviewer's opinion, the best of its kind available. It represents in these days remarkably good value for money, and students intending to read metallurgy have good reason to make it one of their first acquisitions.

Annual Review of Physical Chemistry

Vol. 10. Edited by H. Eyring, in association with C. J. Christensen and H. S. Johnston. Pp. viii+537. (Palo Alto, Calif.: Annual Reviews, Inc., 1959.) 7 dollars.

THE latest volume of this well-known publication includes nineteen chapters, fewer than usual but the chapters are longer. Each has a very full list of references, and a notable feature is the inclusion of much Russian literature. The authors are British, Norwegian and American. Besides familiar topics such as thermodynamic properties, electrolytes, heterogeneous equilibria and spectra, there are chapters on copolymers, proteins, nuclear and paramagnetic resonance, and high temperatures. Each chapter covers a wide field of literature; but in spite of detail and the necessarily brief treatment the book can be read with interest and should be intelligible to physical chemists generally. The authors have taken a good deal of trouble in this direction and have been very successful. It is impossible in a brief notice to indicate the contents of the chapters, but I found those on electrolytes and high temperatures of particular interest; other readers will certainly have different choices. This series of volumes should enable physical chemists to keep up to date in fields outside their own particular interests. The book is very well produced and the price is reasonable.

J. R. PARTINGTON

ROCKET AND SATELLITE INSTRUMENTATION

INSTRUMENTATION for rockets and satellites was the subject of a one-day symposium organized jointly by the British Interplanetary Society and the Society of Instrument Technology on September 1. The meeting was held at Manson House, London, and attended by more than one hundred members of the two societies and others. The morning session, at which Dr. W. R. Maxwell, vice-president of the British Interplanetary Society, took the chair, was devoted to papers and discussion of the instrumentation in the space-vehicle, while the afternoon session, under the chairmanship of Mr. C. C. Eltenton, president of the Society of Instrument Technology, was concerned with instrumentation at the ground stations.

The first paper, by Mr. M. O. Robins, of University College, London, formed a very appropriate introduction to the subject since it outlined the British space research programme as constituted in June of this year. In this context he defined space research to mean scientific research carried out by using the technique of rockets, either for vertical sounding of the atmosphere or for the launching of Earth satellites. Historically the British effort started with the first steps taken in the autumn of 1953 by the Gassiot Committee of the Royal Society which resulted in the development and launching of the *Skylark* rocket at Woomera in 1957. This reliable and versatile vehicle has enabled a variety of valuable scientific measurements to be made up to heights of 100 miles and more. These, carried out mainly by university groups, have included investigations of upper-atmosphere winds and temperatures, electron density, solar radiation and cosmic rays. Experiments planned for the near future include measurements of the geomagnetic field, observations on ultra-violet wave-lengths and ionospheric investigations using radio propagation methods.

The effort made in Britain to extract the maximum of scientific information from optical and radio observations of the Earth satellites launched by other countries had been very effective. The data obtained had already yielded new information about the ellipticity of the Earth, air density and the ionospheric regions. The positional information also enabled a satellite 'prediction service' for observers in the United Kingdom to be operated.

Turning to the British plans for the direct use of satellites, Mr. Robins spoke of the arrangements whereby British-designed instruments will be carried in the *Scout* satellites to be launched in the United States, and of the possibility that British satellites might be launched by a rocket system based on the *Blue Streak* and *Black Knight* designs. For the first British *Scout* payload, the main objective of the experimental programme will be the direct study of the electrical properties of the ionosphere. Present arrangements envisage three *Scout* payloads for the United Kingdom, and experiments for the second are being worked out.

Design studies of possible British satellites and of the investigations to be carried out in them are in progress. Three types of satellite are envisaged. The first, which would weigh about 1,750 lb. and go into a circular orbit of 300 miles height, could carry a telescope and spectrometer for ultra-violet astronomy of stars. The second, of 500 lb. in weight, might be capable of penetrating to distances of 10,000 miles and would enable studies to be made of the Earth's atmosphere, gravitational and magnetic fields. A third and smaller satellite capable of very elliptical orbits is also being considered.

The instrumentation for the first Anglo-American *Scout* satellite was described by Dr. A. P. Willmore, of University College, London. The satellite, which would be launched by a four-stage rocket using exclusively solid propellent motors, would be approximately 20 in. in diameter and would weigh in the region of 100–150 lb. Its orbital inclination would be above 50°, and its perigee and apogee heights about 200 and 600 miles respectively. The responsibility for the instrumentation would be divided between the U.S. National Aeronautics and Space Administration and the British universities; the former providing such parts as the telemetry and power supplies and the latter the scientific apparatus.

In all there will be six experiments on board the satellite: three ionospheric experiments designed to measure the density and temperature of the electrons and the composition of the positive ions, two to measure the intensity of radiation from the Sun in the ultra-violet and the X-ray parts of the spectrum, and in the last the primary cosmic-ray spectrum will be observed. The electron density in the ionosphere will be measured in two ways. In Prof. Sayers's experiment the capacitance of a parallel plate condenser immersed in the ionosphere will be measured at a frequency of a few megacycles per second, and from it the electron density calculated. In the method devised by University College, London, an electrode, consisting of a 2-cm. diameter disk mounted flush with the outer skin of the satellite, is maintained at a potential of 1 V. or so, negative with respect to the ionosphere. By varying this voltage sinusoidally the curvature of the voltage-current characteristic is determined and the density and temperature of the electrons deduced. The experiment to analyse the composition of the positively charged particles employs a similar technique using a spherical probe on a 12-in. long arm.

Ionization chambers and proportional X-ray counters will be used to monitor the emission of ultra-violet light, and soft X-rays from the Sun in order to correlate ionospheric storms with disturbances occurring in the atmosphere of the Sun.

Dr. J. Ring, of the University of Manchester, dealt in more detail with ultra-violet measurements from satellites. The main difficulties of ultra-violet measurement from the ground are due to absorption, scintillations and background radiation produced by the atmosphere and these could be overcome by satellite-borne instruments. There are, however, many difficulties in the design and operation of the instruments, the principal ones being alignment and the recovery of information gained. For example, the examination of a particular star by means of a spectrograph would necessitate alignment and follow-

ing to 10″, but, even if a resolving power of 1 Å. over a 2,000 Å. range were required, a band-width of only 100 c./s. would be needed for the transmission of the data. If, on the other hand, the intensity of the whole sky were to be measured at a given wave-length, then, although there was no alignment problem, the band-width of data transmission required would be many times greater. Dr. Ring described some of the work already done with rockets and satellites, and looked forward to future developments. It is planned to place into orbit an 8-in. telescope with television camera and also 36-in. and 50-in. telescopes. Although the first two objectives may be attained within three years it will probably be ten years before a 50-in. telescope is in orbit. He thought, however, that astronomical observations would really come into their own when manned satellites were launched.

The afternoon session was opened by Dr. B. G. Pressey, who described the ground equipment used for radio observations on satellites at the Radio Research Station of the Department of Scientific and Industrial Research. These observations had a three-fold purpose: to provide positional information, to obtain information from the instruments in the satellite and to study the propagation of the waves transmitted from the satellite. The instrument principally used for satellite tracking is the interferometer, in which the direction of arrival of the radio-wave is deduced from a measurement of the phase difference between the waves received on a pair of spaced aerials. Equipments for reception on 20, 40 and 108 Mc./s. are installed at the Radio Research Station, and the 'Minitrack' system, developed in the United States, which operates on frequencies 136–137 Mc./s., is now in course of erection on the same site.

The equipment available for the reception and analysis of satellite signals on frequencies from 20 Mc./s. to several hundred megacycles per second was described. It was the general practice to record the signals on magnetic tape—up to four channels simultaneously—and to analyse the records afterwards. Measurement of the Doppler frequency shift was carried out with the aid of a reference signal of high stability, the radio beat-note produced by mixing it with the satellite's signal being measured automatically on an electronic counter. The direct measurement of the difference between the frequency shifts on two signals on harmonically related frequencies was also described.

As an example of the methods of recording and decoding telemetry signals, the extraction of cosmic-ray data from the signals from *Sputnik* 3 was described. The signals, which consisted of a group of four pulses, were displayed on a cathode-ray tube using a linear time-base, and photographed on to a moving film so as to produce a raster type of record. From this record time intervals between the changes in pulse durations could be readily measured, and ray intensities and count-rates calculated. The method used to decode the more complex systems such as that used in *Explorer* 7 were also indicated.

A later paper by Messrs. D. J. McLauchlan and T. T. Walters, of the Bristol Aircraft Co., provided a detailed description of the 'Timtape' equipment developed for the processing of time-multiplexed telemetry data from test missile firings. The input is a magnetic tape derived from the Royal Aircraft Establishment 24-channel telemetry system. After separating the channels the equipment interprets the data relative to the calibration-levels and converts them from analogue to digital form. The output is in the form of photographic records and punched cards. Although designed specifically for one telemetry system, 'Timtape' should be capable of reducing data from other systems without extensive modification.

The remaining paper differed from the others in that it dealt with rocket propulsion instrumentation. In presenting it Mr. A. W. T. Mottram, of Bristol Siddeley Engines, Ltd., reviewed the techniques used for the measurement of the performance of liquid-propellent rocket engines. The most important quantities to be measured are thrust and propellent-flow, and these are required to a high degree of accuracy. Measurement of system pressures, flows and thrust under fluctuating conditions demand less accuracy since their purpose is limited to the establishment of engine behaviour and the qualitative assessment of system defects. The prime requirement is for reliability, for which reason the simplest type of instruments were recommended. The best basic-thrust measuring transducer is a rubber-bonded hydraulic capsule with a pressure transducer of the unbonded-wire strain-gauge type. A free turbine flow-meter had proved to be the best for determination of propellent-flow, and Bourdon gauges were recommended for the measurement of pressure.

The symposium provided a useful review of the instrumentation used in satellites and on the ground for investigations of the upper atmosphere. The full texts of the six papers, together with the discussions on them, will be published in the *Journal of the British Interplanetary Society*.

B. G. PRESSEY

SPECTRUM OF RADIATION BACKGROUND UNDER WATER

By GORDON K. RIEL, JOHN P. DOLFIS and DONALD G. SIMONS

U.S. Naval Ordnance Laboratory, White Oak, Maryland

THE investigation of physical phenomena occurring in the sea has, in many cases, lagged behind similar investigations on land and in the atmosphere. This is certainly true in the field of radiations from cosmic rays and other naturally occurring sources. A detailed knowledge of these radiation backgrounds is necessary to evaluate any underwater programme in which detection of radiation is required. An analysis of the radiation background is especially important, because, while the sea provides some shielding from cosmic radiation, it contains several radioactive nuclides. This work has an added importance since any programme of measurement of radiation which is to be carried out in the sea will be

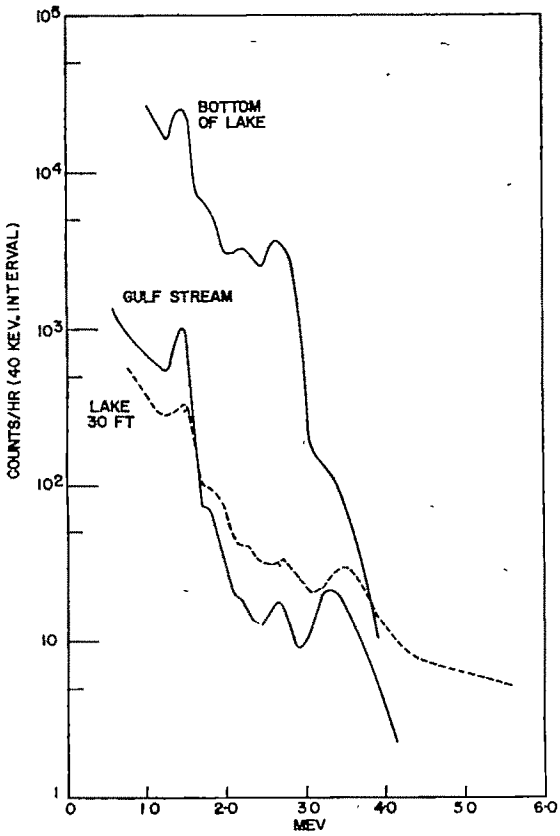

Fig. 1. Spectrum of natural radiation measured under water

almost invariably of a low-level nature, thereby requiring an extensive knowledge of the background sources present and their intensities. Such low-level counting programmes may include: certain types of nuclear research problems which require low cosmic-ray backgrounds, tracer studies of ocean currents, tracer measurements of corrosion or leakage, measurements of the concentration of radioactive nuclides in sediments and biological specimens, and measurements of the effectiveness of radioactive waste disposal.

Hitherto, the problem of obtaining such information in the sea has been made difficult because of its relative inaccessibility to specialized nuclear instrumentation. Consequently, radiation measurements involving energy analysis were limited to laboratory examinations of samples taken from the sea. These methods, while instructive and useful for particular problems (for example, backgrounds from biological specimens), were inherently unable to present a true picture of the background radiations under the surface of the sea. The recent availability of transistorized, light-weight, multi-channel analysers, however, has made it possible to conduct spectral measurements of γ-radiation and cosmic radiations *in situ*.

The experimental phase of a programme to measure the energy spectrum of background radiation directly in the sea was begun in January 1960. The results presented here are from these tests and represent, to our knowledge, the first such direct measurements of the naturally occurring radiation backgrounds. A scintillation spectrometer consisting of a 5-in. diameter by 6-in. long sodium iodide (thallium) crystal, and a transistorized 128-channel analyser for pulse-height sorting, was used for this test. The sodium iodide crystal and associated electronics were encased in a sealed probe and lowered from a surface ship by means of cables up to 1,000 ft. long. A single-conductor armoured cable was used to supply voltage to the probe and return the signal to the ship. On board ship the 128-channel analyser recorded digitally the energy spectrum within a pre-selected range.

Fig. 1 shows the energy spectrum of radiation measured under the water. The curve labelled 'Gulf Stream' gives the cumulative results of two tests at a depth of approximately 400 ft., and a third test at about 1,000 ft. The total counting time of these three tests is 21 hr. These tests were conducted in the Gulf Stream near Fort Lauderdale, Florida. Included for comparison are measurements which were made at mid-depth and in the bottom sediment of the fresh-water of Tridelphia Lake, Maryland. Although the surface background is not shown, it was similar in distribution and magnitude to that found in the bottom of the lake. The general trends of the backgrounds obtained in the sea and lake are lower by an order of magnitude than that at the Earth's surface. This, of course, is to be expected because of the shielding that the water furnishes from cosmic-ray events and from naturally occurring radioactive chains.

The spectral results show essentially three major energy peaks at 1·46, 2·6, and 3·3 MeV. and two minor peaks at 1·8 and 2·2 MeV. These energies are present in both the fresh- and sea-water. The most prominent peak is that of 1·46 MeV., which is due to potassium-40. This is higher in magnitude in the sea than in fresh-water. (No correction has been made for the potassium-40 content of the detector probe itself.) The higher activity in the salt-water is due to the fact that potassium salts, being mostly soluble, concentrate in the ocean. It should also be noted that potassium-40 gives the major background contribution of all the radiation sources present by more than one order of magnitude. Thus, if no energy discrimination is used, the radiation detector will be sensitive almost exclusively to changes in the concentration of potassium-40. Below 1·46 MeV., the scattered potassium-40 radiation masks all other sources.

The peak at 2·6 MeV. corresponds to the 2·61 MeV. γ-ray from thallium-208 in the natural thorium-232 chain. Since these elements are primarily present in compounds of very slight solubility, they concentrate in the bottom sediment. Furthermore, some activity can be expected in the shallow lake water due to mixing of the sediment and washing of soils into the lake by ground run-off. Thus, in addition to the higher cosmic-ray background in the shallow water which tends to increase the rate of count throughout the entire spectrum, a further increase in activity in the 2 6 MeV. region was expected in the lake and at lake bottom. This was clearly demonstrated when the probe was embedded 18 in. into the sediment of the lake bottom. Even though the amplitudes of all of the peaks mentioned were increased in the sediment as compared with the water, the increase of the 2·6, 2·2, and 1·8 MeV. radiations from the heavy elements is an order of magnitude larger than that of the 1·46 and 3·3 MeV. radiations.

The small break at 2·2 MeV. is probably due to the 2·2-MeV. radiation of bismuth-214 from the natural uranium-238 chain or bismuth-212 from the thorium-232 chain. Similarly, the break at 1·8 MeV. may be

due to the 1·8-MeV. γ-rays from bismuth-212. These breaks are also due, in part, to the Compton edges from the 3·3- and 2·6-MeV. peaks respectively.

The exact source of the prominent peak at 3·3 MeV. is not known at the present time. Laboratory tests have shown that this radiation exists as a contaminant of the steel pressure vessel itself, and is not a true source present in the water. Measurements are now in progress to check this further and to try to identify this source of radiation.

Events at energies higher than those originating from the naturally occurring isotopes are assumed to be of cosmic-ray origin. The energy spectrum up to 9 MeV. was measured in the Gulf Stream. There were no peaks from 4 to 9 MeV., and the relationship of count-rate to energy as obtained from the spectra in this range can be represented empirically by :

$$N_E = 54 \exp - 0{\cdot}72E$$

where N_E is counts per hr. in a 40-keV. interval, and E is energy in mega electron-volts.

In the Gulf Stream, the count-rate above 8 MeV. was 240 counts per hr. with 400 ft. of cable, and 70 counts per hr. with 1,000 ft. of cable. Note that the length of cable is quoted rather than depth, since no accurate measurement of depth was available. In the lake, the count-rate above 6 MeV. from 10 to 50 ft. in depth can be fitted by the following function :

$$N_D = 220 \exp - 0{\cdot}21D$$

where N_D is counts per minute at depth D in feet.

One difficulty in measuring γ-ray spectra under water is that the radiation is partially degraded in energy by scattering in the water. This tends to smear out the radiation spectrum. Therefore, the features of the resulting spectrum are not as sharp as would be obtained with non-distributed sources. The unfavourable geometry makes estimation of the concentration of radioactive nuclides difficult. A new probe designed to improve the counting geometry is under construction. It will be capable of exploring the radiation at depths in the seas beyond the practical reach of cable support. This will be achieved by lowering the new probe with a free-diving vehicle. Further tests are also planned using the present equipment.

THE SENSE OF HEARING

It is probably true to say that the eye has received, and continues to receive, from both physiologists and psychologists more attention than has the ear. Nevertheless, speech is one of the most important characteristics of human beings, and the sense-organ with which it is heard deserves therefore to be given due honour. A session of Section I (Physiology) of the British Association, held in Cardiff on September 2, took hearing as its central topic, and left no doubt that this sense is as fascinating as any other.

The main feature of the session was the presidential address to the Section by Prof. W. Burns (Charing Cross Hospital Medical School). He considered the response of the ear both to normal and to intense sound, starting by describing the extraordinary sensitivity and flexibility of the organ. It can detect pressure changes in the atmosphere so small that the actual receptor cells are moved through only the diameter of a hydrogen atom, so that any further increase in sensitivity would merely result in the Brownian movement of the air becoming audible; and yet the ear can also operate for short periods at pressure-levels a million times greater. Part of the secret of this extraordinary performance lies in the mechanical linkage which transmits the sound from the ear-drum to the inner ear where the sense-organs themselves are. The bones which form this linkage terminate in a small piston having only one-twentieth of the area of the ear-drum, and this piston therefore transfers a considerable pressure per unit area to the fluid inside the closed container of the inner ear. In addition to this aid to sensitivity, some protection against loud sounds is provided by the mechanical linkage since muscular contractions can increase its resistance to movement when such sounds are heard and so reduce the sound-level actually reaching the sense organs.

The receptors themselves are arranged, as has long been known, along the basilar membrane which lies inside the coiled tube known as the cochlea. The basilar membrane runs from end to end of this tube, being narrow at the end where the sound enters and wide at the far end : it was of course suggested at one time that it resembled a set of piano-wires resonating independently to different frequencies of sound, but this does not fully correspond to modern ideas. It would seem rather that a change in pressure at the entrance to the cochlea sets up a travelling wave in the basilar membrane which starts at the narrow end, sweeps up towards the far end, getting larger as it goes, and then dies away. The point at which the greatest displacement of the membrane occurs depends on the mechanical properties of the system and thus varies for different frequencies of stimulation. In general, high frequencies mainly affect the narrow end of the membrane while low frequencies involve the entire length.

The sense-organs themselves are cells about the size of a red blood corpuscle, which rest on the basilar membrane with small bristle-like projections (hairs) sticking up into another membrane, the tectorial membrane, which forms a second 'shelf' above the basilar membrane. The displacement of these membranes causes the hairs to be bent. Now there is a potential of about 150 mV. between the inside of the cells and the fluid in which the hairs terminate. The size of this endocochlear potential depends on the extent to which the hairs are bent at the time, and alternating movements of the membranes will therefore produce an alternating potential, the cochlear microphonic, which can be picked up by electrodes in a number of places in the ear. The microphonic follows sound stimulation very closely with no sign of the all-or-none characteristics of the sensory nerve, and each negative phase of the microphonic is followed by the occurrence of nerve impulses in the auditory nerve. It seems likely therefore that the electrical energy stored in the hair cells somehow

produces the firing of the nerve fibres, although the link between the two is still unknown. The stored electrical energy thus acts as a kind of biological amplifier, triggering off considerable effects from a small input of sound energy.

The message in the auditory nerve, then, carries information about the frequency and the intensity of the sound. Different frequencies of sound give rise to maximum stimulation of different hair-cells and therefore of different nerve fibres: at least this is so at frequencies above 2,000 c./s. or so. Below that frequency each wave of the stimulus gives rise to a burst of impulses in the nerve, and the frequency of the impulses therefore conveys information about the frequency of the stimulus. The higher the intensity of the sound, the greater the number of fibres which become active in the auditory nerve: and, at high frequencies of stimulation, intensity will also be reflected in an increased frequency of firing of the fibres.

Perhaps the most important practical implications of Prof. Burns's paper arose from the question of effects of noise on the ear. On the basis of present knowledge, he suggested that special steps must be taken to preserve the hearing of industrial workers if they are exposed throughout their working life to noise above particular levels. The noise should be analysed into octave bands, and protection begun if the sound pressure-level in the octave below 4,800 exceeded 80 db. above the usual arbitrary zero of 0 0002 dyne/cm. The corresponding criteria for successive octaves down the spectrum were 80, 85, 85, and 90 db. If these minimum levels were exceeded, steps should be taken to reduce the exposure of the workers, and to check their hearing regularly by audiometry. Since occupational loss of hearing tends to appear first at 4,000 c.p.s. and spreads only later to lower frequencies, it can be detected and the workers moved to safer employment before the deafness becomes too damaging socially. This is the surest way of detecting the most susceptible people, although it is being widely assumed that the amount of temporary deafness produced by a short experimental exposure to noise may predict the susceptibility to more permanent deafness after long exposure. Above all, it must be realized that occupational deafness is insidious and need not be noticed by the victim until well advanced: nor is it connected with annoyance, being just as dangerous to people who do not object to noise, and conversely being no hazard at the levels reached by many annoying everyday sounds.

Mr. D. E. Broadbent (Applied Psychology Unit of the Medical Research Council) took up the question of noise, and considered those of its effects which do not involve the ear except as the point of entry of the noise. Many of the alarmist reports often spread about these effects are not supported by the evidence: large-scale studies by the U.S. Navy have failed to find any effect on mental health from noise, nor is there much support for the idea that metabolism is higher when working in noise. The sexual performance of rats remains normal after exposure to very high levels, and although the adrenals both of rats and men appear to be active at such levels, there is no evidence of pathological changes as a result. Some recent German researches do suggest a possible effect on the peripheral blood vessels, which constrict in noise, but the chronic effects of this response need further investigation. In addition, of course, there are widespread changes in the body at the onset of an unfamiliar noise, as there are in any new situation. These changes (increased pulse-rate, lowered skin conductance, etc.) are really a response to novelty, and cannot be used as arguments against noise without putting in jeopardy other stimuli which have the same effect: for example, meeting a strange member of the opposite sex.

The efficiency of mental work is definitely impaired by noises of more than 90 db., but has not been proved to be so by any fainter noise. The effect takes the form of momentary lapses, between which work may be perfectly normal. Mr. Broadbent was particularly concerned to make a distinction between these relatively slight effects on health and efficiency, and the annoyance caused by noise. The latter was very widespread and natural, even though it had no connexion with the former: even animals try to avoid loud noises, and sounds which they associate with pain; and to a behaviourist one object of civilization is to decrease the frequency of those stimuli which are avoided by human beings. Annoyance is thus an adequate reason for noise abatement, and the cause of the latter can only be harmed by exaggerated claims of effects on health and efficiency.

Dr. T. S. Littler (Wernher Research Unit of the Medical Research Council) then spoke about problems in the testing of hearing (audiometry). Since any complex periodic wave can be regarded as the sum of a number of sine waves, and since the ear does to some extent analyse complex sound in this way, the most developed method of testing hearing is to present to the ear sine waves of various frequencies, and determine the lowest intensity at which they are audible. Since the loudness and pitch of short tones vary with their duration, the test tone must be long enough to avoid these distorting effects: furthermore it must start and stop gradually rather than abruptly, since sharp onsets are heard as clicks and do indeed contain frequencies widely different from that intended. The whole test tone therefore, including its gradual beginning and end, should last at least two seconds.

The intensity of a threshold tone can be specified either as the minimum audible pressure or the minimum audible field: the former term means that the sound was delivered by head-phones and the sound pressure-level, produced by the head-phones, measured. The minimum audible field means that the sound was produced by loudspeakers and the level measured in the position where the listener's head was later to be placed. The two measurements will not usually be the same, partly because of the physical differences in the situations, and partly because of the sound of the listener's own pulse and similar disturbances which are more notable with head-phones.

There will not, of course, be found a definite intensity at which sounds change from inaudible to audible: over a certain range, the proportion of test tones heard will increase as the sound pressure rises, and the threshold is best taken as the level at which 50 per cent of test tones are heard. This level can then be compared with that for normal ears: it has been difficult to get adequate measurements of normality, because samples of the general population are liable to include people with slight undetected hearing loss. But recent measurements at the National Physical Laboratory, and by the Royal Air Force, have provided an adequate reference against which any given person can now be compared.

To some extent deafness due to failure in the mechanical linkage of the middle ear can be distinguished from deafness due to damage to the sense-

organs themselves or later stages in the nervous system. This is because audiometry by bone conduction will show no loss in the case of damage to the middle ear. But bone conduction is less well standardized than air conduction. The same may be said of speech audiometry, in which words are presented for identification at various sound pressure-levels: in this case it may in some people be impossible to obtain perfect performance even at levels well above the threshold, and it is clear that the performance of the ear at supra-threshold-levels needs further investigation.

The tenor of the whole session was summed up by Lord Adrian, who, in the discussion, reminded the meeting of Darwin's difficulties in explaining the eye on an evolutionary basis because of its complexity. The ear may well inspire similar feelings of admiration.

D. E. BROADBENT

EDUCATION OF SCIENTISTS

THE respective roles of the universities, colleges of advanced technology, research institutes, and other institutes of higher education in promoting the education of scientists were extensively considered at a meeting of Section L (Education) of the British Association for the Advancement of Science on September 1.

Prof. M. W. Thring dealt with the role of the universities in teaching technology. He emphasized that technology has two aspects: that of applied science, which aims at presenting methods of working out rough-and-ready design formulæ based on first principles, and engineering, which is concerned with accurate design based on more empirical formulæ. The essential difference between pure and applied science is in the aim, and not in the quality of thought or level of fundamentality, the aim of pure science being essentially inquisitiveness, and that of applied science the benefit of mankind. The fundamental aspect of applied science is the development of the coefficients in the differential equations describing the separate parts of the complex processes that occur in industry. The superficial, or descriptive level of applied science is the *ad hoc* solution of practical problems. The corresponding level of pure science is natural history, empiricism, or classification, while the more fundamental aspect of pure science is the *experimentum crucis* to decide between rival theories. Since the only valid 'snobbishness' is that relating to quality of thought, it is unfortunate that many schools have inherited the older idea that there is a 'snobbishness' between pure and applied science. The basic problem is to relate the choice of subject of the students of university standard to the careers which are available for them when they have graduated. There is a great tendency for a boy to choose a subject that he has learned at school, or one which his master studied at university, and since very few applied scientists go in for teaching, this does not produce a correct balance in the choice of careers.

The introduction in Britain of colleges of advanced technology improves the channels leading to careers in applied science, but does not help to improve the proportion of the stream flowing in these channels. The essential problem is thus to show the brightest schoolboys that applied science is worthy of their talents and can give them fascinating careers, and is not just a place for those boys who are not deemed good enough for pure science by their schoolmasters. We need many more brilliant technologists on the boards of industry to give a new look to industry. Prof. Thring said that he has direct personal knowledge of industries which rely on foreign countries for their development work, and always wait until processes have been developed abroad before they take them up in Great Britain. The reason for this is lack of sufficiently brilliant technologists on the boards of the companies concerned.

The increased numbers of boys going to universities in the next decade, which would correspond to 5–6 per cent of any age-group, meant that one has to distinguish clearly between the static and dynamic view of university teaching. The former looks on students as a series of pebbles of predetermined size, and the function of the university is to sieve the larger ones and separate them rigidly from the smaller ones. Such a view does not, however, correspond to the human possibilities of the students concerned. The dynamic view is that all the 5–6 per cent of the age-group are capable of striking sparks of originality and interest, providing the teaching method can bring them out sufficiently. Somehow it is necessary to show the students that both the fundamental scientific laws and the way in which they explain practical processes have excitement and even glamour. So often the choice of a field of work for a student arises quite accidentally because one part of science has a good teacher, when many other branches of applied science could be presented in an equally exciting way. Some parts of applied science are inherently glamorous, such as nuclear fission, electron theory and rocket combustion; other parts require much more careful handling before the student can see the excitement of these subjects. The blackboard and chalk are no longer the only method of arousing the interest of the student. Colour films, television programmes, working models and working diagrams have all to be pressed into service.

In the Engineering Faculty at the University of Sheffield it has been decided that the size of the classes should by all attempts be kept below 50 so as to retain the close personal contact between the lecturer and the students. With larger classes one might just as well have a colour film of a lecture given once and for all by a national authority. Other points which are very important in the dynamic view of university teaching are the introduction of small supervision groups of not more than two or three students for an hour a week, keeping the number of hours of formal instruction as low as possible—the figure of 30 for the absolute maximum is being suggested—and the introduction of research or design-study problems in the final undergraduate year.

Prof. Thring then said that just as industry must have two legs, the production of goods for sale and

the development of new processes and methods to be a viable organization, so a university department must have teaching and research if the teaching is to be at the best possible standard. Hence, the university applied science department must have a strong research school studying the coefficients in the differential equations of the processes that are of interest in applied science, and this teaches the research students to be self-propelling in research. Prof. Thring confirmed that the civic universities are proud of their efforts to make sure that technologists know what is going on in the humanities, but felt that there should be no compulsion in this matter. He regarded the basic unit as the informal discussion group or the coffee party. In the discussion it was agreed that there is a difference between technology and the needs of industry for applied scientists among school-teachers, and various methods of overcoming this were discussed.

Dr. J. S. Tait, of the Northampton College of Advanced Technology, then discussed the role of the colleges of advanced technology in the education of scientists. In the 1890's a number of colleges of technology were formed as a result of Lord Kelvin's views that the universities were not close enough to industry, and those in London were particularly fortunate in that later on they could prepare students for the internal degree of the University of London.

By 1956 the Government decided that it would be sensible to give a small number of selected colleges of acknowledged reputation the opportunity to develop into colleges of advanced technology and discard all their work below university-level. They were to concentrate on producing the high-quality technologists so badly needed by British industry and research organizations. The colleges of advanced technology aim to produce the leaders of to-morrow by giving a good grounding in the applications of science to engineering. The new award of the Dip. Tech. is intended to have the standing of a second-class honours degree, and the colleges of advanced technology are equivalent to the technical universities of the Continent. The Committee of Vice-Chancellors and Principals of the Universities has recommended that holders of the Dip. Tech. should be regarded as eligible for university higher degree courses. The official entry conditions are six subjects in the General Certificate of Education, of which two must be at Advanced Level for grammar school boys, or better than 50 per cent in the Ordinary National Certificate for boys from industry, but of the 700 students taken so far in Dr. Tait's College, more than half have had three Advanced Level subjects at entry, that is to say, they have the minimum university entry requirements. Two-thirds of the total have been grammar school boys, and approximately 15 per cent public school boys. The wastage has only been about 5 per cent a year. The selection has been very severe since industry is paying about £2,000 per student to provide what, in effect, are scholarships without a means test. The student spends from six months to a year in industry before he starts in the college, and this makes a tremendous difference in his mental outlook, giving him a definite aim for his academic studies. The interest of the students in the humanities is fostered by giving them a 2-hr. lunch period during which lectures in the humanities are available. It was emphasized on behalf of the Department of Scientific and Industrial Research that it is prepared to give post-graduate studentships for work at the colleges of advanced technology, but the only qualification which can be given in this case is membership of the College of Technologists, while there is a tendency among students to feel that the Ph.D. is the only postgraduate qualification to which it is worth devoting two or three years of their lives. Prof. Craig pointed out that the technical universities on the Continent have their students for five and a half years full-time, and he emphasized that there were essential differences between the aims of the colleges of advanced technology and those of the universities, both being concerned with getting fundamental ideas across to the student, but differing in depth and generality.

Sir Patrick Linstead reported on the work of the British Association Committee, of which he has been chairman, on the subject of broadening the education of the graduate scientist. The desire for knowledge has three aspects: the desire to know how things work, the need to open the doors to a professional career in subjects in which the student is vitally interested, and thirdly, the need to be a member of the world and play his full part in society. On one hand, the student is exposed to lectures on outside subjects and told how important these are; on the other hand, the need to concentrate on his specialist subjects if he is to get through his examinations is emphasized to him. The scientist cannot be complaisant if he does not know of the humanities because of the increasing importance of scientists in the world. Inventiveness and scientific wisdom can only be supplied by vocationally trained scientists, but they also need a wider training as more and more of them are rising to top administrative positions.

The British Association Committee has concluded that both schools and universities have important parts to play in widening education beyond the formal teaching. The schools require more time for minority subjects in the sixth form. In the universities he agreed that compulsion was undesirable, but four steps were necessary: first, the reduction in the pressure on the main specialist subject; secondly, greater attention to non-scientific subjects which are, in fact, a necessary part of the specialist subjects, such as the use of English and the introduction of the history of science; thirdly, the provision of cultural events, lectures, concerts and library; fourthly, the generous provision of facilities, libraries of cultural books which do not close at 5.30 p.m., halls of residence with coffee bars, and beautiful surroundings. Sir Patrick also discussed the question of full-time postgraduate courses, which he regarded as very important. He directed attention to the fact that it would be necessary to have relatively small numbers in such courses compared with the undergraduate courses, while the elaboration of materials and lectures was very great. It was therefore essential not to have excessive competition between different teaching institutions, but to distribute the subjects between them. Prof. Craig also wanted more postgraduate courses, both specialized in advanced technology with people returning from industry, and as extensions of undergraduate courses to more advanced mathematical methods and fundamentals. These should be immediately after the undergraduate course. Prof. Craig also felt that the history of science should be taught with day-to-day reference to the subject as it occurred, and not starting from the very ancient beginnings of the science.

M. W. THRING

PHYSICS DEPARTMENT

HORMONES AND THE CONTROL OF ROOT GROWTH*

By PROF. H. E. STREET
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THE aspect of the hormonal control of growth which has been most intensively studied is the expansion phase in the growth of shoot cells. The promotion of this phase of cell growth is a characteristic activity of indolylacetic acid, the only auxin which has been isolated from plants and is known to be widely distributed. This emphasis is reflected in the definition[1] of auxins as "those plant growth substances which are characterized by their property of stimulating extension growth of shoot cells in bioassay tests". Current texts of plant physiology have, in consequence, very little indeed to say regarding the natural growth hormones of roots and their role in controlling the growth and differentiation of root cells.

It was from the early studies of the influence of the root tip upon the positive geotropic sensitivity of roots, initiated by Cholodny[2,3], that there developed the widely accepted view that the root tip produces an auxin similar to, or identical with, that secreted by the coleoptile of grasses and that the concentration of auxin thereby established in the root cells is supra-optimal for root growth. The subsequent demonstrations of the presence in roots of substances active in the *Avena* curvature test[4] and their production by isolated root tips, particularly when these are supplied with sugar, supported this view. A number of workers[5–7] did, however, report that externally applied auxins are by no means always inhibitory to the growth of seedling roots, and more recently the careful decapitation experiments of Younis[8] have shown that the removal of the root meristem does not lead to an acceleration of root extension growth although it does, as earlier claimed, reduce the sensitivity of the root to gravity.

New approaches to the study of the hormonal control of root growth have, however, now developed from the application of paper chromatography to the separation of natural growth-active substances[9,10] and from studies of the growth of excised roots in sterile culture.

Chromatography has been used to study the natural occurrence in roots of both auxins[9–15] and substances with gibberellin activity[16]. The chromatographic solvents used have in the former case been those known to effect separation of indoles, in the latter case to effect separation of gibberellins from naturally occurring inhibitors. Most of the auxin studies have the limitation that the chromatograms have been assayed only by the *Avena* straight-growth test[17]; directed, that is, to the detection of auxins as defined by their activity in promoting expansion of shoot cells. The simultaneous use of pea-root segments[11] or excised root cultures (Winter, unpublished) as test objects should increase the value of such surveys when working with root extracts.

There is a measure of agreement between different laboratories as to the pattern of auxin activity found on chromatograms of the 'ether-soluble' fraction yielded by roots[11,12,15]. The work of Thurman and Street[15] reveals activity at the R_F of the "accelerator α" of Bennet-Clark and Kefford[10,11] and of indolylacetic acid; elution and rechromatography of the "indolylacetic acid zone" in various solvents strongly indicates the presence of indolylacetic acid. At a higher R_F there is an acidic inhibitory zone which corresponds, with *iso*propanol/ammonia/water as solvent, to the "β-inhibitor" of Bennet-Clark and Kefford. The chemical nature of both the α and β zones is, however, obscure. Finally, there is activity at the solvent front which, when rechromatographed in 40 per cent ethanol, is shown to be complex and apparently does not contain indolylacetonitrile in detectable amount. These chromatograms of the preferentially 'ether-soluble' constituents of root extracts have so far only given negative results when treated with various indole and other sensitive spray reagents, which may indicate that the active compounds are present in very small amounts.

When the alcohol-soluble material of roots in aqueous solution is exhaustively extracted with ethyl ether or ethylacetate significant auxin activity remains in the aqueous phase. This 'aqueous' fraction has been submitted to chromatography and bioassay in several laboratories[13–15], but the published chromatograms do not reveal a consistent pattern, nor have the discrepancies been satisfactorily explained. Thurman and Street[15], by adopting certain purification procedures, combined with low levels of chromatogram loading as compared with those required for the detection of activity in 'ether' fractions, have demonstrated an indole and ninhydrin reactive zone. Part of the growth-promoting activity of this zone is attributable to the indolic amino-acid, tryptophan, and part to other unidentified ninhydrin-positive substances. The 'aqueous' fraction also yields, at a higher R_F in *iso*propanol/ammonia/water, a broad zone of growth-promoting activity resolvable by rechromatography into discrete growth-promoting ninhydrin-positive zones which do not correspond in R_F with any of the commoner amino-acids. Sugars detected on these chromatograms could be separated from the growth-active zones.

The purpose of describing these results in some detail is to direct attention (1) to the complexity of the picture in these and other studies involving chromatography, (2) to the evidence for the presence of indolylacetic acid albeit at very low concentration, and (3) to the quantitative importance of the preferentially water-soluble constituents, including tryptophan, in the total 'auxin' activity extractable from root cells. To this must be added the recent demonstration by Butcher[16] that tomato roots also contain substances with gibberellin activity as revealed by the dwarf pea assay[18].

The complexity of the indole system in roots is further suggested when one examines by chromato-

* Substance of a paper given before Section K (Botany), at the Cardiff meeting of the British Association on September 7.

graphy (even at low levels of loading) the 'ether' fraction obtained from roots which have been allowed to take up indoles from the external medium. These indoles have, in unpublished experiments carried out in my laboratory by Thurman, been applied at inhibitory but sufficiently low concentrations that the roots can recover from the experimental treatments as shown both by subsequent root growth and depletion of the accumulated compounds on transfer to indole-free medium.

Feeding with indolylacetic acid (10^{-6} gm./ml. for 24 hr.) leads to a marked enhancement of growth-promoting activity at the indolylacetic acid position, to the appearance of Erhlich and nitric–nitrite reactors and to growth-promoting activity at R_F 0·25 (*iso*propanol/ammonia/water). The two strong nitric–nitrite reactors at R_F 0·25 and 0·35 in this solvent, can be resolved into three distinct reactive spots by rechromatography in butanol/pyridine/water. One of these has been shown by hydrolysis to be indolylacetylaspartate, the second corresponds in R_F with indolylacetylglutamate and the third the nature of which is unknown gives a characteristic pink colour with nitric–nitrite reagent (the same compound seems to have been detected by Andreae and van Ysselstein[19] in stem tissue). In addition, the *iso*propanol/ammonia/water chromatograms showed two other indoles, one at the starting line and the second at the R_F of indolylacetamide.

Feeding with indolylacetonitrile (10^{-5} gm./ml. for 24 hr.) gives high growth-promoting activity at the indolylacetonitrile position, but the only other compound detected was inactive in the *Avena* test and corresponded in R_F and Ehrlich reaction to indolylcarboxylic acid. This suggests the operation here, as in some other plant tissues[20], of an α-oxidation of the nitrile via indolylaldehyde without any intermediate formation of indolylacetic acid. Feeding with tryptophan (50 mgm./l. for 24 hr.) leads to the marked accumulation of this amino-acid, but the 'ether' fraction lacks growth-promoting activity (at the low level of loading adopted) and the only ethylacetate-soluble compound detected is probably the malonyltryptophan, previously detected in tomato tissue, both as a natural constituent and as a product of tryptophan metabolism, by Good and Andreae[21].

Two interesting observations may be noted from these feeding experiments. First, indolylacetonitrile feeding does not enhance activity at the indolylacetic acid position or give the Ehrlich and nitric–nitrite reactors associated with indolylacetic acid feeding. Further, when indolylacetic acid and indolylacetonitrile are fed simultaneously to roots, the resulting chromatogram is equivalent to an indolylacetonitrile chromatogram superimposed upon an indolylacetic acid chromatogram. This suggests that if there is any inhibitory effect of indolylacetonitrile on indolylacetic acid metabolism, as reported by Bennet-Clark and Wheeler[22] working with disks of potato tuber tissue, then this is quantitatively unimportant in the root tissue. These new observations, when considered in the light of earlier published physiological studies with indolylacetic acid and indolylacetonitrile[23,24], strongly support the view that the activity of indolylacetonitrile on root growth is not explicable in terms of its acting as a precursor of indolylacetic acid. The second interesting observation is that the relatively high levels of indolylacetic acid and indolylacetonitrile and of the indolylacetic acid–amino acid conjugates established in these feeding experiments rapidly decline on transference of the roots to indole-free medium, suggesting their rapid further metabolism. It should be emphasized that these feeding experiments were only designed to detect major ether-soluble products arising from the absorbed indoles and would not detect protein-indole complexes reported by Seigel and Galston[25] to arise from feeding auxins to pea root apices.

As already indicated, 'active' compounds detected in root extracts have been so defined primarily by reference to their ability to promote the expansion of shoot cells. Clearly, therefore, it is important to study the effects of known plant hormones and chemically related compounds on root growth. Using root cultures growing under sterile and defined nutritional and environmental conditions the physiological activity of such substances can be readily described in terms of root morphology, cell division, cell expansion and tissue differentiation. Comprehensive studies of this kind have already been initiated with indolylacetic acid and indolyacetonitrile and revealed their contrasted effects on cell division and cell expansion[23,24].

One of the problems raised by such studies was that auxins seemed to be, at sufficiently low concentrations, inactive, and at higher concentrations only inhibitory to root growth; a situation which took us back to the Cholodny hypothesis that auxins function only as inhibitors of root growth. Recent work[26,27] has, however, shown that appropriate manipulation of the nutritional conditions of culture, particularly in respect of the carbohydrate status, enables significant enhancements of root growth to be obtained in response to treatments with auxins and also with gibberellins and kinetin. Further, since the standard conditions of root culture have been worked out in relation to a very few species, in fact primarily from work with certain tomato root clones, it is not surprising that the bringing into culture of the roots of new species, under probably sub-optimal conditions, has also served to show that very marked stimulations of root growth can be obtained from the applications of low concentrations of auxins and related compounds[28,29].

Work involving the application of mixtures of auxins, gibberellins and kinetin to root cultures has shown that the rate of growth, the relative contributions of cell division, expansion and differentiation to growth, the degree of apical dominance and so on are, under certain conditions, determined less by the concentration of any one factor than by the balance between them[16]. Comparative studies between species of the factors controlling the persistence of meristematic activity in root apices also point to the operation of more than one hormonal factor[30]. These physiological results, when considered against the background of the complex picture revealed by chromatography, suggest that in root growth and differentiation the balance between a complex of growth factors may be determinative in a way similar to that so dramatically exposed by Skoog *et al.* in their studies on growth and differentiation in shoot callus cultures[31].

Recently, in work with cultures of cereal roots, there has been obtained evidence of a further aspect of the hormonal control of root growth. Roots of cereals have, in general, proved resistant to culture[32]. Root tips excised from seedlings, when transferred to standard root culture media, show initially a high growth-rate, but this declines rapidly and ceases within 2–3 weeks. Subculture of the root tips enhances this decline and clones cannot be established in culture.

However, Roberts and Street[28] succeeded in establishing clones of excised Petkus II rye roots by incorporating tryptophan into the culture medium. Further, the observation that, in this case, D- and L-tryptophan and indolylacetic acid were all equally effective suggested that the active substance was not tryptophan itself but some compound for which it acted as a precursor. This view was strengthened when it was found that tryptophan samples, if incorporated aseptically and without heating, were either inactive or of very low activity and that activation occurred during autoclaving. Rye roots apparently ceased growth, in the absence of hormonal concentrations of a tryptophan derivative, for lack of some essential growth hormone.

In unpublished experiments, Scott, Carter and Sutton have now studied the growth in culture of excised roots of the Atson variety of wheat and found that the level of growth and its persistence can be dramatically enhanced by illuminating the cultures. Further, that autoclaved tryptophan very nearly reproduces in dark-grown cultures the enhancement of growth achieved by illumination. In this case, however, indolylacetic acid does not effectively substitute for tryptophan; the wheat roots are apparently much less able to metabolize indolylacetic acid to the required active compound.

Now it is known that, under certain conditions, the growth of excised roots of maize[33], *Lycopersicum pimpinellifolium*[34] and tomato[35] is also enhanced by low-intensity illumination, and work on the action spectrum of this light effect with both tomato and wheat indicates a peak of activity in the red. This work prompts me to ask whether light is an essential requirement for the growth of all roots in culture; in which case the roots of most species so far successfully cultured presumably receive sufficient illumination during the manipulations involved in subculture to permit active growth during the subsequent dark incubation period. If this is so, then it can be suggested as one possibility that the growth of roots normally depends on the translocation to them of some specific hormone synthesized in the shoot; the photochemical synthesis of this hormone can, however, also be achieved in root cells exposed to light. In the light-responsive excised wheat root we may have a system in which it will be possible to characterize and study the biosynthesis of the hypothetical 'rhizocaline' (root hormone supplied by the shoot) first so called by Bouillene and Went[36] but afterwards invoked by a number of workers.

This review, despite its incompleteness, may nevertheless have shown that our knowledge of the hormonal control of root growth has reached a point which could lead to very fruitful further research. This will, however, require the isolation and identification from root extracts of active hormones which, on present evidence, can be expected to be present in very low concentrations; the isolation of the enzymes concerned in the synthesis and metabolism of these growth hormones and the intensification of physiological studies. If such studies are to be pursued with sufficient intensity to have a successful outcome it will require a considerable re-orientation of the research resources at present devoted to the study of what may be broadly called the field of plant hormone research, a field in which extensive practical applications are based upon a most slender body of fundamental knowledge.

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OBITUARIES

Mr. A. L. Hetherington, C.B.E.

ARTHUR LONSDALE HETHERINGTON, who died on August 21 at the age of seventy-eight, was educated at Highgate School and Trinity College, Cambridge. On leaving Cambridge, he taught for two years at his old school and then served for two years in Burma in the Indian Educational Service. He returned to Britain in 1908 as a junior examiner in the Board of Education. He acted as secretary of the Board's Advisory Committee on University Grants and as assistant secretary to the committee which framed the scheme of reconstruction for the University of London. During 1914–19 he was secretary of the Carnegie United Kingdom Trust.

In 1919, Hetherington was appointed to the Department of Scientific and Industrial Research, but was immediately loaned to the Treasury to act as secretary of the newly formed University Grants Committee. He was promoted assistant secretary in

1922 and until his retirement in 1943 was in charge of the grants to postgraduate students for training in research, to individual research workers and the grants to the co-operative research associations. He thus assumed responsibility, without any industrial background, for the research association movement in Britain at the most critical and difficult period of its history.

The novelty of this scheme for Government assistance to research in industry was wearing off, and the post-war boom years were coming to an end. Industry was generally indifferent to science and often suspicious of the co-operative aspect of the associations. Money was tight both in industry and Government, and the associations were compelled to function with very limited resources. Most of them were doing useful work, as evidenced by the book Hetherington wrote with Sir Frank Heath on their early history; but the results achieved were seldom of a kind to make a ready appeal to industrialists imbued with a profound faith in traditional methods. It was largely due to Hetherington's skill as an administrator and to his personality that the movement survived these lean years to play a notable part in the Second World War. His work demanded much tact and patience—virtues which did not come to him naturally. It was a great satisfaction to him to see the associations expand after the War to occupy the important position in British industry they hold to-day.

Hetherington's early training fitted him admirably to deal with the scientific grants to individuals; but even here he had his difficulties, as during the 30's more than one influential, but unenlightened, Civil Servant made no secret of his opinion that many of the grants, especially those for training research students, were little more than unemployment doles.

Hetherington's official work was lightened by two hobbies. The first was his keen interest, as collector and expert, in Chinese porcelain. In this field his important book, written with R. L. Hobson, on "Early Ceramic Wares of China" brought him an international reputation. He also took a leading part in the formation of the Oriental Ceramic Society. His second interest was in turning on the lathe. Here recognition of his skill led to his becoming a Master of the Turners' Company, the honorary freedom of which was bestowed on him in 1932. He took special interest in the turning properties of many little-known Empire timbers.

Finally, Hetherington had quite a talent for versification, and frequently amused his colleagues with mildly satirical verses on matters of topical interest to the Department of Scientific and Industrial Research.

O. F. BROWN

Dr. W. D. Douglas

THE death on August 5 of Dr. W. D. Douglas removes another of the now thinning ranks of first-generation aircraft scientists. He was born in Ireland on August 2, 1887, and educated as an electrical engineer at Trinity College, Dublin. For some years he served as a hospital X-ray operator, and then joined the staff of the Royal Aircraft Establishment and specialized in the properties of materials, especially timber and adhesives, which were the common materials of aircraft structures. He became a leading authority on their properties.

In the 1930's, he was in charge of the mechanical testing of aircraft structures and components and materials. Under his guidance the science of testing large structures grew from small beginnings to something like its present degree of sophistication. His advice on the design and strengthening of structures was eagerly sought by aircraft designers.

Douglas's knowledge of the mode and cause of failure of materials was invaluable to the Air Ministry's Accident Investigation Department, and it became usual for the pieces of crashed aircraft to be sent to him. After painstaking re-assembly and examination of scratches, dents and fractures, he was often able to decide the sequence of catastrophe and the cause of failure. The techniques he developed form the basis of present-day aircraft accident investigation. Re-organization during the Second World War put Douglas in charge of the Materials Department at the Royal Aircraft Establishment, the three divisions of which covered chemistry, metallurgy and non-metallic materials.

On retiring from the Civil Service in 1946, Douglas joined the furniture firm of Harris Lebus as its first head of research. In this unique position he spent nine fruitful years, asking questions, seeking answers and giving sound advice. He represented the firm on technical committees, and when the Furniture Development Council was started in 1949, Douglas joined its research committee and was most helpful in formulating programmes and in guiding the Council's research officers. He played a major part in the development of the performance tests for furniture, which are now incorporated in British Standard Specifications. Furniture satisfying the standards is marketed under the 'Kite' mark.

Douglas retired from Harris Lebus in 1955, but continued to serve most effectively on the Furniture Development Council.

In personal characteristics he was a modest man, and the most helpful and sincere of friends to those in need; but he could also be a worthy adversary. A devoted husband and father, he leaves a widow and son.

C. GURNEY

Dr. Peter L. Goldacre

DR. PETER L. GOLDACRE, a senior research officer in the Division of Plant Industry of the Commonwealth Scientific and Industrial Research Organization, Canberra, Australia, died after a brief illness on April 16, at the age of thirty-four. Paradoxically, at the time of his death from cancer, he was engaged in incisive and rewarding investigations into the nature of the chemical factors controlling cell division in plants.

Goldacre was educated at Sydney Boys' High School and the University of Sydney. He joined the Division of Plant Industry of the Commonwealth Scientific and Industrial Research Organization, in 1947, as one of the first two plant biochemists to be appointed to this agency. His early work, reflecting his biochemical training, was largely enzymological. He was the first to characterize the 'indoleacetic acid oxidase' complex as being composed in part of a peroxidase. Later, at the California Institute of Technology, where he obtained his Ph.D. degree in 1952, he was instrumental in discovering the activating effect of substituted monophenols on this enzyme complex. During these investigations, he also discovered that 2,4-dichlorophenol is a specific inhibitor

for the enzyme catalase, and thus permits the demonstration of the related enzyme peroxidase in such tissues as the liver, where its presence is normally masked by the preponderance of catalase.

By the time he returned to Australia, Goldacre had become keenly aware that many important questions in biology were not ready for investigation by classical biochemical techniques. He made the important and difficult decision to shift his research emphasis to the mechanism underlying differentiation of plant cells. His experiments on the auxin-induced initiation of lateral roots in cultured excised flax roots convinced him of the existence of a cell division inducer (kinin) elaborated by the inhibited, pre-existing lateral root primordia. His search for rich sources of kinin-like materials in tissues undergoing cell division led to the discovery of 'Kineapple' (*Nature*, 184, 555; 1959), a yet uncharacterized, highly active inducer of cell division from young apple fruitlets. In collaboration with several colleagues in Canberra, he was attempting the isolation of this material from three-quarters of a ton of apple fruitlets at the time of his death.

Peter Goldacre's outstanding characteristics were his honesty and easy-going informality, together with his impatience with pretension and sham. He loved camping and the outdoor life; he had a powerful physique and excelled at swimming and other sports. Six months before his fatal illness, he had attended the Fourth International Congress on Plant Growth Regulation at Yonkers, N.Y., and appeared in vigorous good health. The sudden knowledge of his impending death did not materially alter his essentially humorous and compassionate outlook on life.

He leaves his wife and three young children, the youngest born only a few months before his death. To those privileged few who knew him well, he will be remembered as one of Nature's noblemen. The tragedy of his early death lies in the fact that he had so much to give to many who had not yet come to know him.

ARTHUR W. GALSTON

NEWS and VIEWS

Education in Industry

THE British Association for Commercial and Industrial Education has issued reports on two of its recent conferences. The first, "Education for Survival", contains the papers presented at the proceedings of the East Midland Group and is noteworthy for a stimulating account of technological education in Britain by Dr. B. V. Bowden, principal of the Manchester College of Science and Technology. The list of members attending indicates that speakers on subjects like the training of non-apprentices and the attitude of trade unions to apprenticeships were preaching mainly to the converted. The Association would perform a valuable service to industry if it could persuade recalcitrant managing directors of the need for training apprentices and others. The second conference dealt with "The Implications of the Crowther Report", and the speakers, who included the Minister of Education, underlined its main findings and recommendations. The value of what might have been a useful report is diminished by its appearance some five months after the Conference. Information about both reports may be obtained from the Director, British Association for Commercial and Industrial Education, 26*a* Buckingham Palace Road, London, S.W.1.

British Rubber Producers' Research Association

THE current report of the British Rubber Producers' Research Association gives an account of the progress made during 1959, both in the fundamental study of the structure and properties of natural rubber and in the application of scientific knowledge acquired in recent years to the problems of the industry (Twenty-second Annual Report. Pp. 53. 1960). On the fundamental side, work on the biosynthesis of rubber in the tree has been made possible by the installation of a tropical greenhouse at Welwyn Garden City. The attack on this elusive problem includes the study of the structure of the latex vessels by the electron microscope, and the chemical examination of cell constituents. The chemical processes of vulcanization, that is, of the formation of a network of long-chain molecules, and the converse processes of ageing or network breakdown continue to be the subject of intensive study; progress in this field, though necessarily slow, is continuous. Of particular interest is the elucidation of the mechanism of surface cracking by ozone and the role of anti-ozonants. It is well known that this type of degradation is dependent on the state of stressing of the rubber, and it has now been shown that the effect of the anti-ozonant is to raise the critical stress for crack growth, while leaving the rate of growth above this critical stress unchanged. The somewhat related problem of fatigue failure has been shown to be associated with the growth of flaws having dimensions of the order of 0·01 mm. The report gives examples of the application of the knowledge obtained from these fundamental investigations to the production of rubbers and rubber compounds having more desirable physical and chemical properties. This work is designed to ensure that natural rubber is not left behind in the competition with the synthetic materials now available. The report is available from the Association, 19 Fenchurch Street, London, E.C.3.

Comparative Efficiency of Indexing Systems

A REPORT by Mr. C. W. Cleverdon on the first stage of an investigation into the comparative efficiency of indexing systems, an investigation supported by a grant to the Association of Special Libraries and Information Bureaux by the National Science Foundation, has now been issued by the College of Aeronautics, Cranfield, on behalf of Aslib (Pp. v + 166. Cranfield: The College of Aeronautics, 1960). The grant of £10,000 was made in July 1957 for a study of the comparative efficiency of the Universal Decimal Classification, the alphabetical subject catalogue, a faceted classification system, and the Unitern system of co-ordinate indexing, which in this first stage involved the indexing of 18,000 research reports and periodicals in the general field of aeronautical engineering, about half of which dealt with high-speed aerodynamics. The present

report is essentially a factual account of this first stage and any firm conclusions must await the result of using a piece of test equipment in a test programme for which the National Science Foundation has awarded a further grant. Meanwhile besides describing the general organization of the programme and giving a detailed analysis of the problems encountered, the report includes various statistical details and an account of some supplementary indexing undertaken by other organizations and individuals in co-operation. When the test programme is completed it should be possible to analyse the results so as to ascertain in detail the reasons for success or failure in locating information and eventually to state with reasonable certainty exactly what requirements an information retrieval system must meet and propose methods for the design of such a system.

Co-ordination of Research

A VALUABLE means of co-ordinating research in engineering over an 'academic' region is being carried out by the Academic Board for Higher Technology of the Northern Advisory Council for Further Education (Thirteenth Annual Report, 1959/1960. Pp. 32. Newcastle upon Tyne: Northern Advisory Council for Further Education, 1960). The Board has accepted proposals put forward by Prof. W. Fisher Cassie, of the University of Durham, in which he recommended that the institutions for higher technology in the region should be asked to send to the Board their proposals for research projects. In this way, "the Board would be informed of the whole pattern of research and would be able to advise on the use of expensive apparatus and on the possibility of a number of institutions sharing in a research of some magnitude". The Board also accepted recommendations put forward by Prof. A. F. Burstall that more provision should be made for training in engineering design. As a first step a sub-committee was appointed to report on the organization of short courses for designers. Industry will warmly welcome this initiative.

Magnetic Data for the International Geophysical Year

THE 1957 and 1958 volumes of the Observatories' Year Book covering the International Geophysical Year have recently been published (Air Ministry, Meteorological Office. The Observatories' Year Book. 1957. Pp. vi+120. (M.O. 680.) 50*s*. net. 1958. Pp. vi+128. (M.O. 681.) 55*s*. net. London: H.M. Stationery Office, 1960). They contain the autographic records and eye observations of terrestrial magnetism at Lerwick and Eskdalemuir observatories and of atmospheric electricity at Lerwick and Kew. They also contain the log of the auroral watch at Lerwick and a general auroral table for the British Isles. These two volumes have been published out of turn, the otherwise latest volume published being that for 1950, in order to make the fundamental magnetic observations made at the Scottish observatories during the International Geophysical Year available to geophysicists as early as possible. The volumes for 1951–56 are expected to be published during the next twelve months.

The Sarawak Museum Journal

THE *Sarawak Museum Journal*, under the enthusiastic editorship of Mr. Tom Harrisson, Government ethnologist and curator of the Museum, is always of interest to many outside Borneo. The current issue (9, No. 13–14 (New Series), July–December 1959) includes papers on ethnology, history, prehistory, Welfare States, natural history and some book reviews. Notes on "An All-round Museum in a small Country" are as applicable elsewhere as they are in Borneo. Other articles include some carbon-14 datings from Niah caves, an account of the Piltdown forgery from the point of view of orang-utang teeth from Borneo or Sumatra, and notes on cock-fighting, the Dayah national game.

Education in the Primary School

To help teachers in primary schools, the National Union of Teachers is issuing a new series called "Curriculum Studies". The first, "Mathematics in the Primary School", has been prepared by R. A. Swallow, who has specialized in the teaching of mathematics to primary school children over many years. The booklet is clearly written, full of problems which can be presented to children at differing ages, and based on his own experience of children. The second, "Science in the Primary School", explains how science in the primary school should be developed and describes means of doing this. The author, Cedric Griggs, should now follow the sequence of Mr. Swallow's booklet and present a programme of science teaching to develop coincidentally with young children's emerging interests. Both booklets can be obtained from the Schoolmaster Publishing Co., Hamilton House, Hastings Street, London, W.C.1, the former price 2*s*. 6*d*. and the latter 2*s*.

New Technique in Insulation Testing

THE new 'Megger' insulation tester, series 3, mark 3, manufactured by Evershed and Vignoles, Ltd., incorporates some advanced features made possible by new manufacturing techniques and materials. The instrument consists of a hand-driven generator and a direct-reading ohmmeter. The moving element of the ohmmeter consists of two coils, the control and deflecting coils, arranged so as to oppose each other. There is no control spring and the deflexion of the movement depends on the ratio of the currents in the two coils. The turning effort of the new instrument is considerably less than that required for earlier models. A clutch-less nylon gear-train transmits the handle torque to the generator and provides remarkably smooth and consistent operation. In addition to the insulation testing range, the instrument operates over a continuity range 0–100 ohms with a scale of shape permitting readings as low as 0·1 ohm. The continuity testing voltage is obtained from a new miniature generator so that no battery is required and thus constant readiness for use is ensured.

Evaluation and Presentation of Spectro-Analytical Results

IN the pocket booklet entitled "Evaluation and Presentation of Spectro-Analytical Results" the author, A. B. Calder, directs attention to the various types of error which arise in chemical and instrumental analysis (London: Hilger and Watts, Ltd., 1959. 5*s*. net). The errors are classified into two groups, determinate or constant errors, and indeterminate or accidental errors. Their mathematical treatment is dealt with in some detail and then finally the application of the treatment to various spectro-analytical problems is discussed. Throughout, references are given to fuller treatments,

but sufficient warning and guidance are given to indicate to the reader the statistical nature of certain problems encountered in analytical spectroscopy. The importance of indicating how the errors are distributed in multi-stage analytical techniques and the saving in operational time which can often be attained, without loss of accuracy, by the correct interpretation of the analytical data, are emphasized.

Hydrogen in Jupiter

ALTHOUGH molecular hydrogen has long been regarded as a constituent of the atmosphere of Jupiter, direct spectroscopic evidence has been lacking. Jupiter has a known mass and size, and the resulting calculated mean density is surprisingly low. When this was considered in relation to the central condensation of the planet as determined from the motions of its satellites, it became clear that much of the planet must be made up of a light substance. The surface gravity on Jupiter is sufficient to retain light gaseous elements, and it seemed likely that hydrogen might be an important constituent at least of the outer layers of Jupiter, and perhaps also of the interior. The spectroscopic detection of molecular hydrogen has proved to be extremely difficult, and it is only possible if a very large quantity of hydrogen is present. The detection rests on a few extremely faint lines of the quadrupole rotation–vibration spectrum of the molecule. It has now been accomplished in the spectrum of Jupiter by C. C. Kiess, C. H. Corliss and Harriet K. Kiess (*Astrophys. J.*, 132, 221; 1960), who found four of the quadrupole lines. In their paper the authors also direct attention to an unexpected excess continuous absorption, which is so far unidentified, but which closely resembles a known nitrogen tetroxide absorption. Objections to this identification can be raised on the grounds that the hydrogen would act on the tetroxide as a reducing agent, but no other identification has yet been suggested.

Banana Fruit Development

N. W. SIMMONDS has reported on experiments on the development of banana fruits and seed fertility, various synthetic auxins and auxin-antagonists being applied to young fruits in lanolin emulsions (*Ann. Bot.*, N.S., 24, 212; 1960). Auxins stimulated the formation of edible pulp in both seedy and parthenocarpic bananas and induced varying degrees of seed fertility. Of the auxin antagonists tried, coumarin stimulated parthenocarpy and induced seed sterility, three others were not or only slightly active, and thiourea markedly inhibited parthenocarpy. Study of the relation between size of mature fruit and seed content indicates that developing seeds stimulate the growth of pulp, and that the amount of stimulation is roughly proportional to the level of parthenocarpy. Fruit development in the banana seems to fit in with Luckwill's general scheme of dual hormonal stimulus.

Pharmacology of Psychotropic Drugs

THE number of chemical compounds with an effect on the higher centres of the central nervous system has greatly increased in recent years; and the remarkable properties of some of them have aroused much interest in their modes of action, which are now better understood because of improved knowledge of the physiology of the central nervous system. A paper by the Director of Research, Dumex, Ltd., Copenhagen, examines systematically the effects of some of the better known of these psychotropic drugs on the various levels of the central nervous system; their antagonistic and synergistic effects; and the relationship between these effects and the effects on other functional systems and on behaviour. Although the picture revealed is complex and there are many gaps, psychotropic drugs fall into certain classes according to the effects they have, and a system of classification could be developed on this basis. ("The Comparative Pharmacology of Some Psychotropic Drugs". E. Jacobson. Offprint from *Bull. World Health Org.*, 21; 1960. 5*s.*, 1 dollar or Sw. Fr. 3.)

Nomenclature of Human Chromosomes

THE discovery that some errors of sexual development and other congenital defects in man were associated with karyotypic abnormalities has aroused considerable interest, and research in this field is growing rapidly. Already four different states of numerical unbalance of the sex chromosomes have been identified, as well as three primary autosomal trisomic conditions, several examples of karyotypic mosaicism, and other cases attributable to reciprocal translocation and to deficiency. Various systems of numbering of the chromosomes have been used by different research groups, making the comparison of their results difficult. A meeting with the object of trying to devise an agreed nomenclature was therefore arranged by Dr. T. T. Puck, of the University of Colorado, and held in Denver during April 9–11. All those who had contributed to studies of human somatic chromosomes up to the end of 1959 were invited to take part and nearly all were able to attend. Prof. D. G. Catcheside (who acted as chairman), Prof. H. J. Muller and Prof. C. Stern were also present as councillors. A system was agreed on and a statement embodying it and other information relating to the identification of human mitotic chromosomes has been published (*Lancet*, i, 1063; 1960). The statement was signed by all the members, who included five from the United States, three from Britain, three from Sweden, one from France and one from Japan, in addition to those already mentioned. It is hoped that the proposed standard system will be generally adopted, and that any who may prefer to use another scheme will refer to the proposed system and show clearly in what way their own system differs.

Bibliography of Indology

THE National Library, Calcutta, has published the first volume of "A Bibliography of Indology" (Vol. 1: Indian Anthropology. Compiled by J. M. Kanitkar. Edited, revised and enlarged by D. L. Banerjee and A. K. Ohdedar. Pp. xi+290. (Calcutta: National Library, 1960.) Rs. 5.00. 8*s.*). It is in fact a catalogue of more than 2,000 publications on the archæology and anthropology of the sub-continent, with frequent notes and extracts from reviews describing the contents of the works. Added are author and subject indexes which enable the reader to use conveniently the references. The result is a very useful bibliography, if not entirely complete, particularly on the prehistoric side.

University News: Belfast

A CONTRACT has been signed between the Queen's University of Belfast and the United States Navy European Research Contracts Office. Under this contract, in the first year, the University will be supplied with a *Deuce* electronic digital computer and

with money for additional research staff. In return, Prof. D. R. Bates, Dr. A. Dalgarno, and several other members of the Applied Mathematics Department will undertake theoretical investigations on some problems of importance to the Advanced Research Projects Agency (on behalf of which the U.S. Navy Office is acting). In anticipation of the signing of the contract the erection of a building for the computer has been authorized and a new lectureship in digital computing has been established. A digital computing unit has been set up with the Applied Mathematics Department, and Dr. Dalgarno has been appointed director of this unit.

Birmingham

THE University has accepted the offers of Harry H. Payne, Ltd., and of the Harry Payne Trust to make further payments of £1,250 per annum and £1,000 per annum, respectively, to the Harry Payne Fund for a period of seven years from 1961. The Harry Payne Fund was established in the University in 1954 with gifts of £1,000 per annum each from Harry H. Payne, Ltd., and the Harry Payne Trust for seven years. The Fund is used to support a lectureship in employer/employee relations. The lectureship is held by Dr. N. S. Ross, senior lecturer in employer/employee relations.

The following appointments to lectureships have been made: Dr. G. M. Bennison (geology); Dr. T. S. M. MacLean (electrical engineering); Dr. D. A. Wilkins (botany).

London

DR. P. E. POLANI has been appointed to the Prince Philip chair of pædiatric research tenable at Guy's Hospital Medical School. The title of reader in hæmatology in the University of London has been conferred on Dr. Sidney Shaw in respect of his post at Charing Cross Hospital Medical School, and that of reader in bacteriology on Dr. H. I. Winner in respect of his post at the same School.

Massachusetts Institute of Technology: Department of Nutrition, Food Science and Technology

THE Food Technology Department of the Massachusetts Institute of Technology is to be enlarged and renamed the Department of Nutrition, Food Science and Technology. Dr. N. S. Scrimshaw, director of the Institute of Nutrition of Central America and Panama and regional adviser on nutrition of the Pan American Health Organization (the Regional Office for the Americas of the World Health Organization), has been appointed head of this Department.

Dr. Scrimshaw, who is at present an adjunct professor of public health nutrition in Columbia University and a visiting lecturer in the Harvard School of Public Health, will assume his new duties on August 1, 1961. He will continue his association with the Institute of Nutrition of Central America and Panama as a technical director.

The Night Sky in November

FULL moon occurs on Nov. 3d. 11h. 58m. U.T., and new moon on Nov. 18d. 23h. 47m. The following conjunctions with the Moon take place: Nov. 5d. 18h., Aldebaran 0·4° S.; Nov. 9d. 00h., Mars 6° N.; Nov. 21d. 15h., Jupiter 5° S.; Nov. 21d. 19h., Venus 7° S.; Nov. 22d. 08h., Saturn 4° S. In addition to these conjunctions with the Moon, Venus is in conjunction with Jupiter on Nov. 19d. 02h., and with Saturn on Nov. 28d. 07h., on both occasions Venus being 2° S. Mercury is too close to the Sun at the beginning of the month for normal observation, but it becomes visible as a morning star later in the month; it will be visible low in the south-east before sunrise, rising about two hours before the Sun on November 23. There is a transit of Mercury on November 7, partly visible at Greenwich. At ingress, exterior contact takes place at 14h. 34·4m., and interior contact at 14h. 36·4m. Only the earlier part of the transit will be visible in Great Britain; sunset occurs at 16h. 20m. at Greenwich and Mercury leaves the solar disk at 19h. 13m. The last November transit of Mercury was in 1953, and the next will be in 1973. Telescopic aid will be necessary to observe the transit. Venus is an evening star, setting at 17h. 50m., 18h. 00m. and 18h. 30m. on November 1, 15 and 30, respectively. During this time its distance from the Earth decreases from 119 to 102 million miles, the visible portion of the apparent disk is from 0·823 to 0·744, and its stellar magnitude from −3·4 to −3·6. Venus is visible in the south-west after sunset. Mars rises at 20h. 05m., 19h. 20m. and 18h. 10m. at the beginning, middle and end of the month, respectively. It is in Gemini, reaching stationary point on November 21 and then beginning to move westward among the stars. Its stellar magnitude is −0·5 and its distance from the Earth on November 15 is 69 million miles. Mars is now a very prominent object and can be seen almost all night. Jupiter is low in the south-west at sunset, and sets about two hours after the Sun. Conditions are unfavourable for observation. Saturn is in Sagittarius, east of Jupiter, and sets about three hours after the Sun. Conditions are unfavourable for observation. Occultations of stars brighter than magnitude 6 are as follows, observations being made at Greenwich: Nov. 6d. 5h. 05·6m., 318 B. Tau. (*R*); Nov. 15d. 4h. 02·0m., η Vir. (*R*). *R* refers to reappearance. The Taurid meteors are active near the beginning of the month, but conditions are unfavourable. The Bielids are active about November 14, with a radiant near R.A. 1h. 32m., Dec. +43°. This shower has recently been recovered photographically, and conditions are favourable, so that there is hope that it may again be seen visually. The Leonids are active on November 15–17, conditions being favourable; the radiant is near R.A. 10h. 08m., Dec. +22°.

Announcements

PROF. REBECCA C. LANCEFIELD of the Rockefeller Institute has been awarded the third T. Duckett Jones Memorial Award of the Helen Hay Whitney Foundation. The award, amounting to 6,500 dollars, was conferred for "her long and continuing studies which are so largely responsible for the present knowledge of the biology of hæmolytic streptococci".

PROF. JOHN MCMICHAEL, professor of medicine in the University of London at the Postgraduate Medical School, Hammersmith, has been appointed a trustee of the Wellcome Trust in place of Sir Henry Dale, who retired from the Trusteeship in July 1960, and was succeeded as chairman by the Rt. Hon. the Lord Piercy. Sir Henry Dale will continue to serve the Trust in an advisory capacity as scientific consultant.

ERRATUM. In the article entitled "Dwarf Mistletoes" in *Nature* of October 8, p. 112, the author of the paper surveyed is incorrectly given as "J. Knight"; the paper is in fact by Dr. Job Kuijt.

SCIENTISTS IN THE PUBLIC SERVICE

SPECIAL PROMOTIONS

SPECIAL posts have been created in the Civil Service as in previous years under provisions included in the White Paper on the Scientific Civil Service (Cmd. 6679, 1945) to provide for the promotion of individual research workers of exceptional merit. The promotions were effective from July 1, and include the following.

Deputy Chief Scientific Officer

MR. R. BENJAMIN joined the Admiralty Signal Establishment in 1944. During the following years his many contributions to radio and radar research and development were notable for their remarkable insight and brilliant execution. Promotion was rapid and he became a special merit senior principal scientific officer, in 1955, at the age of 32. By that time he was already established as an international authority on the theory, design and use of circuits in the video and pulse fields. His practical application of this knowledge to the processing and display of information, together with a major contribution to the concept of the accompanying radar, have borne fruit in the latest naval 3-D air-defence system which has been demonstrated with such conspicuous success. In addition to a continuing concern with advanced radar systems since 1955, Mr. Benjamin has been exploring new techniques of automation and computation to be applied to data processing and weapon control in virtually the whole field of naval warfare.

MR. L. G. CARPENTER, head of the Metallurgy Department, Royal Aircraft Establishment, joined the Establishment as head of the Research Section of the Instrument Department in 1937, and in 1940 was responsible for development of the first gyro-stabilized bomb site to go into Royal Air Force use. In 1940 he was transferred to the charge of the Research Section of Armaments Department concerned with bomb fuzes, bomb ballistics and the air-to-ground rocket weapon. In 1944, he was appointed head of the General Armaments Division and in 1946 head of the High-Temperature Materials Group in the Metallurgy Department. This group was the first (1947) in the United Kingdom to prepare titanium in a pure state and determine its properties. He has guided research on metal fatigue, properties of materials at high temperatures, the use of graphite for the hot parts of rockets and as a fuel container for nuclear reactors and the study of gas/solid reactions. His recent personal work has been concerned with the absorption of oxygen and nitrogen by hot titanium and the oxidation of gold. He is at present engaged on the reaction of rarified beams of nitrogen with solid surfaces and the required vacuum techniques.

DR. L. ESSEN, of the National Physical Laboratory, is internationally well known for his pioneer work on precise frequency standards for accurate measurements of frequency and time-interval. His first major contribution, the Essen quartz-ring oscillator, proved greatly superior to any previous frequency standard and to any mechanical clock for precise time-keeping in observatories and standard laboratories. More recently he was responsible for introducing the cæsium atomic beam resonator as a natural standard with a frequency stability and reproducibility of 1 part in 10^{10}. With his co-workers in Britain and in the United States he has used it to calibrate quartz clocks and monitor standard frequency transmissions, thereby establishing invaluable data on the performance of quartz clocks and different cæsium standards, the propagation of radio signals, variations of the Earth's rate of rotation and the value of the second of (ephemeris) time in terms of the cæsium standard. His determination in 1947 and 1950 of the velocity of propagation of microwave radiation revealed the fact, since confirmed by other observers in the microwave and optical regions, that the previously accepted value of the velocity of light was too low by 1 part in 20,000. His work as an experimental physicist has been nationally and internationally recognized by several awards and he was recently elected a Fellow of the Royal Society.

DR. C. TIMMS joined the scientific staff of the Metrology Division at the National Physical Laboratory in 1936. There he worked with Dr. G. A. Tomlinson, whose work on the standards of accuracy of gear-cutting machinery he has since continued and developed. This work played a large part in the marked improvement effected during the Second World War in the accuracy and reliability of naval and marine reduction gear drives. He is now a national authority on all aspects of gear metrology, and recently was invited to give the annual Viscount Nuffield Lecture to the Institution of Production Engineers on this subject. He has also carried out fundamental work in the measurement and assessment of surface finish, and has been largely responsible for the development of the branch of precision engineering measurement referred to as dynamic metrology. Dr. Timms became head of the Mechanisms, Metrology and Noise Control Division of the National Engineering Laboratory in 1950, and is now applying his knowledge and experience to improvement of the performance of machine tools, particularly in the application of precision circular diffraction gratings to measurement and correction of errors.

Senior Principal Scientific Officer

DR. R. N. COX of the Armament Research and Development Establishment has a wide background of research in experimental and theoretical fluid dynamics and is an expert in the field of hypersonics research.

Dr. R. G. Hopkinson is in charge of that part of the Building Research Station research programme which deals with the lighting of buildings; his particular research interest is the psycho-physics of illumination in relation to design for daylighting and artificial lighting. Good lighting has an important influence on building design, and Dr. Hopkinson's work has contributed greatly to the definition of the quality of lighting on a metrical basis.

Mr. D. G. King-Hele of the Guided Weapon Department, Royal Aircraft Establishment, is a versatile mathematician, whose work on satellite orbits is now internationally known.

Dr. D. McLean of the Metallurgy Division, National Physical Laboratory, is engaged on the investigation of dislocation structure in iron and iron alloys using the thin-film technique in the electron microscope.

Mr. E. C. Maskell of the Aerodynamics Department, Royal Aircraft Establishment, is an outstanding aerodynamics worker, particularly in the field of slender wings and jet flaps.

Mr. W. R. Piggott joined the Department of Scientific and Industrial Research in September 1939. After an early association with Sir Edward Appleton in certain special radio projects during the War, he joined the staff of the Radio Research Station and began his studies of the ionosphere for which he is so well known. Mr. Piggott has made an intensive investigation of the absorption of radio waves by the ionosphere, and pursued this and related topics in great detail during the International Geophysical Year: in the latter respect he has made valuable analyses of the observations made at Halley Bay by members of the Royal Society Expedition. His outstanding contribution to knowledge of the upper atmosphere is demonstrated by the numerous papers he has published, including a special report issued by the Department concerning the design of aerials to take the best advantage of the ionosphere for long-distance transmission.

Mr. L. P. Smith has been head of that section of the Meteorological Office which specializes in meeting the requirements of agriculture and horticulture since 1949. His success in this form of operational research has been noteworthy, and he has made many practical and easily assimilated contributions to good husbandry. His studies have included relationships between weather conditions and the spread of blights and diseases of plants and animals.

Dr. N. Uri joined the Research Establishment and Experimental Factory, Aberdeen, of the Ministry of Agriculture, Fisheries and Food in 1954 as a Senior Government Research Fellow, and was established as a principal scientific officer in 1956. The applied objectives of his work have been the prevention of deterioration by oxidative rancidity in food, particularly foods with low water content produced by freeze-drying. He has developed a theory on the effect of the polarity of the environment on trace metal catalysis in relation to the onset and speed of oxidative rancidity in fats. He has devised a new method of testing the stability of fats based on metal catalysis. He has also investigated the anti-oxidant properties of naturally occurring substances such as quercetin and the synthesis of new anti-oxidants.

Mr. W. Watt of the Metallurgy Department, Royal Aircraft Establishment, is a research worker in the field of high-temperature materials, especially ceramics and interstitial graphite.

Similar promotions have been made by:

(1) Agricultural Research Council: Senior Principal Scientific Officer

Dr. R. A. Beatty of the Unit of Animal Genetics, Edinburgh, is engaged on work in the common ground between genetics, embryology and reproductive physiology.

Dr. R. M. C. Dawson of the Biochemistry Department, Institute of Animal Physiology, Babraham, Cambridge, works on phospholipids and their metabolism.

Dr. R. F. Glascock is head of the Department of Radiobiochemistry at the National Institute for Research in Dairying, Reading, and has specialized in the application of the isotopic tracer technique to biochemical problems.

Dr. C. G. Johnson is a member of the Entomology Department of the Rothamsted Experimental Station, Harpenden, Herts. He is best known for his work on the aerial dispersal of insects.

(2) U.K. Atomic Energy Authority: Senior Principal Scientific Officer

Dr. T. E. Cranshaw has worked at Harwell for ten years. During the first eight years he worked on extensive air showers produced by high-energy cosmic rays. In 1954 he designed and built the apparatus at Culham Airfield which was the first to use the principle of covering a large area by a lattice of identical units, and with which many properties of air showers were investigated. In 1959, Dr. Cranshaw performed an experiment to measure a possible difference between the charges of the proton and the electron, which was shown to be smaller than one part in 10^{20}. More recently he has worked on the Mossbauer effect and its application to relativistic frequency shifts.

Mr. R. D. Lowde, during his thirteen years at the Atomic Energy Research Establishment, Harwell, has been in particular an exponent of neutron inelastic scattering techniques as a means of studying the solid state. He was the first to demonstrate the crystallographic phenomena that are the basis of the modern neutron-diffraction methods of investigating lattice vibrations and the dynamics of spin systems in magnetic substances. In recent years he has carried through a series of investigations in the theory and practice of these methods; the principal results have been the finding of effects due to 'spin waves' in metallic iron and due to magnetic 'critical phenomena' near the Curie temperature of the same material. In addition to his work in neutronics and magnetism, he has published researches in electronics and crystallography, and many papers on scientific instruments and methods.

(3) Nature Conservancy: Senior Principal Scientific Officer

Mr. M. V. Brian is officer in charge of the Furzebrook Research Station of the Nature Conservancy. He is well known for his contributions on social insect populations.

ASTRONOMY IN CANADA

THE April and June issues of the *Journal of the Royal Astronomical Society of Canada* (54, 79, 126; 1960) contain abstracts of reports read to the National Committee for Canada of the International Astronomical Union at a meeting held in Ottawa on November 27, 1959. These reports give a comprehensive view of research programmes at present being undertaken by Canadian institutions, and testify to the virility of Canadian astronomy.

The Dominion Observatory at Ottawa has made important contributions to positional astronomy, and this work is continuing. Two programmes are international in scope, being shared by meridian circle observers at fifteen observatories. These are the observation of 1503 *FK*3 supplementary stars, and a programme of 3754 *AGK*3 reference stars required for the photographic survey of improved positions and proper motions. Much work is done in connexion with the Time Service, including a co-operative effort to determine the relation between Universal Time and Ephemeris Time by direct lunar photography using a Markowitz Moon camera. Work at Ottawa is by no means confined to positional astronomy, and investigations are in progress on meteor astronomy and meteorites, solar physics and radio astronomy. An intensive search of air photographs of Canada has revealed a number of circular features, some of which may be the remains of meteorite craters. These are being studied by geophysical techniques, and in two cases rock cores have been drilled. It is considered highly probable that the craters at Hollerford, Ontario, and Deep Bay, Saskatchewan, are due to meteoritic impact. An 84-ft. radio telescope has been erected near Penticton, B.C., and installation of equipment is in progress. A programme on 21-cm. hydrogen radiation will soon be undertaken.

At Queen's University a modest programme of astronomical research has been started. Measurements on the scintillation of radio sources have produced results relating to the ionosphere, to rapid variations of the geomagnetic field, and to radio bursts from the Sun. Much radio equipment is in the course of construction, with the view of counting cosmic radio sources.

The David Dunlap Observatory of the University of Toronto is the leading Canadian institution with a large teaching schedule in astronomy. Recently there has been a marked increase in student enrolment in astronomy courses, and there are at present five students taking the full graduating option in astronomy, and six graduate students. Recently accepted theses have included calculations on the interior structure of sub-dwarfs, and photometric and spectrophotometric studies of visual binaries and the determination of their ages. Some work on stellar radial velocities is still in progress, although no new large programmes in this field have been laid out in recent years. The long-established work on globular clusters is continuing; about 4,500 photographs have been accumulated. Many cluster variable stars have been found and periods determined. A supplementary bibliography on individual clusters is being prepared and will shortly be published. Spectroscopic studies of hot carbon stars have been made, and it has been shown that the photo-ionization of neutral carbon is probably responsible for the opacity in the atmosphere of *R* Coronae Borealis. Investigations of galaxies have led to the identification of a large near-by cluster of galaxies in Canes Venatici, the recalculation of the absolute magnitudes of supernovæ and a redetermination of the Hubble constant of expansion of the universe. The radio astronomy programme at Toronto is varied in nature. It includes the measurement of absolute fluxes of the Sun and of selected sky points, and thermal sources are being developed to provide the calibration of the radiometer.

Several Divisions of the National Research Council are pursuing research on astronomical and related problems. Meteor work has been in progress for many years, and both visual and radio techniques are used. A photographic programme of meteor spectroscopy has been undertaken. Auroral and upper atmosphere research is also in progress. Work in radio astronomy includes regular observations of the total flux of radiation from the solar disk and the measurement of the absolute fluxes from bright radio sources. The existing radio astronomy site near Ottawa is now becoming unsatisfactory because of the large amount of interference arising from the expansion of the city. This has led to the establishment of a new quiet site for radio astronomy in Algonquin Provincial Park at Lake Traverse. Radio astronomical and geophysical investigations are also undertaken at several establishments of the Defence Research Board; most of this work is directed to studies of solar–terrestrial relations, the ionosphere and the aurora.

At the Dominion Astrophysical Observatory at Victoria many astrophysical investigations are in progress. Much time has been given to observations of eclipsing binaries in which one star is a cool supergiant and the companion a smaller hot star. The eclipses last many weeks, and observations at ingress and egress enable the atmospheres of the super-giant components to be studied. Five such binaries have been observed. The outer atmospheres of the supergiants contain local condensations of matter in violent mass motion, with velocities of 20 km./sec., or more, relative to the surface. The super-giants have radii, masses and luminosities of respectively 200, 20 and 3,000 times the corresponding solar quantities. Other cool stars are being observed and their spectra analysed by conventional methods. The hot *O*-type and Wolf-Rayet stars are being analysed. They also show large mass motions in their atmospheres; their atmospheres tend to be unstable, showing shells or halos, and it is likely that matter is ejected from these stars. Variable stars of the β Cephei type are being followed in detail, and cometary spectra are obtained whenever an opportunity offers itself. Much effort at Victoria is devoted to stellar motions. The radial velocities, absolute magnitudes and distances of many early-type stars are being obtained, both for individual stars and for members of clusters and associations. Several long-term programmes of radial velocity observations are also under way. New instruments under construction

include a fast grating spectrograph for the 72-in. telescope and a microphotometer recording directly the intensities of spectrum lines, and a Coudé spectrograph for the new 48-in. reflector is being designed.

An astronomical programme at the University of Western Ontario deals with the photometry and spectrophotometry of peculiar *A* stars. Observations are being made to determine which of these stars are variable and to study the nature of the light variability. The variations in their spectra are also being studied. A programme of laboratory work on molecular spectra has included the measurement of intensities in many astrophysically important bands, the photography of many bands and the determination of lifetimes of various states. An experimental study of the physical basis of the Hanbury Brown–Twiss intensity interferometer has been undertaken, and further work on this is in progress.

R. H. GARSTANG

THE ROCKEFELLER FOUNDATION

THE President's review from the Rockefeller Foundation annual report for 1959 covers a year of appropriations totalling more than 34 million dollars; 6,769,070 dollars went to programmes in the agricultural sciences, 12,300,071 dollars to those in medical and natural sciences and 4,049,350 dollars to those in the social sciences, while 291 Fellows from 39 countries began advanced study outside their own countries, and 339 other Fellows continued work through earlier awards, besides briefly dealing with the Foundation's operating programmes. Five main topics are discussed. The India International Centre, established at New Delhi in March 1959, with the support of 35 of the 38 universities in India, as well as Government support, is intended to provide a forum for fruitful cultural and intellectual exchange in a congenial setting where foreign and Indian leaders of thought may live together: it should serve as a place where scholars and scientists from Indian universities can meet and live with foreign cultural leaders and provide for more frequent contacts and exchange among the widely scattered Indian universities. A small publishing programme is also planned. Besides a grant of 710,200 dollars for building and selected expenses the Foundation has made allocations of 123,935 dollars for five years towards the operating expenses of the Centre.

To assist the New York University to meet the national needs for research and training defined by the Brooklyn Museum conference as necessary to ensure adequate standards of conservation of the nation's immense art heritage, the Rockefeller Foundation has provided 500,000 dollars towards the initial expenses of establishing a laboratory at the University's Institute of Fine Arts new quarters and, on a declining basis during ten years, towards certain operating expenses. The Foundation has already awarded fellowships to three members of the staff of the All-India Institute of Medical Sciences, in which, it is estimated, the Government of India will have invested the equivalent of more than 9 million dollars by March 1961, as well as six travel grants to members of the faculty and administrators since 1957, and appropriations totalling 300,000 dollars for teaching and research equipment. Still more recently, some 500,000 dollars have been released to meet foreign exchange requirements for the construction of the hospital clinic complex. At September 1, 1959, 50 postgraduate students were enrolled, of whom 40 (selected from 60 applicants) were preparing for teaching and research in the basic medical sciences, but only 13 out of 94 applicants could be accepted for postgraduate studies in the clinical fields. There are now 215 undergraduate students, and the first group will complete the basic course of study at the end of 1960.

Dean Rusk also directs attention to the unexpected dividends on virtually a world-wide basis which the Foundation's modest agricultural programme, began in Mexico in 1943, is now paying. When the project has been completed, descriptions will have been published of virtually all the races of maize in Latin America and seeds of all races will be in cold storage in three centres in Latin America with duplicate samples in storage in the United States. The seed of these maize races is available to corn breeders in all parts of the world, and the collections, which are serving as models for similar banks involving other crop plants, have been drawn upon extensively and have been widely used by maize geneticists in the United States in connexion with analyses of genetic systems of the maize plant, while classification of the living races of maize has permitted identification of many varieties in the prehistoric collection of maize from archæological sites. The Foundation has also joined forces with the Ford Foundation in establishing an international research institution to meet the urgent need for rice improvement, and, in co-operation also with the Government of the Philippines, an International Rice Research Institute is being planned on a site adjacent to the College of Agriculture of the University of the Philippines at Los Baños, towards which the Ford Foundation has appropriated 6·9 million dollars for construction and equipment and the Rockefeller 160,000 dollars for operating costs in 1960; the Institute should be in full operation by the end of 1961.

Besides this major advance, the operating programme in agriculture in 1959 saw the inauguration of the Inter-American Food Crop Improvement programme, and as a result in the Central American Corn Improvement Project there are now in the six countries concerned 23 full-time specialists instead of 5 part-time. Development of centres for fundamental research to increase knowledge of varietal improvement, soil fertility, cultural practices and the control of plant diseases is being encouraged. Besides referring to progress in the Mexican, Columbian, Indian and Chilean Agricultural Programmes, Dean Rusk emphasizes the virus research programme of the Foundation for which 1,194,640 dollars was appropriated in 1959, under which 110 agents known or suspected of being arthropod-borne are being investigated, 60 of which fall into four major groups, and very good evidence is available that 84 are transmitted by mosquitoes.

It is becoming increasingly evident that infection of man with an arthropod virus is usually accidental,

and the great problem in the temperate zones is to explain how the arthropod-borne viruses are maintained during the colder months when active insect vectors are scarce or absent. Recent investigations have shown that the young forms of several species of ticks parasitize birds, and it is thus possible that an infected tick could be transported over long distances by migrating birds. The extent and distribution of infections of man with the arthropod viruses can be determined by antibody survey work, and results of a study of residents of Athens provided evidence that the antibodies persist for at least 30 years following infection. Very valuable information has been obtained in extensive antibody surveys in the Caribbean region and a surprising finding of these immunity surveys is the wide distribution and high rate of infection with some of the recently discovered viruses.

BRITISH AGARICS AND BOLETI

A RECENT check-list of British agarics and boleti* is a logical development from the revised list (1948) of Pearson and Dennis, and embodies a number of suggestions that were put forward in that work. Many unjustified names have been dropped, and a number of new records for Britain have been added. The system used follows in the main that of Singer (1949), thus being narrower than that used in the earlier list. The work is not just the compilation that the title suggests; there are 536 pages in all, including the ancillary accounts, and the work has involved a critical study of actual material of almost three-quarters of the species listed.

Part 1*A* is a systematic list of genera that will be of assistance to foray secretaries and others who make lists of collections. Part 1*B* is the check-list proper—an alphabetical list of genera and species with synonyms, misdeterminations, authorities and references. Part 2 is a list of epithets of specific, varietal and formal rank that have been used in the past, and will be of value in translating old names in terms of the present list. Two papers published in association with the list (Part 3 by P. D. Orton, and Part 4 by F. B. Hora; *Trans. Brit. Mycol. Soc.*, 43, Pt. 2) set out a discussion of taxonomic principles which justifies the treatment given. The view is put forward that genera and species must be accurately fixed as soon as possible, but that as yet we have insufficient information on which to erect varieties and forms. Much useful advice to collectors and taxonomists is given here. Comments on the genera used in the list are given; there is a summary of changes in genera and their subdivisions; validations of new combinations and descriptions of new species are found; and there are critical notes and keys to help understand and use the system.

The work is a massive and comprehensive undertaking, and the authors are to be congratulated on their foresight in visualizing it and on their energy in carrying it to completion. It would be strange if all mycologists were to agree with the decisions taken here: there will no doubt be those who will complain at the changes. But in the long run the sooner a stable and workable system is reached the better. This work is a major step in this direction. D. PARK

* New Check List of British Agarics and Boleti. By R. W. G. Dennis, P. D. Orton and F. B. Hora. Supplement (1960) to *Transactions of the British Mycological Society*.

ENDEMIC AND EPIDEMIC GOITRE IN ITALY

THE almost legendary disease of epidemic goitre re-appeared in 1940 in the Italian Alps and Piedmont, attacking thousands of soldiers in the Province of Cuneo, and in subsequent years spreading to the civil population of the other provinces of Piedmont. It died out in this part of Italy in 1945, but continued to flare up in small foci in Lombardy, Liguria, Emilia, Tuscany and Venetia up to 1948 (*World Health Org.*, 14, No. 8; 1960).

The epidemic appeared in an area where endemic goitre had existed for a long time, raged for several successive years from spring to autumn, affected groups or individuals coming from outside the epidemic areas, and spread to regions from which endemic goitre had disappeared decades before.

The Italian epidemic of 1945–48 affected not only man but also dogs and pigs in some localities. At Monferrato it was shown that goitre appeared both in individuals drinking water from the mains and in those drawing their water from wells and tanks. Most of the goitres disappeared after some months, but some persisted and a few were still visible after some years. Administration of iodine brought no improvement and had no prophylactic effect.

Most of the authors who have studied the Piedmont epidemic admit a relationship between epidemic and endemic goitre. This relationship, however, has been questioned in the case of Tuscany, where epidemics without endemic goitre have been known. An analysis of recent data and of the data available on successive epidemics from the year 1700 have led A. Costa and M. Mortara to the conclusion that the two forms of goitre are diagnostically identical. They emphasize, in particular, the cerebral symptomatology that is clinically manifest to a greater or lesser extent in the two forms, and are inclined to the view that the central nervous system is affected, with elective, but not exclusive, localization in the autonomic centres in the diencephalon. Costa and Mortara consider that the cerebral phenomena manifested in acute epidemic goitre might provide some clues to the cerebral changes that result in the cretinism and deaf-muteness of endemic goitre. An important fact is that endemic cretinism is still to be found in its old sites—the Alps and the southern Apennines, including several surrounding hill and plain areas—but does not appear in association with endemic goitre in the south of Italy. Cretins are rare in the

new generations, and among them myxœdema and dwarfism due to thyroid insufficiency are less frequent.

War difficulties and the comparative lack of knowledge about the symptoms of thyroid dysfunction impeded research at the time of the Piedmont epidemics. Most of the tests were normal. Neutropenia was observed with lymphocystosis, and the blood iodine level was high. No serum antibody to human thyroglobulin was found.

In the Piedmont the uptake of radioiodine is generally greater than normal in the mountain, hill and plains foci of endemic goitre, and the iodine taken up is organically fixed in the thyroid. The excretion curve of radioiodine is slow in comparison with that in hyper-thyroidism. Thyroid clearance of iodine is high, kidney clearance is normal. Body growth, bone maturation, and sexual development in children are the same in endemic and non-endemic areas.

During the epidemics of goitre in the endemic area, the environmental factors traditionally considered to influence the disease—water, malnutrition, deficiencies, consanguinity, and shortage of iodine—all received attention. But none of these factors seems to be responsible for endemic goitre or for the Piedmont epidemics. The epidemic spread gave rise to the hypothesis of an infectious origin, with transmission by an intermediate host favoured by hot weather—for the epidemics occurred mainly in summer. In Umbria, the heavy consumption of *Brassicæ* containing goitrogenic factors, and in mountain areas a diet lacking in proteins and in some essential amino-acids were blamed. Endemic goitre is essentially rural in character, and Costa and Mortara consider that its frequent occurrence in localities where sheep are raised in stables may be more than a simple coincidence. The possible influence of radiation has not been ruled out, but radon has been sought in the atmosphere and in the water, and atmospheric radioactivity has been measured, without any relationship with endemic goitre being found. The iodine content of air and water and the excretion rate of iodine have shown no significant differences between endemic and non-endemic areas.

Goitre is not a static disease in Italy. It was widespread in the last century and the first decade of this century; then its prevalence decreased. It appears now that the descending curve has been arrested. Goitre has become more common in central and southern Italy, and has flared up in localities of northern Italy which had for some time appeared free from it. In certain areas the epidemics seem to have left endemic goitre in their train. The phenomenon of epidemic goitre in Italy has given rise to observations and research that are not paralleled in other countries; but so far its origin remains unexplained.

SOME CHARACTERISTICS OF GEOMAGNETIC MICROPULSATIONS (*Pc*)

By Prof. J. A. JACOBS and K. SINNO*

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A DETAILED investigation[1] has been carried out on geomagnetic micropulsations recorded by rapid-run magnetograms during the International Geophysical Year (1957–1958), from seventeen observatories as widely distributed geographically as possible (see Table 1). The results from these seventeen observatories were recorded photographically, not only on rapid-run magnetograms with a recording speed of 20 mm. per 5 min., but also on standard speed magnetograms with a recording speed of 20 mm. per hr.

Micropulsations (*Pc*) are defined as continuous pulsations usually appearing on the daylight side of the Earth, lasting for many hours with periods in the range of 10–60 sec., and amplitudes of the order of a few tenths of a gamma in middle latitudes. However, if the evidence of all investigators over a wide area is considered, it becomes apparent that these micropulsations do not correspond to a single wave-band but to two wave-bands, the first a shorter-period micropulsation (about 15–30 sec.) and the second a longer-period micropulsation (about 30–90 sec.). Fig. 1 shows the spectrum of micropulsations which have been investigated by several workers from stations all over the world, and clearly illustrates the division into these two different wave-bands.

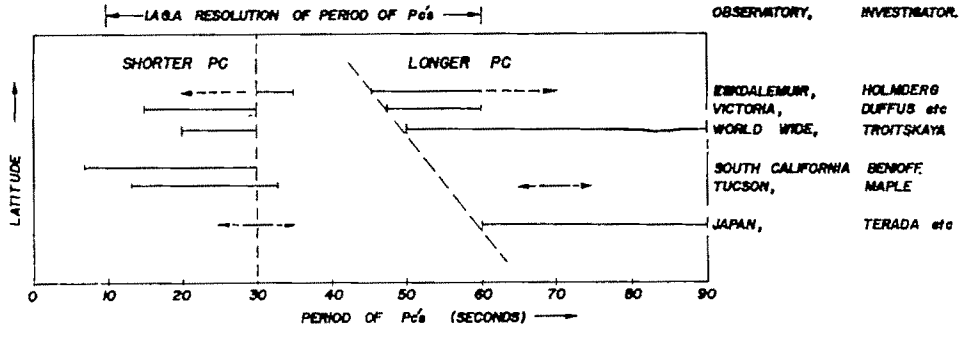

Fig. 1. Latitudinal distribution of spectrum of micropulsations (*Pc*) with periods greater than 10 sec. as reported by different investigators from data shown on the right-hand side

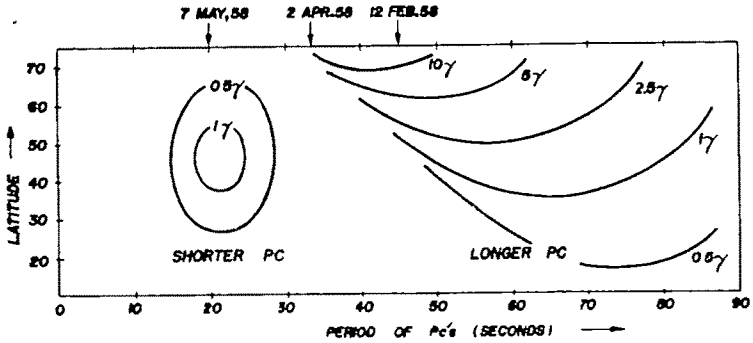

Fig. 2. Equi-amplitude contours of micropulsations (*Pc*), derived from Fig. 1

Typical of longer-period micropulsations were those observed on February 12 and April 2, 1958, which have periods of 33 and 45 sec., respectively. These examples have coherent, synchronous wave-forms over a wide area. It is also worth noting that micropulsations of this type often have amplitudes up to ten gammas or more in polar regions.

A pulsation appeared on May 7, 1958, with a period of about 20 sec. and with maximum amplitude at about lat. 50°. Many similar examples (such as those which occurred on February 8 and May 28, 1958) have been found: they all have in common comparatively short periods (from about 15 sec. to 30 sec.). Those shorter-period micropulsations show different periods at different latitudes, although it is not possible to be definite on this point since the speed of the rapid-run recordings is too slow for any fine resolution.

Combining the results of previous investigations with the distribution in latitude of the amplitude of micropulsations which has been derived in the present analysis, equi-amplitude contours can be drawn as shown in Fig. 2. The different distribution in latitude of the amplitude of the two wave-bands of micropulsations and the geographical variation of period of the shorter micropulsations lead to the conclusion that the longer and shorter period micropulsations are probably caused by hydromagnetic waves in the upper and lower parts of the outer atmosphere respectively.

Between about 2300 and 2400 U.T. on February 12, a series of very intense (longer-period) micropulsations were observed. They continued for about 1 hr. and appear as thick traces on ordinary magnetograms because of the slow paper speed (see Fig. 3). Of special interest are the pre- and post-oscillations of this particular micropulsation. The figure shows clearly the intense pulsation of about 6-min. period which prevailed during the previous 2 hr. and after the micropulsation. Usually this type of pulsation is observed in polar regions and is frequently associated with micropulsations. They are nearly synchronous over a very wide area, from the Arctic to the Antarctic, and on occasions appear in equatorial regions as well. Moreover, the polarization is nearly linear at each station. This type of pulsation has been designated a long-period continuous pulsation (*LPc*).

Sometimes beating oscillations of micropulsations, which appear mainly in middle latitudes, occur simultaneously with these linear pulsations in polar regions. The periods of both the beating micropulsations (*Pc*) and the pulsations (*LPc*) are about the same, namely, 3–7 min. (ref. 2). Moreover, the ideal equivalent overhead current-systems which have been drawn for the examples on February 12 are

Table 1. STATIONS SUPPLYING OBSERVATIONS USED IN THIS REPORT

Station	Abbreviation	Geographical Lat.	Geographical Long.	Geomagnetic Lat.	Geomagnetic Long.
Point Barrow	*PB*	71° 18′ N.	156° 46′ W.	68 6° N.	241 0° E
College	*Co*	64° 51′ N.	147° 50′ W.	64·7° N.	256 5° E.
Big Delta	*BD*	64° 09′ N.	145° 51′ W.	64·4° N.	259 0° E.
Healy	*Hy*	63° 51′ N.	149° 00′ W.	63·6° N.	256 5° E
Sitka	*St*	57° 08′ N.	135° 20′ W.	60 0° N.	275·4° E.
Lovo	*Lo*	59° 21′ N.	17° 50′ E.	58·2° N.	105 8° E.
Fredericksburg	*Fr*	38° 12′ N.	77° 22′ W.	49 6° N.	349·9° E
Tucson	*Tu*	32° 14′ N.	110° 57′ W.	40 4° N.	312 1° E.
Kakioka	*Ka*	36° 14′ N.	140° 11′ E.	26·0° N.	206 0° E.
Honolulu	*Ho*	21° 18′ N.	158° 08′ W.	21 0° N.	266·4° E.
Guam	*Gu*	13° 27′ N.	144° 45′ E.	3 9° N.	212 8° E
Koror	*Kr*	07° 16′ N.	134° 32′ E.	3 3° S.	203 5° E.
Apia	*Ap*	13° 48′ S.	171° 46′ W.	16 0° S.	260·2° E.
Hermanus	*Hr*	34° 24′ S.	19° 13′ E.	33 3° S.	80 3° E.
Byrd Station	*By*	79° 59′ S.	120° 01′ W.	70 6° S.	336 0° E.
Little America	*LA*	78° 18′ S.	162° 10′ W.	74 0° S.	312·0° E.
Wilkes	*Wk*	66° 15′ S.	110° 31′ E.	77 8° S.	170 0° E.

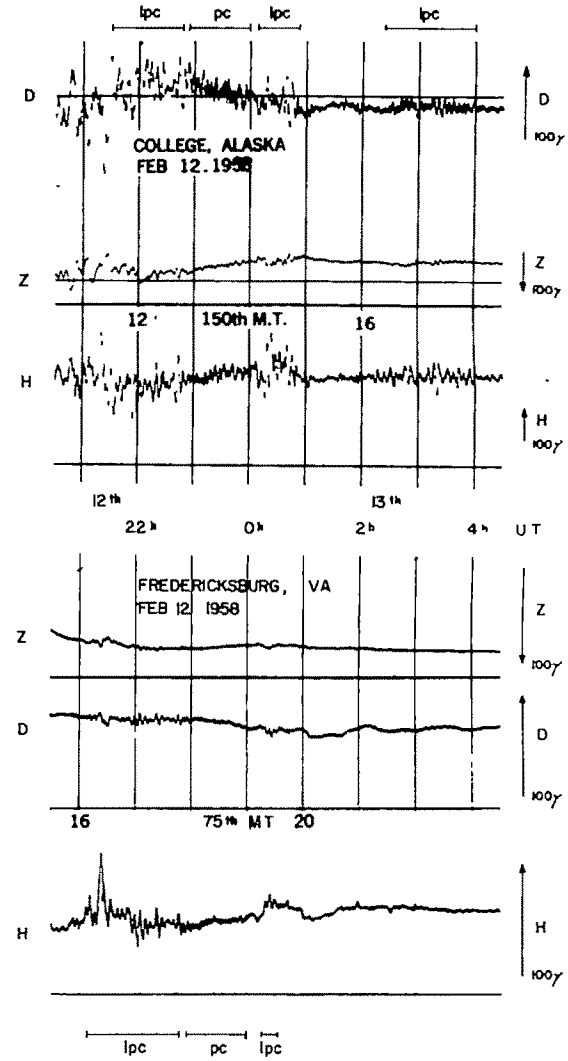

Fig 3. Examples of micropulsations (*Pc*) and long-period continuous pulsations (*LPc*). Traces are from ordinary magnetograms at College and Fredericksburg on February 12–13, 1958

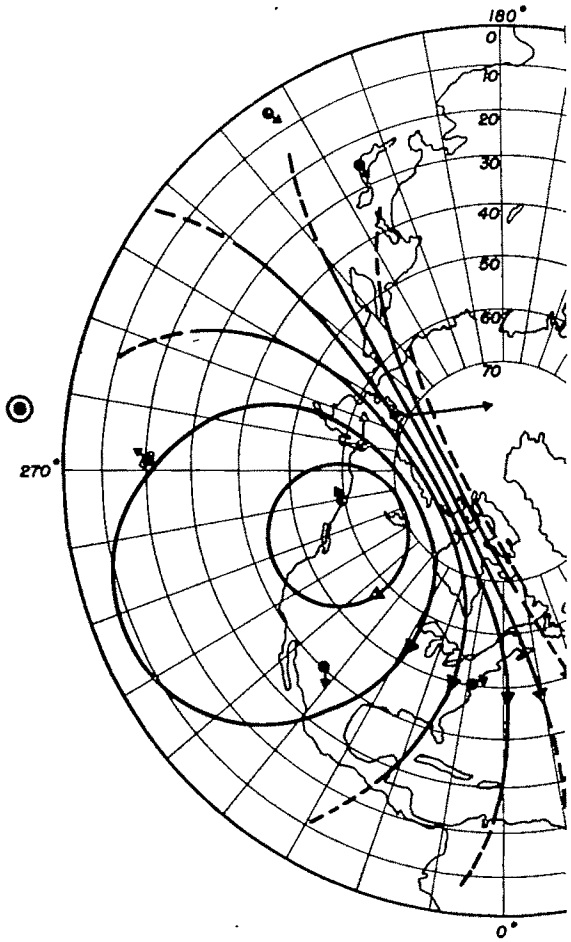

Fig. 4. Equivalent overhead current system for micropulsations (*Pc*) at 2345–2350 U.T. February 12, 1958. Electric current between successive lines is 5×10^3 amp.

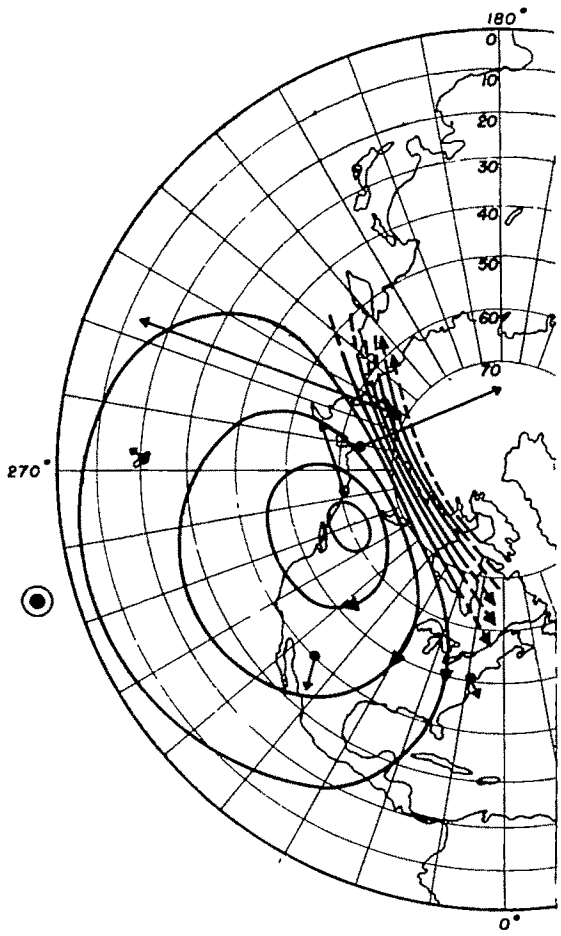

Fig. 5. Equivalent overhead current system for long-period continuous pulsations (*LPc*) at 2215–2230 U.T. February 12, 1958. Electric current between successive lines is 5×10^4 amp.

strikingly similar for both except in the polar region (see Figs. 4 and 5). The close relations between them indicate that both pulsations have a common source, probably outer atmospheric oscillations.

We wish to acknowledge the sources of data from the various geomagnetic stations and the International Geophysical Year World Data Centre *A*. The research was supported by the Geophysics Research Directorate, Air Force Cambridge Research Center.

* On leave of absence from the Radio Research Laboratories, Kokubunji, Tokyo.

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SMALL-ANGLE X-RAY SCATTERING BY PILE-IRRADIATED GRAPHITE

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PREVIOUS attempts to study the nature of radiation damage in graphite by small-angle X-ray diffraction are reported as being unsuccessful[1]. This was because the scattering due to radiation-induced defects was small in comparison with that due to defects already present before irradiation. The purpose of the present communication is to report that small-angle scattering of intensity much greater than that found with unirradiated graphite has been observed with specimens of polycrystalline artificial graphite of reactor grade heavily irradiated (*Dido* doses 5×10^{20}–17×10^{20} n.v.t. measured thermal flux) at temperatures in the vicinity of 150° C.

The specimens were in the form of solid half-cylinders and were examined in reflexion using a Philips 1050 diffractometer and nickel-filtered copper $K\alpha$ radiation. With $\frac{1}{6}$° divergence slits the minimum scattering angle (2θ) at which observations could be made was 3°. All the measurements were made under identical conditions. The variation of scattered intensity with 2θ is shown in Fig. 1 for three irradiated specimens and a typical unirradiated specimen. A fourth specimen, irradiated at 300° C., showed no

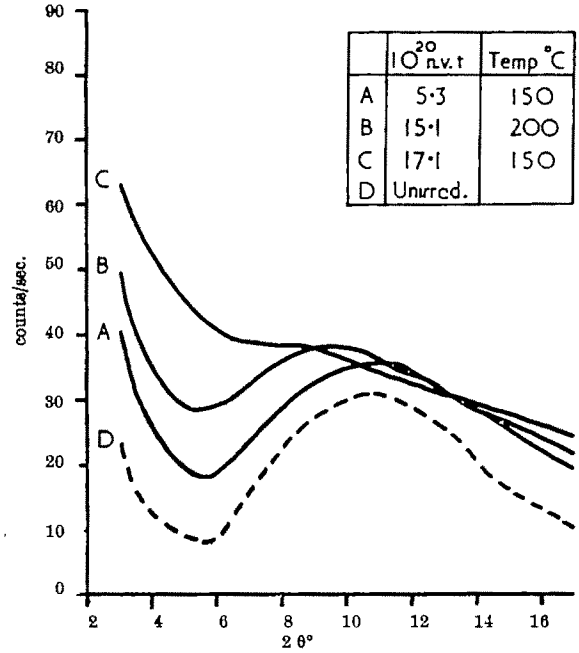

Fig. 1. Low-angle X-ray scattering from irradiated graphite

increase in small-angle scattering within the observable range of 2θ.

The component of the intensity attributable to radiation damage was obtained by subtracting from each irradiated intensity distribution the intensity distribution of an unirradiated specimen cut from the same block of graphite in the same orientation relative to the direction of extrusion. This procedure compensates for slight block-to-block variations in the pre-irradiation small-angle scattering and also for variations in the degree of preferred orientation. The latter is manifested as differences in the height of the diffuse peak in the vicinity of $2\theta = 11°$ which is due to the short wave-length 'white' X-rays reflected by the 0002 graphite lattice planes. Radiation

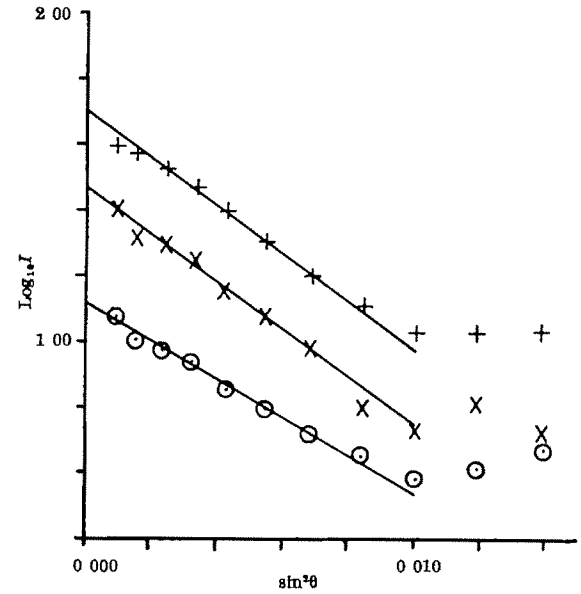

Fig. 2. Slope analysis (Table 1 · A, ○; B, ×; C, +)

Table 1

Specimen	Dose (n.v.t. × 10^{20})	Temperature of irradiation (°C.)	$\bar{R}$ (Å.)	R_{disk} (Å.)	N (per cent)	N (per cent) / (n.v.t. × 10^{20})
A	5 3	150	2 46	3 5	4 3	8
C	17 1	150	2 77	3 9	13 2	7·7
B	15 1	200	2·73	3 9	8·9	5 9

damage results in broadening of the crystalline X-ray reflexions, but in the case of this 'white' radiation 0002 peak the change is very slight and introduces a negligible error into the small-angle scattering curves derived by the subtraction procedure. However, radiation broadening of the copper $K\alpha$0002 peak in the vicinity of 25° results in major differences which extend as low as $2\theta = 11°$, and as the subtraction procedure cannot compensate for this the curves are in error above this value of 2θ.

The slope-analysis method was applied to the scattering distributions thus derived without making specific corrections for vertical divergence[2], and it can be seen from Fig. 2 that the plots of log I versus $\sin^2\theta$ are good approximations to straight lines up to $\sin^2\theta = 0\ 009$ ($2\theta = 11°$). The slopes of these plots give the average 'radius of gyration' $\bar{R}$ of the scattering centres. Values of $\bar{R}$ are listed in Table 1 together with values of $R_{disk} = \bar{R}\sqrt{2}$. R_{disk} is the average radius of the scattering centres if they are assumed to be disks of a thickness much less than their diameter. The intensity distributions are not sufficiently accurate to give any reliable indication of the shape of the scattering centres; but it is likely that in irradiated graphite they are disk-like aggregates of interstitial atoms, sandwiched between the graphite layers and formed by clustering of the atoms displaced by neutron bombardment, as already suggested[1].

Interpretation of the present results in terms of this picture presupposes that the observed scattering is entirely due to the clusters of interstitials, and neglects any contribution from the vacancies which must exist in comparable numbers. This is justifiable in that single interstitials probably have a far greater degree of mobility than the vacancies at the temperature of irradiation, and are therefore more likely to form clusters under the influence of the strain fields set up in the adjacent graphite layers. Such clusters of ten or more atoms would have a small-angle scattering power much larger than that of the more numerous single vacancies since the small-angle scattering power of an individual centre is proportional to the square of the number of electrons it contains.

The log I – $\sin^2\theta$ graphs show little decrease in slope with increase in $\sin^2\theta$, a feature which normally indicates that the scattering centres are all much the same size. In the present case one would expect a range of sizes, but perhaps there is some feature of the mechanism of formation which leads to one size being more probable than any other under given conditions. This size as characterized by R_{disk} increases with dose.

The supposition that the scattering centres are disks of interstitials enables an estimate of their concentration to be made from the absolute magnitude of the total intensity scattered by them, which in the present case was measured by comparison with the integrated intensity of the 002 reflexion of finely powdered rock-salt. The concentration of interstitials, expressed as a fraction N of the number of atoms per unit volume in the perfect graphite lattice, is

related to the total scattered intensity $I_{tot.}$ by an equation of the form :

$$I_{tot.} = KN\alpha R_{disk}$$

where R_{disk} is the value of the radius given by the slope analysis, α is the number of interstitials/unit area of disk and K is a constant in which are combined various physical and instrumental factors. The value given to α was $0 \cdot 2$ interstitial/Å.^{2}, which corresponds to occupation of one in every two interstitial sites within the periphery of a disk, that is, an average distance of $2 \cdot 44$ Å. between adjacent interstitials. If a higher density is assumed, for example, occupation of every site, the interstitials would be $1 \cdot 45$ Å. apart and would have to be graphitized to a high degree.

The values of N are given in Table 1 together with the number of interstitials/10^{20} n.v.t., which agrees closely with estimates made by other experimental and theoretical methods[3]. It is perhaps noteworthy that the specimen irradiated at 200° C. shows a lower value of N/n.v.t. than those irradiated at 150° C., a point which it is intended to verify in further experiments.

So far it has been tacitly assumed that the scattering observed here is true small-angle scattering. In several instances supposed small-angle scattering from inhomogeneities in a crystal lattice has since been shown to be multiple Bragg reflexion from distorted lattice planes[4]. Though it is difficult to perform quantitative calculations on this type of multiple reflexion it seems that the intensities observed in the present experiments are at least two orders of magnitude larger than the maximum possible by multiple reflexion. Further, neutron-diffraction experiments[5] in which the wave-length employed was such as to place all reflexions from lattice planes beyond the cut-off, that is, $\sin\theta > 1$, definitely indicated the presence of point defects in graphite irradiated to a level comparable with the present specimens. Owing to the difficulties inherent in neutron diffraction, these experiments did not show whether or not the defects were clustered, but the number of defects detected agrees reasonably well with the present ones. Thus it can be argued that neutron diffraction shows that point defects occur in irradiated graphite in sufficient concentration to cause true small-angle X-ray scattering provided they cluster in a manner similar to that postulated here. The observed small-angle scattering interpreted in this way gives a reasonably self-consistent picture which is also consistent with theoretical calculations and other types of experiment.

This work will be continued, and it is hoped that in future the use of plane-polarized X-rays in which the plane of polarization can be rotated[6] will permit an experimental distinction to be drawn between true small-angle scattering and multiple Bragg reflexion.

I am indebted to the Head of the United Kingdom Atomic Energy Authority's Culcheth Laboratories where this work was carried out, and to the Director of the Central Electricity Generating Board Berkeley Nuclear Laboratories, for permission to publish this article. I also thank Drs. A. L. Sutton and G. K. Williamson for helpful discussions and advice.

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SUCROSE CRYSTALS

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Layer Growth

IN an earlier article[1], I was able to report having found that sucrose crystals grew layer-wise, just as Drs. Bunn and Emmett had previously described the growth mechanism of crystals of many salts. I am now able to report that a sucrose crystal immersed in a very slightly sub-saturated solution dissolves by a receding layer mechanism. In a growth cell under the light microscope, one may vary the degree of saturation of the mother syrup by temperature control, and by this means produce advancing or receding layer fronts at will. If a crystal is immersed in very slightly sub-saturated syrup, faint etch pits form first. Later, as the natural gradient of exhaustion of the contact layer becomes established, the receding layers become visible, first near edges and corners, then spreading over the whole crystal surface, and even in the etch pits. I have been able to record this, both by photo-micrography and by ciné-micrography.

Drs. Dunning and Albon[2] have reported spiral growth in sucrose crystals nucleated and grown under laboratory conditions, but have not hitherto been able to observe them in commercially grown crystals (private communication). Having now observed a large number of growing and dissolving crystals under the microscope, my impression is that certainly in crystals which have been grown under the practical conditions of varying supersaturation and occasional sub-saturation the layer fronts are so strongly developed as to continue to efface spirals by overgrowth, just as they overgrow pockets of solution in making fluid inclusions. I feel that spirals and layers should be regarded as two distinct, and not necessarily connected, mechanisms by which crystal growth may take place. The latter become more strongly developed with increasing crystal size, also after partial dissolution or mechanical damage. It is becoming increasingly evident that, even on an apparently dry sucrose crystal, the surface should be regarded as in a state of dynamic, not static, equilibrium.

Thin Films

Crystallization in thin films (up to a hundred or so microns in thickness) exhibits different phenomena, according to the nature of the bounding media. These may conveniently be grouped in three cate-

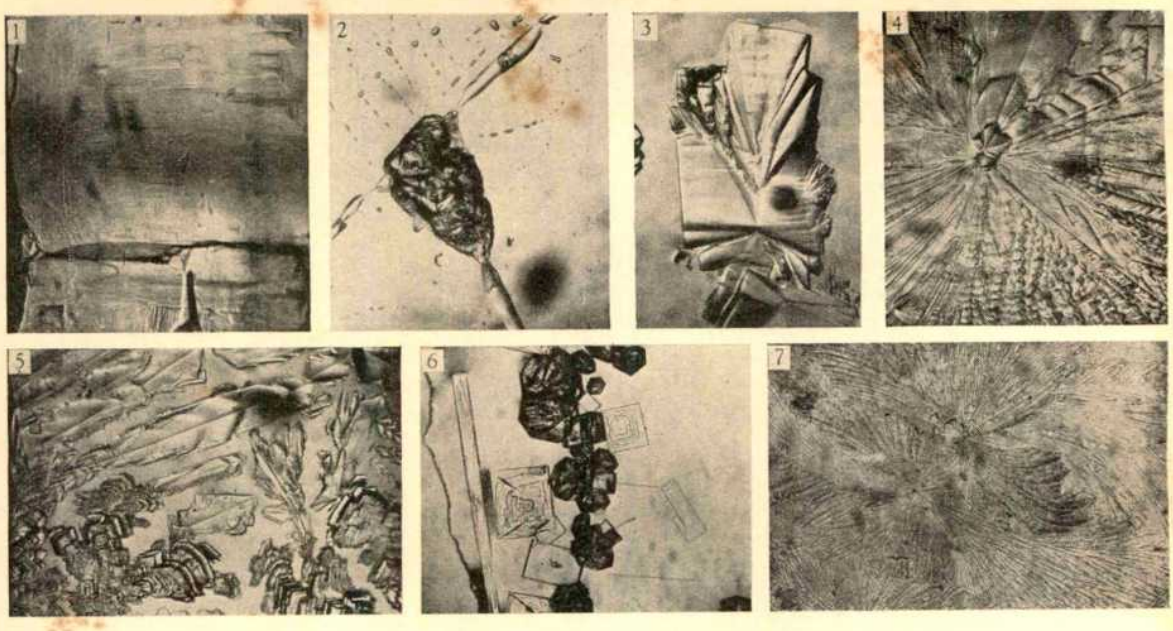

Fig. 1. Mild dissolution : etch pits and receding layers
Fig. 2. Drainage system at 3·5 supersaturation. Mass/nucleation hazard, also how spherulitic crystals commence exploring growth
Fig. 3. Disordered crystal at 2·4 supersaturation ; note spherulitic eruptions
Fig. 4. Radialite from film, showing part-rhythmic growth
Fig. 5. An example of rhythmic dendritic exploring growth
Fig. 6. Sodium chloride grown in vapour-pressure controlled film ; whisker, acicular, tabular, etc., forms
Fig. 7. Radialitic carpet of sucrose from film only one or two microns thick. Note curvature

gories ; (*a*) glass or plastic (relatively inert) ; thus glass/syrup/glass ; (*b*) atmosphere with controlled humidity (causing migration of water molecules to or from the solution) ; thus glass/syrup/air ; (*c*) sucrose crystal (offering or receiving sucrose molecules to or from the solution) ; thus crystal/syrup/air.

(*a*) The first system has very wide application to problems of form, rate of growth, etc. By adopting techniques on the lines of microbiological work one may avoid intrusion of external nuclei. By warming a supersaturated solution to the temperature of saturation before using, one may seed a film of the syrup, by means of a needle dipped in specially prepared nuclei, without producing fresh nucleation by mechanical hazard. Probably the most challenging demonstration by this system is that of the greatly varying rate of growth of different nuclei when introduced into the same medium. By seeding with two needles carrying different types of nuclei, and with one drawing a horizontal and the other a vertical line, then 'incubating', any difference in the natural rate of growth of the two types of nuclei should be revealed. By this means it appeared that particles of pulverized crystal at first grew more rapidly than whole seed crystals, until the regular crystal form had taken shape. On extending the growth period, however, there appeared far more difference in size between neighbouring crystals of the same origin than appeared overall between those from the different origins.

Another application is to the study of the effect of various impurities on crystal form, for example, increasing proportion of raffinose, which produces first a lengthening in the axis ratio, then striking wedge-shaped forms.

Still another application is to study whether crystals can display any form of 'inheritance'. Can a seed crystal, produced in circumstances favouring a characteristic form, carry forward the special feature if transferred to a different medium ? I have tested this by transferring crushed portions of the spherulitic form produced at high supersaturation to solutions of low supersaturation. The broken edges were repaired, but growth was so slow that normal nuclei, developed in the new medium, rapidly outgrew the spherulitic fragments. An example of internal rather than external specialized form is that reported by Drs. Dunning and Albon[2], who found spiral growth on crystals nucleated and grown in sucrose solution containing up to 1 per cent of dextrose to have a highly significant heightening of the step as compared with that in pure sucrose solution, hence probably an increased growth-rate. I have not been able by the above means to satisfy myself with evidence of effective 'inheritance' in this case.

By applying non-sucrose components to one exposed edge of an '*a*' type film, after seeding, diffusion may reveal the effect of the component thus introduced on the resulting crystallization, as a prelude to a more controlled investigation.

(*b*) The glass/syrup/air system offers a remarkable facility for attaining and maintaining any desired degree of supersaturation without the handicap of virtually uncontrollable nucleation in the higher range. It also renders possible the production of controlled crystallization in films of thickness down to the millimicron range.

To eliminate rogue nucleation, the solution should be sub-saturated when placed on the slide. Extremely thin films may be obtained by dilution and drainage. The prepared slide is placed in a desiccator, controlled by means of moist salts, glycerine, etc. If the desiccator is suitably constructed, both observation and photo-micrography may be made *in situ*.

Both the natural hazard of nucleation and the resulting crystal form are very strikingly affected by

the degree of supersaturation. With sucrose, nucleation is maximal at about 3 supersaturation, at which stage perhaps one nucleus may form per 24-hr. at 20° C. in a 0·3 gm. film. At less than 1·5 and greater than 5·0 supersaturation, weeks may elapse without a single nucleus forming naturally. Supersaturation has been expressed in the form recommended by the International Commission for Uniform Methods of Sugar Analysis, 1958, namely:

$$\frac{\text{gm. sucrose/100 gm. water at temperature } t}{\text{gm. sucrose/100 gm. water in saturated solution at temperature } t}$$

Regarding the influence of supersaturation on crystal form, at the 1·1 level normal to industrial production, euhedral crystals form. At 1·5 signs of disorder appear, this increasing as supersaturation increases. At 2·5 supersaturation spherulitic multi-crystals appear, together with some abnormal mono-crystals, which by this stage show occasional eruptions of multi-crystal segments, frequently at rhythmic spacing on the mono-crystal. By 4·0 supersaturation practically all nuclei are spherulitic. When grown in a thin film the spherulitic nucleus develops two-dimensionally, that is, 'radialitically', this proving most illuminating on details of structure. Normally, adjoining ray crystals are in harmony of orientation, as with a fan, but the full 360° may include several such groupings, each of different orientation. I have recorded layer growth, also hour-glass and veil inclusions on radialite crystals, just as with normal mono-crystal forms[3]. My impression is that all these phenomena, culminating in spherulitic nucleation, are the outcome of the build-up of the exothermic heat of crystallization even to the point of local fusion. Mosaic may result from one form of the above disorder.

If the film has been gelled with agar or gelatine the spherulitic nucleation occurs even as low as supersaturation 1·6, and two easily recognized variant forms ensue. With agar, sharply contoured layer growth scales abound; whereas with gelatine, multitudes of gentler curves take the place of the more normal rectilinear radialites.

If crystals are allowed to grow in a thin layer of solution in a covered Petrie dish exposed to atmosphere of 50–60 relative humidity, the upper surfaces of the crystals become exposed. Surface forces cause solution to be drawn up and continue crystallization, until the residual film is so thin that this flow ceases. Alternatively, one may commence with a film of similar thinness and permit nucleation therein. In either case, the formed crystal then develops an 'exploring growth'—reminiscent of *Amoeba*—which is truly delightful in its rhythmic beauty. Familiar contour angles may be recognized, repeating in nodal and anti-nodal intensity, strongly reminiscent of Liesegang precipitation. A little reflexion on the manner of growth will indicate that each complete pattern, though apparently so complex, is yet as truly a mono-crystal as any simple euhedral crystal. These truly dendritic forms normally develop rectilineally, but sometimes exhibit curvilinearity, developed by faults, to permit growth to enter a zone richer for growth. This exploring growth can proceed in films so thin as to render crystals invisible in the light microscope, and can develop crystals with truly dry surface areas. It is extremely slow, continuing for weeks.

(c) The crystal/syrup/air system is normally met in industrial application, and will be dealt with more fully elsewhere. It is pertinent to report here that the remarkable ability of syrup to dry almost to the amorphous and extremely slowly crystallizing form, contributes considerably to problems of bulk storage. Probably all the crystal forms described above may be formed during the granulation or drying of commercial sugar.

Though my work has been mainly with sugar, the system of crystallizing in vapour-pressure controlled films, will obviously have wide applications. Sodium chloride so treated has yielded encouraging results. Exploring growth is shown, and whisker growth appears to occur sub-surface, since I have photographed whiskers growing under other crystals. The subsequent development from whisker to needle, also of strikingly clear tabular crystals, is easy to follow and is being filmed, as are many of the sucrose phenomena described herein.

For those interested in this work, a wide and rapidly increasing range of photomicrographs is now available of the diverse forms of sucrose crystallizing under this vapour pressure control.

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[2] *Nature*, 180, 1248 (1957).
[3] *Nature*, 182, 715 (1958).

PROTEINS INDUCED IN PLASMA BY ŒSTROGENS

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THE fact that at least two—and probably several—of the proteins of egg yolk are synthesized in the liver of the hen and transferred via the blood plasma to the ovary (where they are deposited as granules in the ovum) is well established[1–3]. However, recent articles by Prof. R. H. Common and Chi-Ching Mok[4] and Joubert and Cook[5], convey the impression that much of the data available in the literature, some of it our own[1,3,7–9], has failed to come to the attention of workers interested in the elucidation of the proteins involved in avian reproduction. Further, because of the limitations of techniques employed in any single laboratory, much confusion exists with respect to the nomenclature, chemical constitution and physical orientation of these proteins. We have therefore prepared the following critical analysis.

First, the administration of œstrogen to the hen, pullet or rooster results in the amplified appearance of at least three major protein components in the

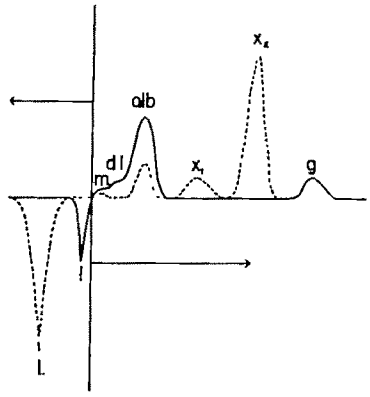

Fig. 1. Composite ultracentrifuge patterns from plasmas of control and œstrogenized birds. Areas under the peaks are equivalent to concentration. Negative peaks are due to the high proportions of lipid in such fractions. Areas defined by the solid line indicate control values. Those defined by the broken line indicate values for œstrogenized bird. *l*, Light lipoprotein; *m*, mucoprotein; *d.l.*, dense lipoprotein; *alb.*, albumin; X_1, X_1-phosphoprotein; *g*, globulin; and X_2, X_2-lipoglycoprotein

plasma; there are the two mentioned by Common and Chi-Ching Mok (phosvitin and lipovitellin) and also a light lipoprotein varying in flotation-rate upwards from S_f 15 (ref. 9). (We have chosen not to apply a generic name to this protein, and have used the term X_1-phosphoprotein in place of phosvitin and the term X_2-lipoglycoprotein in place of lipovitellin, for several reasons that will become evident.)

The appearance of $X_1 - X_2$ in the serum is not the only change in the plasma of œstrogenized birds. In addition, there are absolute decreases in albumin, globulins, normal light lipoproteins (Sf 0–15), dense lipoproteins ($-S$ 0–10), and mucoproteins (ref. 9 and unpublished work). The severity of the decreases is proportional to the amount of œstrogen administered and to the increases in components induced by œstrogen. A schematic diagram of these changes as they might appear in a composite ultracentrifuge pattern of chicken plasma is presented in Fig. 1.

Secondly, the implication must be questioned that phosvitin, lipovitellin and a component referred to as γ-livetin[4] are present in the plasmas in the form of complexes with each other that are similar to the complexes formed when egg yolk or the serums of œstrogenized birds are greatly diluted with distilled water[1]. Of course, in the native egg yolk of the hen, the X_1 and X_2 proteins (plus lighter lipoproteins and a relatively small amount of nucleoprotein) are present in the form of giant complexes termed granules. (Such granules comprise approximately one-fifth of the total volume of the egg yolk, and on isolation and dissolution with 10 per cent sodium chloride have been demonstrated to contain all the X_1 and X_2 in egg yolk[3].) However, since the X_1 present in yolk granules retains a high percentage of bound calcium, the granule complex must be very different from the complex which forms when either plasma X_1 and X_2 or egg yolk X_1 and X_2 are diluted with distilled water. In these latter cases, the complex appears to result from the removal of naturally bound calcium from the X_1 phosphoprotein (this phosphoprotein contains 10 times more calcium per unit weight than does casein of milk) exposing numerous negative charges on the X_1 molecule which readily combine with the positive charges made available on the phospholipid portion of the X_2 protein. The amount of calcium associated with serum X_1 in the native state is sufficient to neutralize the negative charges of the phosphoserine in the molecule so that no complex is formed; and, indeed, phosphorus and calcium analysis of the X_2 (lipovitellin) component of serum show it to be uncontaminated with X_1. As for γ-livetin, its existence has never been demonstrated in plasma or serum.

The term γ-livetin was introduced by Joubert and Cook[5] to account for a protein component of egg yolk that, when resolved in the ultracentrifuge, trailed behind a fraction which they termed a complex of γ-livetin, phosvitin and lipovitellin (Fig. 2).

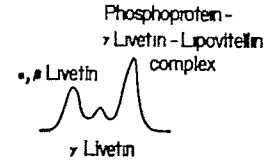

Fig. 2. Schematic sketch of egg yolk ultracentrifuge patterns as obtained and interpreted by Joubert and Cook (ref. 6)

These workers claimed that they were unable to resolve γ-livetin in quantity from this so-called complex in 5 per cent sodium chloride, but that it could be resolved in larger amounts in the presence of phosphate buffer (pH 7·6), barbiturate buffer (pH 9·0) or glycine buffer (pH 10·4). We have discovered that yolk X_2 lipoglycoprotein splits into smaller molecules when placed in an alkaline medium and that X_1 phosphoprotein tends to conjugate (thus sedimenting faster) in the same medium. Thus, the γ-livetin that Joubert and Cook observed was probably the alkaline breakdown product of X_2 which, according to our experience, shows a somewhat similar sedimentation-rate (approximately S 4–5) to that of X_1, in 10 per cent sodium chloride.

In work carried out at about the same time[3], we had examined the ultracentrifuge patterns of egg yolk proteins in 10 per cent sodium chloride solutions and were not able to resolve as much of the so-called γ-livetin as Joubert and Cook did in their buffered experiments. Furthermore, because of previous experience with yolk proteins of the frog[7], in which case we had isolated the trailing component by ultracentrifugation and characterized it, we had suspected that the so-called γ-livetin was actually the natural form of the phosphoprotein from which phosvitin is derived. Subsequent centrifugal isolation of this fraction in the partition cell for the preparatory ultracentrifuge and chemical characterization revealed it to be nearly pure phosphoprotein (X_1), containing approximately 10 per cent phosphorus[1] and 50 per cent serine (unpublished work), of which almost 50 per cent was phosphoserine. (Our best sample of phosvitin prepared by the method of Joubert and Cook[5] gave this same amino-acid analysis.) Furthermore, protein, calcium, phosphorus and lipid analysis of the remaining X_1 plus X_2 lipoglycoprotein fraction (see Fig. 3) revealed that no significant amount of phosphoprotein was actually complexed with the X_2 lipoglycoprotein (lipovitellin) in 10 per cent sodium chloride, nor could there have been any large amount of 'heavy X_1' present, having the same sedimentation-rate as X_2. (We use the term 'heavy X_1' to describe an, as yet, theoretical molecule having twice the molecular

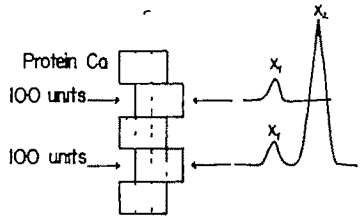

Fig. 3. Layering of proteins in partition cell for the ultracentrifuge

weight of X_1 as we have described it and consisting, in theory, of two units of the X_1 having the sedimentation constant S 4·75. Turtle egg yolk X_1-phosphoprotein appears to have approximately twice the molecular weight of hen egg yolk X_1, but its structure has not yet been determined.)

A complex of X_1 with X_2 would have increased detectably the sedimentation-rate of the X_2. The possibility of a third, fourth or nth component present as an impurity in the X_2 peak cannot be excluded, but X_1 does not seem to be one of these, and γ-livetin, if present, cannot be complexed with X_2, since it would, in such an orientation, again completely modify the sedimentation-rate of X_2.

Thirdly, from the foregoing, it is obvious that at least phosvitin as obtained by the chemical procedures of Joubert and Cook[5], or by the electrophoretic separations of McCully, Maw and Common[10], is a derived protein of a form considerably different from its physiological counterpart. In its natural state, phosvitin contains approximately 7 per cent calcium, as determined by calcium analysis of phosphoprotein (X_1) isolated ultracentrifugally from either serum or egg yolk. During the chemical or electrophoretic isolation of phosvitin, nearly all the calcium is removed. (75 per cent of the calcium associated with the phosphoprotein is irretrievably lost by a single precipitation in distilled water) and often a considerable amount of the phosphorus is removed by hydrolysis. These losses, together with a possible breaking of the phosphoprotein backbone, are reflected by a much slower sedimentation constant for egg yolk phosvitin (S 3·0) as compared with egg yolk X_1, its naturally occurring counterpart (S 4·75) and a much faster rate of migration on paper at a pH of 8·6 (ref. 10).

Lipovitellin, as prepared by Joubert and Cook[5], sediments at nearly the same rate as the naturally occurring egg yolk dense lipoprotein (X_2 isolated by ultracentrifugation); but in the chemically prepared form it is usually contaminated with both lipovitellenin and livetins. Pre-isolation of the egg yolk granules was found by us to eliminate the livetins, since these are found only in the yolk fluid. The egg yolk granules contain only phosphoprotein and dense and light lipoproteins in significant proportion, and the light lipoproteins can be floated off by ultracentrifugation. The dense lipoprotein (lipovitellin) contains a considerable amount of polysaccharide, and approximately 20 per cent of its weight is due to the presence of lipid, mainly phospholipid[3]. Many workers tend to obtain higher lipid values for this component, due to contamination with lipovitellenin (or light lipoproteins), which are co-precipitated with the phosphoprotein and lipovitellin on dilution with distilled water.

Finally, it should be emphasized that the natural form of phosphoprotein from egg yolk (X_1) is only half the size of its serum precursor as measured under our conditions, although it contains the same proportions of phosphorus and calcium[3], and the natural form of the dense lipoprotein of egg yolk (X_2) is only half the size of its serum precursor, although it contains the same proportions of total lipid and phospholipid[3]. Thus, striking alterations have taken place in the molecules during the transfer from blood to yolk granule or from yolk granule to solution. In confirmation of these changes, when aliquots of egg yolk X_1 and X_2 and serum X_1 and X_2 were mixed and centrifuged together, the ultracentrifuge pattern shown in Fig. 4 was obtained.

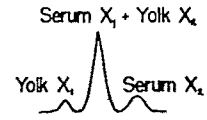

Fig. 4. Sedimentation pattern of a mixture of egg granules, proteins and serum from an œstrogenized rooster

It is mainly because we do not yet know the exact nature of these and possibly other alterations that we prefer to use the terms serum X_1 and X_2 and egg yolk X_1 and X_2. These terms both link and distinguish the four different components which may, or may not, be relatively homogeneous materials. The terms phosvitin and lipovitellin, however, refer to proteins which are known to be altered and mixed, and thus do not show due respect for the integrity of these important physiological entities.

These investigations were partly supported by contract *AT*–04–1–*GEN*–12 between the Atomic Energy Commission and the University of California, Los Angeles; aided, in part, by grants from the Eastern Seal Foundation, Society for Crippled Children and Adults; Ayerst Research Laboratories, Inc.; Squibb Institute for Medical Research; the Josiah Macy, Jr., Foundation; and U.S. Public Health Service Grant-in-Aid No. *A*-3793 (*RI*).

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THE communication by Miss C-C. Mok and me in *Nature*[1] stated our belief that we had identified phosvitin in hen's serum for the first time. Dr. Schjeide and Dr. Urist suggest that their extensive researches on the proteins of avian yolk and serum were unknown to us. In point of fact, their observations, as reported in certain of their papers[2,3], had encouraged us to persevere in attempts to isolate phosvitin from hen's serum by chemical procedures. Our communication, like our work, deals with a relatively very limited part of the wide range covered by the researches of Dr. Schjeide and Dr. Urist, but we regret the omission of any reference to their

researches, the more so as a full publication of our own restricted study has been delayed.

In one of their papers[4], published prior to our communication, Dr. Schjeide and Dr. Urist point out that their serum X_1-phosphoprotein and their egg yolk X_1-phosphoprotein, which are ultracentrifugal entities, have a common origin and that both are phosphoproteins of high serine content but differing in sedimentation behaviour. They also point out that consideration of these results, in conjunction with those of other workers, led them to the conclusion that the phosvitin of Meecham and Olcott[5] is a relatively pure X_1-phosphoprotein. The different ultracentrifugal behaviour of serum X_1-phosphoprotein and yolk X_1-phosphoprotein, however, could indicate that the 'phosvitins' from them might differ in such properties as contents of nitrogen, phosphorus and serine. This could scarcely be established except by preparation and analysis of these phosvitins. Our reported results showed that phosvitin prepared from hen's serum by the method of Joubert and Cook[6] had the same contents of nitrogen and phosphorus, and showed similar behaviour on zone electrophoresis on paper as did phosvitin prepared from egg yolk by the same method. This, of course, does not mean that the serum X_1-phosphoprotein and yolk X_1-phosphoprotein of Dr. Schjeide and Dr. Urist are the same portein, but it does suggest that these two ultracentrifugal entities would yield similar, if not identical, phosvitins when subjected to the isolation procedure of Joubert and Cook[6].

The criticism in the foregoing communication that our phosvitin preparation is a derived protein, and in that sense an artefact, may very well be valid; and if so, then we would have been more correct to have said that we believed this to be the first occasion on which phosvitin had been prepared from hen's serum by a biochemical procedure rather than "as the first occasion on which phosvitin had been identified as a constituent of the hen's blood". For the same reasons, we consider that our communication would have been more correctly entitled "Preparation of Phosvitin from the Serum of the Hen". We also suggested[1] that two lipoprotein zones observed on paper electropherograms of egg yolk and hen's serum might be related to a lipovitellin–phosvitin–γ-livetin complex and to lipovitellenin. In the light of later work, we now regard this suggestion as invalid, at least in so far as it relates to lipovitellenin. The resolution of lipoprotein zones on such electropherograms is greatly affected by the nature of the buffer.

Certainly ultracentrifugal studies, such as those of Dr. Schjeide and Dr. Urist, are likely to separate entities much more closely related to the physiological entities present in serum than are biochemical procedures or zone electrophoresis. Indeed, it is not at all easy to relate the results of zone electrophoretic experiments to the results of free electrophoretic studies, such as those of Clegg and his collaborators (for example, refs. 7–9). At the same time, simpler biochemical procedures and zone electrophoresis are more widely available techniques than ultracentrifugation and free electrophoresis; and to that extent it may be worth while to persist with the simpler techniques and to attempt to relate the results to those established by more elaborate and fundamental approaches, such as those of Dr. Schjeide and Dr. Urist, whose communication provides a timely synopsis.

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NEW EVIDENCE FOR A RELATIONSHIP BETWEEN ION ABSORPTION AND PROTEIN TURNOVER IN PLANT CELLS

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SALT absorption in plants is clearly an energy-requiring process; but the mechanism by which it is achieved remains obscure[1]. Experiments with metabolic inhibitors such as cyanide, azide, and carbon monoxide have confirmed the dependence on respiration, and indicate the involvement of the cytochrome oxidase system. The effects of 'uncoupling agents' (for example, 2,4-dinitrophenol) on respiration and absorption strongly suggest that ion transport is more closely linked to the supply of high-energy phosphate compounds than to electron transport, but the evidence is not unequivocal[2,3]. Other methods of separating ion absorption from respiration must be exploited if their interrelationships are to be fully elucidated.

Steward and Preston[4] were impressed by the closely similar influence of various external factors on salt accumulation and protein synthesis in potato tuber slices, and a scheme has been proposed whereby the two processes may be linked[5]. Other investigators[6–8] pointed out, however, that active absorption can occur in excised roots and storage tissue cells in the absence of net protein synthesis (compare ion movements in erythrocytes, nerve and muscle cells of animals); and such claims led to the generally accepted view that the correlation sometimes observed is only an indication of a common dependence on respiration. Nevertheless, it remains possible that ion transport is linked to protein turnover (that is, breakdown and re-synthesis) which is a characteristic feature of cyto-

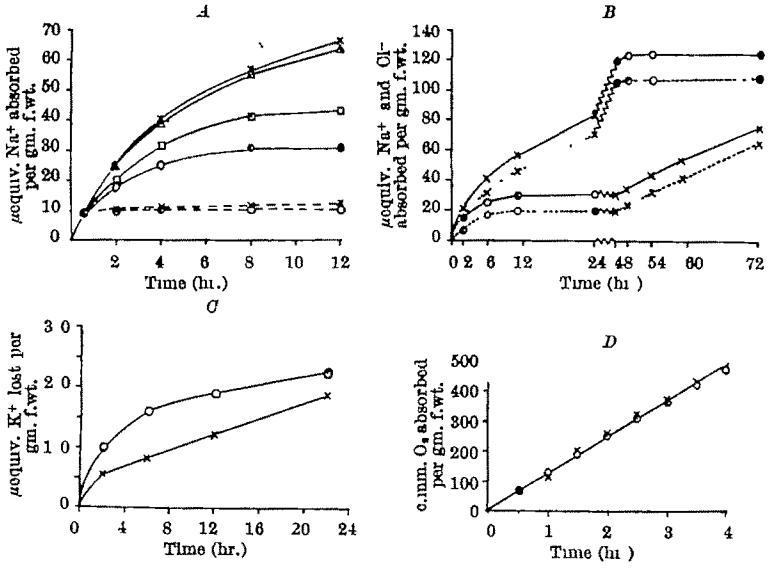

Fig. 1. Effect of chloramphenicol on: *A*, sodium absorption; *B*, sodium and chloride absorption; *C*, potassium leakage; *D*, oxygen absorption, by washed red beet slices. *A*, Sodium uptake from (*a*) 0·01 *M* sodium chloride (×); (*b*) 0·01 *M* sodium chloride + chloramphenicol (0·2 gm. per litre) (△); (*c*) 0·01 *M* sodium chloride + chloramphenicol (1 gm. per litre (□), (*d*) 0·01 *M* sodium chloride + chloramphenicol (2 gm. per litre) (○). (——) 25° C. (- - -) 2° C.
B, Sodium (——) and chloride (. .) uptake from 0·01 *M* sodium chloride (×) and 0·01 *M* sodium chloride + chloramphenicol (2 gm. per litre) (○) at 25° C. After 48 hr., disks were transferred into the alternative medium.
C, Potassium released from disks placed in 0·01 *M* sodium chloride (×) and 0·01 *M* sodium chloride + chloramphenicol (2 gm. per litre) (○) at 25° C.
D, Oxygen absorbed by disks placed in 0·01 *M* sodium chloride (×) and 0·01 *M* sodium chloride + chloramphenicol (2 gm. per litre) (○) at 25° C.

plasmic proteins, even under conditions which do not favour net synthesis. This possibility may be investigated experimentally using antibiotics which are known to be specific inhibitors of protein metabolism, at least in bacteria[9,10].

The effect of bactericides on uptake of salt does not seem to have been investigated hitherto with higher plants, although absorption of some of these substances has been studied[11]. Dumont[12] showed that active transport of sodium ions out of the gills of a crab, *Eriocheir sinensis*, is strongly inhibited by some antibiotics, and unaffected by others.

In the present investigation the effects of chloramphenicol on ion absorption and respiration in red beetroot and carrot root slices have been examined. The first experiment with washed beet slices showed that the antibiotic at a concentration of 1 and 2 gm. per litre (about 0·003 and 0·0006 *M* respectively) causes nearly complete inhibition of sodium absorption within about 8 hr., while at a concentration of 0·2 gm. per litre it is almost without effect (Fig. 1*A*). That the initial physical phase of cation absorption is largely unaffected by chloramphenicol was shown by the absence of an inhibitory effect during the first 2 hr. when an experiment was performed at low temperature. Likewise, the equilibration phase of rapid metabolic absorption observed with washed slices, which is completed in about 8 hr., seems to be insensitive to the inhibitor, but the prolonged slower phase of active accumulation is strongly inhibited (Fig. 1*B*). A comparable effect on chloride, as on sodium absorption, was observed. The difference between the course of absorption of the two ions is attributable to a smaller initial physical component in the case of anion than cation uptake. The concomitant slow leakage of potassium ions from cells during absorption of sodium and chloride is enhanced by chloramphenicol in the early stages of an experiment, but is reduced later (Fig. 1*C*).

The effect of chloramphenicol on sodium and chloride absorption by storage tissues is completely reversible. When red beet disks which had been kept for 48 hr. in an aerated sodium chloride solution containing chloramphenicol were washed and transferred to a solution of salt alone they began to absorb immediately, at a rate comparable to that of the control tissue (Fig. 1*B*). Conversely, absorption of salt by tissue which had been absorbing sodium and chloride for 48 hr. was almost immediately inhibited on transference to a salt solution containing chloramphenicol.

A similar experiment has been performed with washed slices of carrot tissue, and the inhibition reversed 3 times (Fig. 2*A*). A somewhat higher concentration (4 gm. per litre) is required to produce

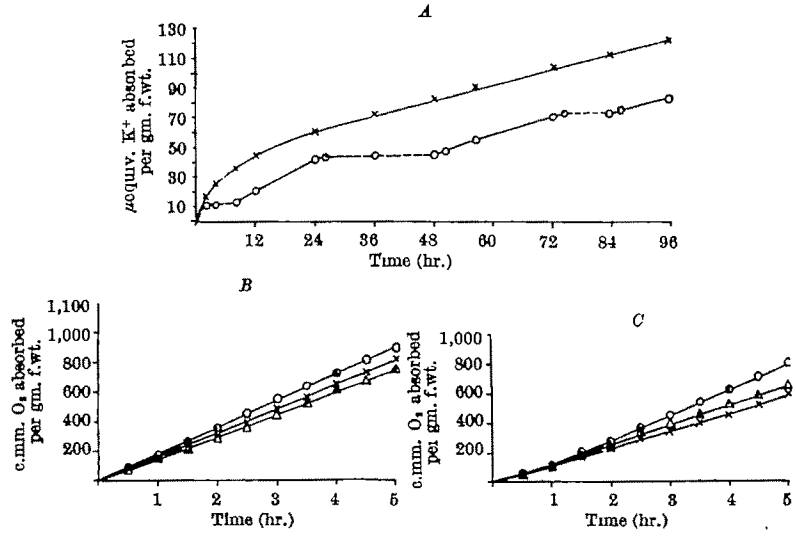

Fig 2. Effect of chloramphenicol on: *A*, potassium absorption; *B* and *C*, oxygen absorption by washed carrot slices at 25° C.
A, Uptake from (*a*) 0·01 *M* potassium chloride and (*b*) 0·01 *M* potassium chloride + chloramphenicol (4 gm. per litre) (○- - -○) and 0·01 *M* potassium chloride (○——○) supplied alternately.
B, Oxygen absorption by disks placed in (*a*) 0·01 *M* potassium chloride (×); (*b*) 0·01 *M* potassium chloride + chloramphenicol (2 gm. per litre) (△); and (*c*) 0·01 *M* potassium chloride + chloramphenicol (4 gm. per litre) (○).
C, Oxygen absorption by disks placed in (*a*) distilled water (×); (*b*) chloramphenicol (2 gm. per litre) (△) and (*c*) chloramphenicol (4 gm. per litre) (○)

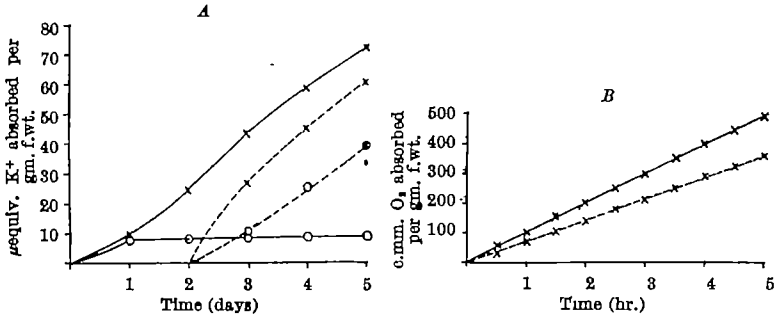

Fig. 3. Effect of chloramphenicol (2 gm. per litre) on *A*, the development of ion absorptive capacity; *B*, the enhancement of respiration, caused by washing red beet tissue at 25° C. in aerated solutions. The freshly cut tissue was washed for 8 hr. in running tap water, and afterwards for 12 hr. in distilled water, before the commencement of the experiment.

A, Uptake of potassium by disks placed in (*a*) 0·01 *M* potassium chloride immediately (×——×); (*b*) distilled water for 2 days, and then transferred to 0·01 *M* potassium chloride (× --- ×); (*c*) 0·01 *M* potassium chloride + chloramphenicol (2 gm. per litre) immediately (○——○) and (*d*) chloramphenicol (2 gm. per litre) for 2 days, and then transferred to 0·01 *M* potassium chloride (○--○)

B, Oxygen absorption by disks placed in 0·01 *M* potassium chloride at 25° C. after (*a*) washing for 48 hr. in aerated distilled water at 25° C. (×——×); and (*b*) washing for 48 hr. at 25° C. in aerated distilled water containing chloramphenicol at a concentration of 2 gm. per litre (×---×)

complete inhibition of absorption in carrot than in red beet tissue.

The effects of chloramphenicol on salt absorption are manifested without any apparent influence on the rate of oxygen absorption in red beet tissue (Fig. 1*D*), and only a relatively small effect was observed in carrot (Fig. 2*B*). Calo and Varner[13] similarly noted the insensitivity of respiration, in both freshly cut and washed potato tuber slices, to inhibition by the antibiotic. In carrot, oxygen absorption is stimulated somewhat by chloramphenicol in the absence of salt (Fig. 2*C*). This is possibly attributable to release of salt from the vacuoles with a result that ions gain access to the respiratory sites in the cytoplasm. The presence of salt in the external medium after the experiment supports this contention.

The observations indicate that inhibition of ion transport induced by chloramphenicol is independent of an effect on respiration. Thus, it seems unlikely that absorption is directly related to electron transport as in the mechanisms suggested by Lundegårdh[2] and Conway[14]. Furthermore, chloramphenicol at the concentration used does not influence protoplasmic streaming in either red beet or in *Elodea* leaf cells (unpublished data), which proves that energy continues to be available at least for some endergonic processes in presence of the antibiotic. Protoplasmic streaming probably depends on a rhythmic folding and unfolding of protein molecules, and it is therefore unlikely that chloramphenicol would inhibit ion absorption if uptake occurred by a mechanism dependent solely on this phenomenon, such as that suggested by Goldacre and Lorch[15].

If it is assumed that chloramphenicol prevents salt absorption by inhibiting the same reaction as that affected in blocking protein metabolism, then a close relationship between the two processes is indicated. Supporting evidence for this conclusion is supplied by the inhibitory effects of nucleic acid antagonists, ribonuclease, and ultra-violet light on both ion absorption[16,17] and on protein synthesis[9,10]. It must be noted, however, that the concentration of chloramphenicol necessary to inhibit ion transport in carrot root slices is at least 10 times greater than that required to prevent growth of carrot callus tissue cultures under the influence of coconut milk (unpublished work). The reason for this discrepancy is still obscure; but differences in the rate of penetration of the antibiotic into the two kinds of tissue may be responsible.

The manner in which ion transport could be linked to protein turnover or synthesis remains to be considered. It must first be emphasized that turnover probably does not involve breakdown of a complete protein molecule followed by immediate re-synthesis, but rather the continuous removal and replacement of individual amino-acids in the polypeptide chain[18]. A similar series of reactions to those involved in the exchange process is probably concerned also in synthesis of new protein, and, in fact, in *in vitro* experiments on incorporation of labelled amino-acids it is difficult to distinguish between exchange and net synthesis. No attempt to do this is made in the discussion which follows. Both processes involve temporary attachment of the protein molecule, or a part of it, to a ribonucleic acid template, and it seems likely that the formation of such a protein-nucleic acid complex diminishes the capacity of the protein to bind ions both by removing available electrostatic binding sites and by reducing its chelating power, thus causing ions to be released. When the turnover site leaves the template and returns to its natural shape, binding capacity is perhaps restored and ions are taken up again. Although probable, this idea is hypothetical since no direct evidence for the reversible release of ions from protein is yet available. The ability of proteins to bind ions with a specificity comparable to that exhibited by ion transport mechanisms is well illustrated by the association of enzymes with specific activating ions.

In order that a molecule may function as an ion carrier it must not only possess the ability to bind ions reversibly, but it must also be suitably located in a membrane. The association of proteins with both surface and internal cytoplasmic membranes is quite certain, but the manner in which they are arranged in relation to the lipid and phospholipid components remains uncertain. It is likely that the membranes are in a state of continuous flux, and as a result of such movements a particular region of a protein molecule may occasionally face towards one surface of a membrane, and then the other, especially when the membrane is thin. Thus, ions which are picked up at a surface in contact with the medium may be released again on the inside where the amino-acid exchange mechanism is located. The proximity of the ribonucleic acid template may prevent the carrier site from binding ions on the inner surface immediately after exchange has occurred, and allow it to traverse the membrane unloaded before accepting ions again from the medium. The characteristic location of microsomes, which are known to be particularly active in facilitating protein turnover and synthesis, on one side of the membranes of the endoplasmic reticulum[19] may be of significance in determining the direction of ion transport across cytoplasm. However, no such arrangement occurs at the vacuolar boundary of a plant cell, and yet ions accumulate in the central vacuole. Moreover, the probable thickness of the tonoplast is such that the mere turn-about of indivi-

dual protein-binding sites is unlikely to facilitate transport across the membrane as a whole. Either the ions are handed from site to site in moving from the outer to the inner surface, or other substances, for example, phospholipids, collaborate in a manner which is yet obscure. Possibly, ions are accumulated first in some of the smaller vacuoles and vesicles with which the cytoplasm abounds, and are then transferred to the central vacuole as a result of coalescence between it and the smaller ones. Vacuole coalescence is a feature of vacuome development in meristematic cells, and may well persist even in mature parenchyma.

Possibly only a few types of proteins are suitably adapted to carry out ion transport in the manner proposed. It has been suggested[20,21], that specific proteins with enzyme-like properties (permeases and translocases) are concerned in the transfer of sugars and phosphate across bacterial membranes. Chloramphenicol may be a specific inhibitor of such carriers functioning in the plant cell, and this possibility needs to be investigated further. It is interesting to speculate that, alternatively, the capacity to bind ions reversibly may be an inherent property of all labile protein molecules, and those which are located in membranes can function as carriers in active transport. All membranous organelles may thus be capable of ion accumulation, such as has been shown in the case of mitochondria[22,23]. Inhibition by chloramphenicol is then attributable to a general effect on protein turnover.

A feature of cells of storage tissues is that when first cut from the dormant organ they are incapable of accumulating salt, but a capacity to do so develops if they are washed for a time in an aerated solution of salt or in aerated distilled water. The development of absorptive ability has been attributed to synthesis or activation of carrier molecules resulting from enhanced metabolism induced by this treatment[8]. An experiment in which disks of red beet were washed either in a salt solution or in distilled water, in the presence and absence of chloramphenicol, has shown that the antibiotic prevents the development of absorptive capacity. Disks washed for 2 days in chloramphenicol (2 gm. per litre) at 25° C., and then transferred to salt, absorbed potassium over the next 3 days at an increasing rate comparable to that of disks placed in salt solution at the start (Fig. 3*A*). Disks washed for 2 days in chloramphenicol and transferred to salt also showed a lower rate of respiration than disks washed for the same time in distilled water before transference (Fig. 3*B*). A similar observation was made by Calo and Varner[13] with potato tuber tissue. The antibiotic evidently inhibits some metabolic activity upon which stimulation of both respiration and ion accumulation capacity depend.

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PHOSPHOLIPIDS CONTAINING PHOSPHATE TRIESTER GROUPS

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THE study of phospholipids has undergone rapid development in recent years not only in respect of the number of papers published annually but also because findings in the fields of respiratory enzymes[1,2], blood coagulation[1], cell structure[1] and transport across cell membranes[1,3] emphasize the importance of phospholipids. Much of this activity has been stimulated by the introduction of new analytical procedures which have greatly simplified the techniques used in this field. Dawson[4] showed that mild alkaline hydrolysis (0·2 *N* sodium hydroxide at 37° for 20 min.) of phospholipids yielded a mixture of glyceryl phosphoryl choline, glyceryl phosphoryl ethanolamine, glyceryl phosphoryl serine, glyceryl phosphoryl glycerol, glyceryl phosphoryl inositol and glycerol-1-phosphoric acid which could be separated by paper chromatography. It was assumed that each water-soluble phosphate ester was derived from one phospholipid and hence the specific radioactivity of each phospholipid, if labelled with phosphorus-32, could be deduced from that of the corresponding water-soluble phosphate ester. Chromatography on silicic acid was shown by Lea, Rhodes and Stoll[5] to effect a separation of phospholipids into well-defined components, and Marinetti, Erbland and Stotz[6] obtained good separations using chromatography on silica-impregnated paper and di-*iso*butylketone/acetic acid/water (40:25:5 by volume).

Table 1. RAT LIVER PHOSPHOLIPIDS

All results expressed as moles per cent of total lipid-phosphorus

	Hanahan *et al* (ref 8)	Shotlander and Collins (ref. 9)
Phosphatidyl ethanolamine and serine	22	18
'Complex' phospholipids	—	39
Lecithin	58	33
Lysolecithin	3	—
Minor components*	13	10
	96	100

* Phosphatidyl inositol, sphingomyelin and phosphatidic acid-like materials.

It was surprising to find that the analytical methods[7] introduced in this laboratory gave results that were at variance with those obtained by the procedures referred to above. In this laboratory the phospholipids are dinitrophenylated using 1-fluoro-2:4-dinitrophenyl-benzene followed by methylation using diazomethane, and the resulting phospholipid derivatives are separated, by low-temperature chromatography on cellulose at −20° using acetone, into fractions soluble and insoluble respectively in acetone, and then each fraction is further resolved by counter-current distribution. Table 1 shows a comparison with the results obtained by Hanahan, Dittmer and Warashina[8], who used silicic acid chromatography. The major difference is in the 'complex' phospholipids which constitute 39 per cent of the total rat-liver lipids and in which the molecular weight is at least double that of the known phospholipids. This fraction has not been detected by other workers.

There are two possible explanations for this discrepancy: one is that the 'complex' phospholipids are degraded by the silicic acid chromatography, and the other is that the chemical treatment (dinitrophenylation and methylation) used in this laboratory[7] results in the production of artefacts not existing in the original phospholipid mixture.

To test these alternatives, rat liver lipids were treated with silicic acid (Mallinckrodt), the lipids recovered quantitatively, dinitrophenylated and methylated and separated by counter-current distribution into two fractions: *A*, that containing phosphatidyl ethanolamine and phosphatidyl serine; *B*, that containing the 'complex' phospholipids. The amounts of these compounds were determined from the content of dinitrophenyl-groups and the results are shown in Table 2. Not only was the proportion in fraction *B* of the 'complex' phospholipids decreased, but also further examination revealed considerable qualitative changes both in respect of their behaviour on counter-current distribution and in their solubility in acetone and in water. The dinitrophenylated and methylated 'complex' phospholipids are insoluble in water and very soluble in acetone but, after treatment with silicic acid, only 6–10 per cent of the total phospholipids had these properties. Of the remaining dinitrophenyl-containing materials in fraction *B*, 4 per cent (of the total phospholipids) were insoluble in acetone and 3 per cent were soluble in water. The small amount of 'complex' phospholipid which appeared to be unchanged had the molar ratio dinitrophenyl-groups/phosphorus = 0·5 but, unlike the original material, choline was not detected. The fall in the amount of 'complex' fraction was not accompanied by a corresponding rise in the phosphatidyl ethanolamine and serine, and thus there was a disappearance of about a third of the total amino-nitrogen (ethanolamine and serine). These results show that silicic acid can degrade phospholipids and that its effect is on the 'complex' fraction. Other workers[5] did not consider the possible presence of unidentified lipids which might be sensitive to silicic acid, but were content to show that silicic acid chromatography was without effect on lecithin and phosphatidyl ethanolamine.

Table 2. EFFECT OF SILICIC ACID ON PHOSPHOLIPIDS

Phospholipids from the same sample of rat liver lipids were treated with silicic acid as shown below, the lipids were then completely eluted and treated as described by Collins and Wheeldon (ref. 7).

All results are expressed as gm. atoms of phosphorus per 100 gm. atoms of total lipid phosphorus.

Fraction	*A* Phosphatidyl ethanolamine and serine	*B* 'Complex' phospholipids
Treatment		
Control	15	32
Lipids (300 mgm.) stood with 12 gm. silicic acid in chloroform-methanol (1:1 by vol.) for 48 hr.	15	20
Lipids (300 mgm.) chromatographed on silicic acid (12 gm.)–'Celite' (6 gm.) Rate of flow 3–4 ml./min Solvents, chloroform-methanol in the proportions used by Hanahan *et al.* (ref. 8)	11	18

While the above evidence demonstrates that silicic acid can degrade some phospholipids, this of itself does not dispose of the possibility that the process of dinitrophenylation and methylation may result in artefacts. Reasons for believing otherwise are discussed in previous papers[7], and are augmented by the following experiment (Table 3) in which the object was to show that the specific radioactivity of the phosphorus, esterified to ethanolamine, in phosphatidyl ethanolamine is greater than that in the complex phospholipids. As the methods available did not separate the serine component, the specific radioactivity of the ethanolamine component was estimated from the specific radioactivity of the combined fraction on the assumption that the radioactivity of the serine component was zero. Although this is not the case[10,11], it is the least favourable assumption that can be made in that it minimizes the differences between the two ethanolamine-containing materials. The phosphatidyl ethanolamine and serine (as the dinitrophenylated and methylated derivatives) were isolated by counter-current distribution and redistributed in heptanemethanol for 120 transfers. A single dinitrophenyl-containing peak was obtained with a partition coefficient of 0·50, in which the molar ratio of dinitrophenyl-groups/phosphorus was 1·0 and which contained 86 per cent phosphatidyl ethanolamine and 14 per cent phosphatidyl serine. The specific radioactivity of this material is shown in Table 3. Because the 'complex' phospholipids contain approximately two atoms of phosphorus to each molecule of ethanolamine or serine, it was necessary to effect a partial hydrolysis before the radioactivity could be related to the amino-compounds. The complex fraction was treated with 0·2 *N* sodium hydroxide in 50 per cent aqueous methanol for 20 min. at 37°, the mixture neutralized with 'Zeokarb-225' (H-form), and the fatty acids removed by extraction with diethyl ether. Paper chromatography in phenol-water of the water-soluble materials showed the presence of two phosphate-containing[12] spots (R_F 0·73 and 0·54). Both spots gave a positive reaction for a *cis*-glycol group[13]; the slower spot has not yet been identified, but the faster-moving material was yellow, indicating

Table 3. INCORPORATION OF RADIOPHOSPHORUS INTO PHOSPHATIDYL ETHANOLAMINE AND THE ETHANOLAMINE-CONTAINING PORTION OF THE 'COMPLEX' PHOSPHOLIPIDS

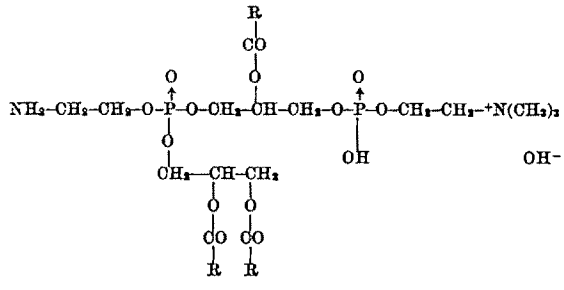
A rat was intravenously injected with 0 8 mc. of sodium dihydrogen phosphate-^{32}P (0·01*M*, *p*H 7·0) in 0 1*M* sodium citrate (*p*H 7 0), killed 90 min. later, the liver lipids extracted, and processed as described by Collins and Wheeldon (ref. 7) and Shotlander and Collins (ref. 9).

	Specific radioactivity (counts/min./μmole P)	Ratio serine-nitrogen to total ammo-nitrogen	Specific radioactivity of ethanolamine moiety, assuming that of serine is zero (counts/min./μmole P)
Phosphatidyl ethanolamine and serine	13,700	0 14	15,900
'Complex' phospholipids (phosphorus esterified directly with ethanolamine and serine)	9,100	0 24	12,000

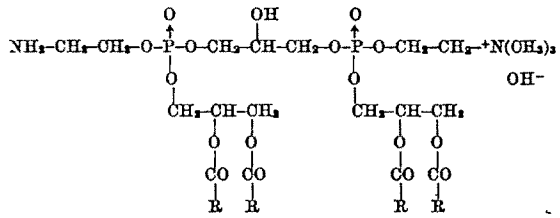
the presence of a dinitrophenyl group. The yellow spot was eluted with water, and analysis indicated that the molar ratio of dinitrophenyl-groups/phosphorus was 1·0, and it was concluded that this was glyceryl phosphoryl N-2:4-dinitrophenyl ethanolamine (or serine, as no separation was obtained in this solvent system). The specific radioactivity and serine content of this material are shown in Table 3. It will be seen that the specific radioactivity of the phosphatidyl ethanolamine is between 1·50 and 1·32 times that of the phosphate ester containing ethanolamine, which was derived from the complex fraction and, as the combined counting and chemical errors do not exceed 4 per cent, this difference is highly significant.

These results show that the dinitrophenylated and methylated 'complex' phospholipids represent a distinct and real fraction, but beyond indicating that they are sensitive to silicic acid, they provide no information as to their structure. Previous work[7] has shown that the molar ratio of dinitrophenyl-groups/phosphorus is usually 0·5 but may be 0·67. Qualitative analysis[7,9] has also shown that choline is present in some but not all the components that make up the 'complex' phospholipid fraction and that inositol is absent. Further information was obtained in experiments in which the dinitrophenylated and methylated 'complex' phospholipid fraction (50 mgm.) was treated with one of the following reagents: triethylamine (0·1 ml. in 10 ml. of diethyl ether saturated with water and left 12 hr. at 20°), tetramethyl ammonium hydroxide (0·1 ml. of a 25 per cent (w/v) aqueous solution added to 10 ml. of diethyl ether saturated with water and left 12 hr. at 20°), acetic acid (8 ml. of glacial acetic acid and 2 ml. water and left 30 min. at 40°). In addition, chromatography on 'Hyflo-Supercel' or on silicic acid (Lights or Mallinckrodt) gave similar results. The total lipids were recovered after treatment, treated with diazomethane and submitted to counter-current distribution. One of the products isolated had a molar ratio of dinitrophenyl-groups/phosphorus of 1·0 and was indistinguishable from the methyl ester of dinitrophenyl phosphatidyl ethanolamine and serine. This methyl ester was not obtained if the preliminary 'hydrolytic' treatment was omitted, and hence one must conclude that the preliminary treatment gave rise to dinitrophenyl phosphatidyl ethanolamine or serine. The only groups present in these compounds which are available for chemical bonding are the free hydroxy group on the phosphorus and the carboxy group on the serine, and it thus follows that the 'complex' phospholipids contain either a phosphate triester or a serine-carboxylic ester. This last alternative is unlikely, not only because it could account for only 24 per cent of the 'complex' phospholipids but also because carboxylic esters such as the glycerides appear to be quite stable to silicic acid chromatography. Thus, one must infer that the 'complex' phospholipids are distinguished from the remaining phospholipids, which are phosphate diesters, by the presence of a tertiary ester of phosphoric acid. The nature of the compound to which the phosphatidyl ethanolamine is esterified has not been fully elucidated, but it is clear that it must contain phosphorus and is in all probability another phospholipid.

Two types of compounds are possible: (1) those in which phosphatidyl ethanolamine is esterified with the free hydroxy group in such a compound as lysolecithin, sphingomyelin or cardiolipin; (2) the second type can be imagined in which phosphatidyl ethanolamine is linked by glycerol (or similar compound) to another phospholipid and the resulting compound would have two phosphate triester groups. The suggested structures are shown below: the first type would be a phosphatidyl ethanolamine-lysolecithin, (I), whereas the second would be, for example, 1-(phosphatidyl ethanolamine) 3-(phosphatidyl choline) glycerol (II). Complete or partial hydrolysis of compounds such as those suggested above would yield products which would be identical with those which are in fact obtained, and this helps to explain their non-recognition in the past. Further, the splitting of the phosphate triester on silicic acid would either yield the classical forms (phosphatidyl choline, ethanolamine or serine) or such compounds as lysolecithin or lysophosphatidyl ethanolamine.



(I)



(II)

The occurrence of lysolecithin in animal tissues has only been reported in recent years, and it is interesting to note that in every case it was isolated either by silicic acid chromatography[5], or by chromatography on paper impregnated with silicic acid using aqueous acetic acid in the solvent system[6], or by counter-current distribution using aqueous acetic acid as a component of the solvent mixture[14]. Both silicic acid and acetic acid have been shown here to be effective

in degrading the 'complex' phospholipid fraction, and lysolecithin has not been detected by the methods in use in this laboratory. The 'complex' or triester fraction has been shown to be present in rat tissues (liver, kidney, heart, lung, brain, spleen and intestine), sheep brain, human blood plasma, influenza virus, yeast and cabbage leaf, and the amounts have varied from 15 per cent for human blood plasma to 60 per cent for sheep brain.

The fact that phospholipids consist of about 60 per cent in the form of phosphate diesters and 40 per cent as triesters means that most investigations on phospholipids have neglected the study of a major portion. The procedure described by Dawson[4] involving alkaline hydrolysis, which has been widely used for the study of the exchange of inorganic phosphorus-32 with phospholipids, cannot distinguish between the diesters and the triesters, as the triesters of phosphoric acid are labile to alkali and a diester would be formed.

The procedure[7] developed in this laboratory suffers from the disadvantage that derivatives of the phospholipids are isolated and not the native materials. In certain fields such as in the study of blood coagulation, this is a serious drawback as the object is the isolation of material with biological activity. Apart from the fact that the native 'triester' phospholipids are more soluble in ethanol than phosphatidyl ethanolamine or serine[7], no work has been attempted on their isolation in an unaltered condition. An analytical method[7] exists for the determination of this group of phospholipids and hence attempts at their isolation can be readily followed. However, the solution to the problem of obtaining the native materials may be as readily solved by chemical synthesis, and in the meanwhile, much work remains to be done on the elucidation of the structures of the phosphate triester phospholipids.

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ACTION OF SPERMINE ON SOLUBLE RIBONUCLEIC ACID AND SOME POLYNUCLEOTIDES

Spermine Fractionation of Soluble Ribonucleic Acid of Rabbit Liver

THE unique biological role of cytoplasmic, or soluble, ribonucleic acid, as an acceptor for acyl-activated amino-acids, and as a donor of the amino-acyl moiety to microsomal protein, has been established[1-3]. Furthermore, it has been found that in any one soluble ribonucleic acid preparation there are a finite number of acceptor sites, presumably one for each polynucleotide chain, and it has been shown by several investigators[2,4,5] that each amino-acid is bound to soluble ribonucleic acid in a fixed amount and independently from other amino-acids. From these observations it has been inferred that there is a specific soluble ribonucleic acid chain for each amino-acid, and indeed it has been possible to separate, at least partially, different species of soluble ribonucleic acid by various experimental procedures. These procedures[6-8] may be based on either (*a*) special properties conferred by the presence of an amino-acid at the nucleoside end, or (*b*) differences in the physico-chemical properties of the various chains. Thus Brown *et al.*[6] were able to prepare in essentially pure form the soluble ribonucleic acid species specific for tyrosine or histidine by taking advantage of the ability of soluble ribonucleic acid labelled with these amino-acids to form diazonium compounds with a polyaminoazostyrene resin at neutral *p*H. On the other hand, partial separation of amino-acid specific soluble ribonucleic acids based on physicochemical properties of the amino-acid-free soluble ribonucleic acid were obtained by Smith *et al.*[7] by column chromatography and by Bowman[8] by electrophoresis on starch. More promising results were obtained by Holley *et al.*[9] through application to soluble ribonucleic acid of the counter current distribution system of Warner and Vaimberg[10].

Purification of soluble ribonucleic acids specific for valine or proline was achieved, as described here, by utilizing the well-known ability of polyamines to form insoluble complexes with polynucleotides[11]. The procedure was based on the assumption that amino-acid-specific soluble ribonucleic acids differ sufficiently in their chemical composition (base composition or sequence) to allow separation. This assumption is in accord with the results of Holley *et al.*[9] and Warner and Vaimberg[10] and is supported directly by the findings of Klee and Cantoni[12] that the specificity of soluble ribonucleic acid for proline, valine or leucine is not related to molecular weight.

Rabbit liver soluble ribonucleic acid was isolated from the '*p*H 5 enzyme' by a sodium chloride extraction procedure to be described in a forthcoming publication. On treatment of soluble ribonucleic acid with a two- to three-fold excess of spermine tetrahydrochloride at *p*H 5·6 and low ionic strength (0·02 *M* sodium succinate buffer in 0·03 *M* sodium chloride) approximately 70 per cent of the ultraviolet absorbing material is precipitated. The sper-

Table 1. SPERMINE FRACTIONATION OF SOLUBLE RIBONUCLEIC ACID

	Amino-acid acceptor units		Specific activity (μmoles of amino-acid/125 nucleotides)		
	Proline	Valine	Proline	Valine	P/V
Rabbit liver					
Soluble ribonucleic acid	100	100	0·115	0 041	2 8
Supernatant	24 8	69	0 092	0·091	1·0
Precipitate:					
Extract 1	10 5	10	0·194	0·066	2·9
Extract 2	26	5	0 276	0 039	7·1
Extract 3	25 7	10	0 316	0 035	9 1

The starting material, and the various fractions were tested as follows for their ability to accept activated amino-acids: the reaction mixtures (0 5 ml.) contained the following components; adenosine triphosphate, 10 m*M*; magnesium chloride, 20 m*M*; sodium chloride, 2 8 m*M*; potassium phosphate buffer, *p*H 7 6, 2 8 m*M*; ^{14}C amino-acid, 0·05 m*M*; and approximately 8 optical density units of soluble ribonucleic acid. Appropriate activating enzymes[14] were added to start the reaction; incubation time, 15 min at 37°. The reaction was stopped by addition of 0·5 ml. of 6 per cent chloroform. The precipitate was washed 3 times with 8 per cent chloroform, once with ethanol, suspended in 0·75 ml. of 6 per cent chloroform, and hydrolysed for 30 min. at 100°. After neutralization with potassium hydroxide, the optical density of this solution was determined and an aliquot was plated and counted. Values are corrected for self absorption. Amino-acid acceptor units thus determined are in counts/min./o d. at 260 mμ.

mine-soluble fraction is 2–3 times richer in valine-specific soluble ribonucleic acid than the starting material. Repeated extraction of the spermine-insoluble fraction with small volumes of phosphate buffer, 0·025 *M*, *p*H 7·2 in 0·05 *M* sodium chloride, yields a fraction enriched by about the same factor with respect to proline acceptor ability. Total recovery in both cases is satisfactory (Table 1). On the assumption that in a single soluble ribonucleic acid chain there is only one acceptor site for the activated amino-acid and on the basis of a chain-length of 125 nucleotides, the partially purified proline specific soluble ribonucleic acid is approximately 25–30 per cent pure, while the valine specific species is about 8–10 per cent pure. (The value of 125 for chain-length is based on a molecular weight of 45,000–55,000, as determined by sedimentation and viscosity measurements[13].)

It is noteworthy that the *p*H at which the fractionation is carried out is relatively critical. Thus, essentially no fractionation was achieved at *p*H 6 or 4·8. At *p*H 5·2 the results obtained are in the same general direction but partition is less precise. Intermediate *p*H's have not yet been investigated. Since the ability of spermine to react stoichiometrically with soluble ribonucleic acid is not dependent on *p*H, these results suggest that the determining feature which permits fractionation of a population of various soluble ribonucleic acid chains relates to the pK_a of the amino group of cytosine (and/or adenosine) in the polynucleotides.

Work by Huang and Felsenfeld using synthetic polynucleotides as model systems provides support for this hypothesis. These results are detailed in the following communication. It is of interest to point out that rabbit liver soluble ribonucleic acid has a high cytosine content[15], as is also the case for soluble ribonucleic acid derived from *E. coli* or yeast[16,17].

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Solubility of Complexes of Polynucleotides with Spermine

Cantoni has shown in the preceding communication that the solubility of soluble ribonucleic acid-spermine complexes is dependent on *p*H. The solubility of nucleic acid complexes with poly-cations has also been the subject of investigations by Razin and Rozansky[1], who studied polyamine-nucleic acid interactions, and by Chargaff *et al.*[2], who used polylysine and other poly-cations to fractionate deoxyribonucleic acids. The results presented in this communication are concerned with the behaviour of complexes of spermine with synthetic polyribonucleotides.

If an equivalent of spermine per mole of polymer phosphorus is added to a distilled water solution of heat-denatured calf thymus deoxyribonucleic acid at *p*H 6·5, a precipitate forms at once and most of the nucleic acid may be separated by centrifugation. Similar results were obtained with the synthetic polyribonucleotides, polyadenylic acid and polyinosinic acid. The polypyrimidines, polycytidylic acid and polyuridylic acid formed somewhat more soluble complexes with spermine, though precipitation was observed in the presence of excess spermine. Under conditions similar to those of some of the experiments described here (polymer phosphate concentration about 5×10^{-5} *M*, buffer concentration about 0·01 *M*, spermine concentration about 2×10^{-4} *M*), addition of spermine to separate solutions of polyadenylic acid, polyinosinic acid, polycytidylic acid and polyuridylic acid resulted in immediate extreme elevation of the absorption spectrum because of scattering from aggregates. Centrifugation at 16,000 *g* in a Servall centrifuge for 10 min. was sufficient to remove from suspension 80 per cent or more of the polyadenylic, polyinosinic and polycytidylic acids. Only 50 per cent of the polyuridylic acid-spermine was removed, but the spectrum of the supernate showed that the remaining material was in an aggregated form. The same solubility properties were observed for all these polynucleotides at *p*H 6·8 (cacodylate buffer) and *p*H 4·1 (acetate buffer).

When polyadenylic acid ($S_{20} = 8{\cdot}4$) and polyuridylic acid ($S_{20} = 5{\cdot}4$) are mixed in 1:1 base ratio in the presence of 2×10^{-3} *M* magnesium chloride, the two-stranded poly (adenylic + uridylic) complex is formed[3]. (Sedimentation coefficients, given in Svedberg units, were measured in 0·05 *M* sodium chloride, 0·005 *M* cacodylate buffer, *p*H 6·8, using

a Spinco model E ultracentrifuge equipped with ultra-violet optical system. According to Fresco and Doty[8] the value of S_{20} found for polyadenylic acid corresponds to a molecular weight of about 4×10^5.) The addition of an equivalent of spermine to this complex at pH 6·8 (or any other pH between 6·8 and 4·5) caused total precipitation. However, if polyinosinic acid ($S_{20} = 6·3$) and polycytidylic acid ($S_{20} = 5·2$) were similarly caused to combine in 1 : 1 ratio[4] by adding magnesium chloride, the complex formed when spermine was added was soluble at pH 7. (All the observations concerning solubility of spermine complexes were made within 2 hr. after addition of spermine. After 24 hr. small amounts of precipitation have been observed in poly (inosinic + cytidylic)-spermine at pH 6·8.)

The solubility of the poly (inosinic + cytidylic)-spermine complex has been studied as a function of pH. To a 1-ml. sample of 5×10^{-5} M poly (inosinic + cytidylic) in 2×10^{-3} M magnesium chloride was added 0·1 ml. of 0·1 M cacodylate or acetate buffer of the appropriate pH. The absorption spectrum was determined in a Cary model 14 spectrophotometer, and 0·04 ml. of $1·25 \times 10^{-3}$ M spermine tetrahydrochloride was added. The spectrum was plotted again both before and after centrifugation at 16,000 g in a Servall centrifuge for 15 min. At every pH between 6·8 and 5·1 there was no change in the absorption spectrum (aside from dilution effects) before centrifugation, and no more than a 5 per cent decrease in optical density after centrifugation. There was no further decrease in optical density with longer periods of centrifugation. However, when pH 4·5 buffer was used the addition of spermine resulted in immediate aggregation and increase of absorption values throughout the spectrum. Centrifugation removed these aggregates; only 70 per cent of the original polynucleotide remained in solution. When the experiment was repeated with pH 4·1 buffer only 30 per cent of the poly (inosinic + cytidylic) was still soluble after centrifugation.

This behaviour is in contrast with that of poly (adenylic + uridylic) in 2×10^{-3} M magnesium chloride. Using conditions similar to those described for poly (inosinic + cytidylic) it was found that poly (adenylic + uridylic) precipitated completely both at pH 6·8 and pH 5·1. In the experiment shown in Fig. 1 equal volumes of 5×10^{-5} M poly (adenylic + uridylic) and 5×10^{-5} M poly (inosinic + cytidylic) (both in 2×10^{-3} M magnesium chloride) were mixed and 0·1 ml. of 0·1 M cacodylate buffer (pH 6·8) added to a 1·0-ml. aliquot. The resultant spectrum (curve A) was the mean of the spectra of poly (adenylic + uridylic) and poly (inosinic + cytidylic) taken separately. Spermine (0·15 ml. of $1·25 \times 10^{-3}$ M) was added directly to the cuvette. The spectrum gave evidence of aggregation and after centrifugation only the spectrum of the poly (inosinic + cytidylic) remained, as demonstrated by direct comparison with a poly (inosinic + cytidylic) control containing the same concentrations of poly (inosinic + cytidylic) and of spermine used in the solution of curve A. Spermine thus effects a complete separation of poly (inosinic + cytidylic) from poly (adenylic + uridylic) under these conditions.

It does not appear likely that the differences in solubility described here were the result of differences in molecular weight. The polyinosinic and polycytidylic acids used in these experiments were precipitable, and so was incompletely combined poly (inosinic + cytidylic), or completely combined polymer at pH 4·1. With smaller polyinosinic and polycytidylic acids (S_{20} equal to 2·6 and 2·1 respectively) the addition of polycytidylic acid-spermine solution to the polyinosinic acid-spermine precipitate caused rapid solution of the polyinosinic acid and immediate appearance of the poly (inosinic + cytidylic) spectrum. The simplest conclusion is that only the well-ordered poly (inosinic + cytidylic) structure[4] is capable of forming soluble complexes with spermine. The precipitation of the poly (inosinic + cytidylic)-spermine complex formed at low pH may be the result of partial derangement of the poly (inosinic + cytidylic) structure as cytosine is titrated[5] in the neighbourhood of pH 4·5. The spectral shifts that occur when the pH is lowered to 4·5 indicate that cytosine is being titrated, though this does not necessarily mean that the hydrogen bonding to inosine has been destroyed[6]. If structure is important, then it must be assumed that the poly (adenylic + uridylic) structure[7] differs from that of poly (inosinic + cytidylic) sufficiently to affect the solubility properties.

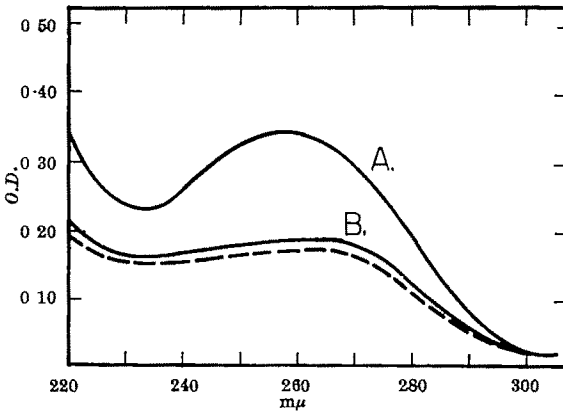

Fig. 1. Absorption spectrum of a solution originally containing $2·3 \times 10^{-5}$ M poly (adenylic + uridylic), $2·3 \times 10^{-5}$ M poly (inosinic + cytidylic), and 0 091 M pH 6·8 cacodylate buffer Total volume 1 1 ml. Curve A, before addition of spermine; Curve B, solid line, after adding 0 15 ml. of $1 25 \times 10^{-3}$ M spermine and centrifuging. Dotted line, a solution containing $2·0 \times 10^{-5}$ M poly (inosinic + cytidylic, 0 080 M cacodylate buffer, and $1 5 \times 10^{-4}$ M spermine. In all experiments spermine was added as the tetrahydrochloride

The similarity of the behaviour of these synthetic polymers to that of soluble ribonucleic acid may be accidental, but there is little doubt that fractionation of ordered polynucleotides may be effected with spermine, and that this fractionation has a pH dependence resembling that of soluble ribonucleic acid. Further investigations with complexes of the co-polymers poly (adenylic; uridylic) and poly (inosinic; cytidylic) are in progress

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LETTERS TO THE EDITORS

PHYSICS

Standard Unit of Pressure in Vacuum Physics

A UNIT of pressure in terms of the height of the column of a liquid manometer is essential, since such an instrument, including the compression manometer (McLeod gauge), is indispensable in the measurement of low pressures. Even in the recent methods[1] developed for measuring pump speeds and calibrating vacuum gauges, in which the only magnitude needed to be determined accurately is a rate of gas flow, manometers are required.

The use of the existing practical unit (mm. mercury) has already been challenged by the tremendous development of the physics and technology of vacuum. This unit is characterized by the following features: (1) It does not express a pressure in the basic terms of force per unit area. (2) It is not related decimally to the absolute units of pressure. (3) Its value is affected by temperature and geographical position. While the third characteristic appears to be a disadvantage which can be eliminated by the application of some corrections, the second characteristic would require fundamental alteration in the definition of the unit.

The pressure h in mm. mercury is evaluated by applying the hydrostatic equation $p = g\,\Delta\,uh$, where p is the absolute pressure in C.G.S. units and $u = 1$ mm. $= 0{\cdot}1$ cm. is the unit of the column height. Since gravity $g = 980\,665$ cm. s.$^{-2}$ and mercury density $\Delta = 13{\cdot}5951$ gm. cm.$^{-3}$ at 0° C. are considered as standard values, we obtain for $h = 1$ mm. mercury:

$$1 \text{ mm. mercury} = g\,\Delta\,u = 1{\cdot}333,22 \times 10^3 \text{ dyn. cm.}^{-2}$$

All previous suggestions[2] aimed at standardization of the pressure unit have not sought to alter this relationship in such a way that p and h would become simply related. In the following I will discuss this possibility as a practical proposition.

The main point is to transform the above relation into:

$$g\,\Delta\,u = 10^n$$

where n is an arbitrary integer. Here only u and g can vary, the latter factor being limited between 978 and 983, the gravity at the equator and pole, respectively. It results that u has two limits $u_1 = 0{\cdot}07482 \times 10^{n-3}$ cm. and $u_2 = 0{\cdot}07526 \times 10^{n-3}$ cm. An acceptable magnitude for practice would be $u' = 0{\cdot}075$ cm. $= 3/4$ mm. From this assumption it follows $n = 3$ and for gravity the value $g' = 10^6/75\,\Delta$ cm. s.$^{-2}$ or $g' = 980{\cdot}7455$ cm. s.$^{-2}$ within one part in 10^5.

Thus we have:

$$p = g'\,\Delta\,u'h' = 10^3h' \text{ dyne cm.}^{-2}$$

The pressure corresponding to $h' = 1$, that is, $p = 10^3$ dyne cm.$^{-2}$, may be taken as standard unit and conveniently termed 'vac'. This pressure unit, 1 vac $= 10^3$ dyne cm.$^{-2}$, corresponds to a mercury column of exactly 0·75 mm. height under the conventional conditions: g' as above and $\Delta = 13{\cdot}5951$ gm. cm.$^{-3}$ at 0° C. Therefore, pressures expressed in vac are measured by taking 0·75 mm. instead of 1 mm. as unit of the mercury column. Since 0·7500615 mm. mercury $= 10^3$ dyne cm.$^{-2}$, 1 vac may for all practical purposes be equated to 3/4 mm. mercury within less than one part in 10^4.

Recommendation of vac as standard unit of pressure would require the adoption of the conventional value g', which is different from the standard gravity. Such a decision will not cause any confusion because the latter value has little use in vacuum physics. However, vacuum physicists will greatly benefit by simplification of conversion to the absolute unit. No complications regarding the recalibration of vacuum gauges are involved.

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Radiative Recombination in Gallium Phosphide Point-Contact Diodes

CAREFUL observation of the radiation emitted from point-contact gallium phosphide diodes under conditions of reverse bias has shown that the luminescence is associated with the recombination of carriers in the breakdown region of the current-voltage characteristic. Electroluminescent radiation has been observed in gallium phosphide by several workers[1-5]. The electroluminescence appears to be associated with p–n junctions formed between the p-type bulk and an n-type skin on the surface of the material and at grain boundaries. From measurements of optical absorption in gallium phosphide, a value for the energy gap at room temperature of 2·19 eV. was deduced. This value is in good agreement with the value of 2·20 eV. for the room temperature band gap measured at Bell Telephone Laboratory[6].

We obtained a measurement of the energy spectrum of the recombination radiation by a simple and convenient arrangement of a diffraction grating and a 35-mm. camera. A diffraction grating with 15,000 lines per inch was attached to the 50-mm. extension bellows of an Exakta camera, and a 100-μ slit was affixed in the focal plane of the lens. With this arrangement, both zero-order and first-order spectra are visible on a single frame. The gallium phosphide luminescence was exposed through the slit to Ansco Super Hypan film for times up to 30 min. Fig. 1 is a print of one such exposure (×10). (The zero-order spectrum is not shown.) The two discrete lines at the left of the figure are the two prominent lines from the spectrum of gallium (4033 Å. and 4172 Å.), and are used for calibrating the spectrograph. They may be obtained by producing an arc between the point contact and the gallium phosphide crystal after the exposure of the recombination radiation has been made. Fig. 2 is a densitometer trace of the negative showing the wave-lengths and energies of the observed radiation. Correcting for the spreading effect due to the width of the slit, the energy of the recombination radiation is here observed to be between 1·96 and 2·19 eV., with a peak density at 2·12 eV. The peak

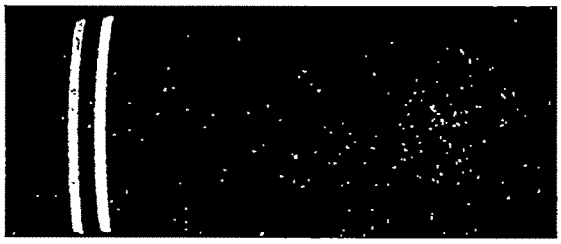

Fig. 1. First-order spectrum of recombination radiation from gallium phosphide point-contact diode

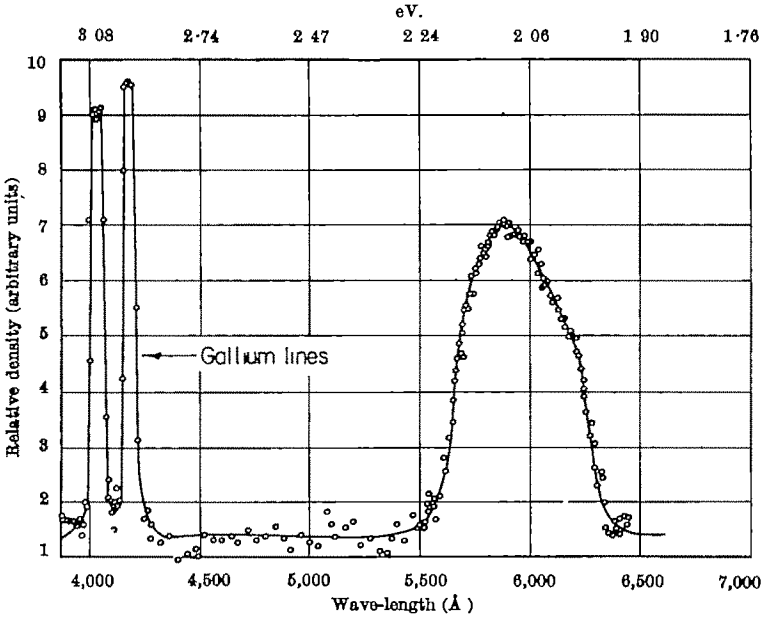

Fig. 2. Densitometer trace of the first-order spectrum of recombination radiation from gallium phosphide point-contact diode

density and minimum energy values correlate with those published by Wolff *et al.*[1]. However, interestingly enough, our maximum energy 2·19 eV. corresponds closely to our measured value of the minimum energy between the conduction and valence bands, and Wolff's maximum energy 2·32 eV. corresponds to his measured value of the band gap. Although the actual operating temperature of the diode was not determined, operation of the device in the breakdown of the reverse characteristic dissipated sufficient heat to increase its temperature significantly. Therefore, deductions concerning the probability of direct interband transitions from our results are not made, pending precise temperature measurement and control of the diode under operating conditions. The point-contact gallium phosphide diodes were prepared from small single crystals of *p*-type material, grown by the vapour-phase transport of the compound. A rather wide range of peak reverse voltages was observed, varying from 10 to 60 V. The slope of the reverse characteristic of the breakdown region also varied from diode to diode, and in some cases multiple slopes were observed.

It has been shown that in some silicon junctions, avalanche breakdown is accompanied by the emission of light at isolated points which are presumably associated with regions where dislocations pass through the junction[7]. Goetzberger and Shockley[8,9] have recently shown that the multiple slopes seen in the breakdown region of some silicon junctions are associated with isolated areas of high density of impurity which penetrate the *p–n* junction. Such a correlation between the onset of luminescence at isolated points in the breakdown region and discontinuities in the slope of the reverse characteristic was observed in our gallium phosphide junctions. The luminescent points appeared to be on the top surface of the crystal and were generally separated from the point contact, indicating that rectification was not restricted to the point contact, but was also evidently associated with a junction between an *n*-type surface skin and the bulk *p*-type material. Fig. 3 is the drawing of an oscilloscope trace of the reverse characteristic of a point-contact gallium phosphide diode. As the voltage was increased, new points of luminescence were observed to appear at the same voltages as the discontinuities in the slope of the reverse characteristic.

Appreciation is expressed to J. F. Miller for preparing the gallium phosphide and to Dr. P. W. Davis for the band-gap determination.

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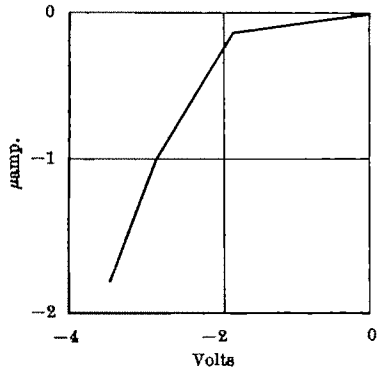

Fig. 3. Reverse characteristic of gallium phosphide point-contact diode

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Determination of Fluid Saturation in Porous Media by a Radio-Frequency Method

A KNOWLEDGE of fluid saturation at any one cross-section is very often required when studying fluid behaviour in porous media. Investigators measuring this have employed a variety of techniques including resistivity methods[1,2], radioactive tagging of a fluid[3], X-rays[4], and light absorption[5]. Very often it is required to know the extent of saturation of water or a water solution in a porous medium. Since water has a high dielectric constant, it has seemed worth while to consider a method which is dependent on this fact, and which would be used primarily for water or water solution. The technique proposed here has its origins in high-frequency titrations[6,7], where a high-frequency signal is fed into an electrode or coil on the titration cell. Changes in composition during the course of a titration are then measured in terms of change in current or voltage of the plate or grid of the oscillator valve or change in frequency of the oscillator. A change in degree of saturation in a porous medium will produce a similar loading effect in an oscillator as a high-frequency titration, and consequently, a similar method of detection may be employed.

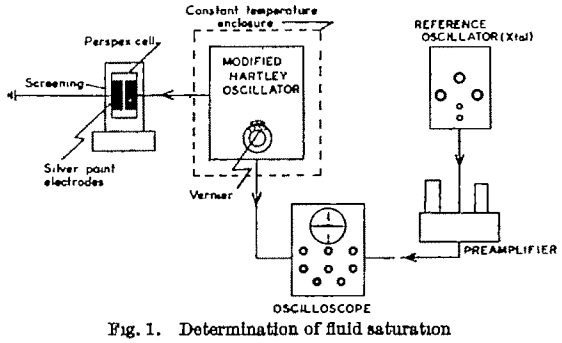

Fig. 1. Determination of fluid saturation

In the present arrangement (Fig. 1) the signal from a modified Hartley oscillator was fed into a silver paint electrode on one-half of a 'Perspex' cell (internal diameter and height 4 and 8·9 cm. respectively) and to the X-plates of an oscilloscope (Heathkit *O*-11). The electrode on the opposite side of the cell was earthed and the cell was screened by surrounding it with a copper shield. The signal from the crystal-controlled reference oscillator (a Heathkit *TO*-1 Colpitts oscillator) was sent to a 4-watt pre-amplifier (General Electric Phono-mic) and the amplified signal fed into the Y-plates of the oscilloscope. Two frequencies were used in the present work, 500 kc./sec. and 1,000 kc./sec., by selecting the appropriate crystal in the reference oscillator. It was found in the initial experiments that the oscillator was quite sensitive to temperature, and a slow frequency drift took place at room temperature. To obviate this difficulty the oscillator was enclosed in a constant-temperature cabinet.

With the cell empty, the variable oscillator was tuned to the frequency of the reference oscillator by means of a vernier on the variable capacitor of the oscillator. The point at which both signals were in phase on the oscilloscope served as an initial reference point. The cell was then packed with an unconsolidated silica sand of -30 $+40$ U.S. sieve size and the oscillator re-tuned to reference oscillator frequency. This point served as a reference point for the subsequent measurements with a fluid in the porous medium. The extent of fluid saturation of the packed cell was measured by the change in capacitance in the Hartley circuit in terms of vernier divisions, at balance, from that for the dry medium. Removal of the cell from the oscillator signal cable for unpacking could result in a capacitance change when the cell was replaced: however, with experience it was found that the initial reference point could be attained by adjustment of the position of the cable.

A series of fluid saturations was obtained by mixing a known quantity of fluid, in this case distilled water or 0·05 *N* sodium chloride solution, with a known quantity of sand and packing the resultant homogeneous mixture into the cell, *in situ*. Porosity of the medium was $34{\cdot}3 \pm 0{\cdot}3$ per cent for the complete range of saturations up to 100 per cent. Measurements were made of change in capacitance or frequency change in terms of difference in vernier reading (reading for cell with fluid minus reading for cell without fluid) over the range of saturations from 0 to 100 per cent.

When fluid saturations exceeded 30–40 per cent a slow frequency drift took place, always in the same direction. This was attributed to gravity drainage. When conditions had stabilized, vernier settings could be reproduced for the same fluid saturation to within less than $\pm 0{\cdot}1$—the total vernier difference being of the order of 50 divisions, for 0–100 per cent fluid saturation. The overall effect of gravity drainage was to cause a difference of vernier reading of up to 0·4 of a division from the initial reading—this corresponded to a variance in the fluid saturation of up to 5 per cent. Since this distribution of fluid could not be handled quantitatively the readings for a particular fluid saturation were taken at time $t = 0$, that is, before any drainage took place. The effect of gravity drainage on the capacitance or vernier reading is illustrated for a number of fluid saturations in Fig. 2. It can be seen that the system may take as much as one hour to become stable. The curves illustrating the relationship between fluid saturation and capacitance (vernier reading difference) are shown in Fig. 3. It is apparent from the general shape of the curves that the greatest sensitivity of the method is in the regions of low saturation. In addition,

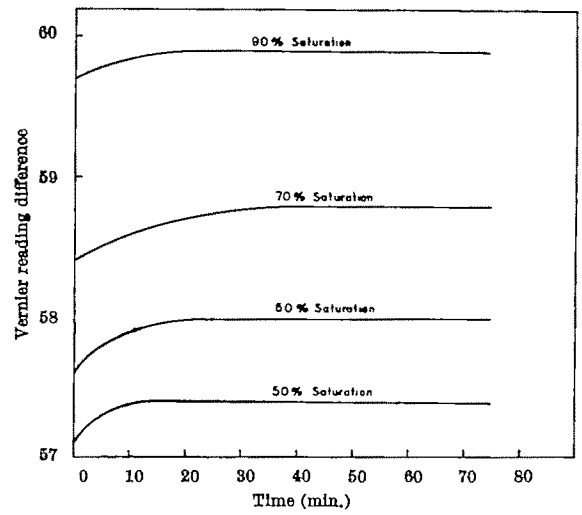

Fig. 2

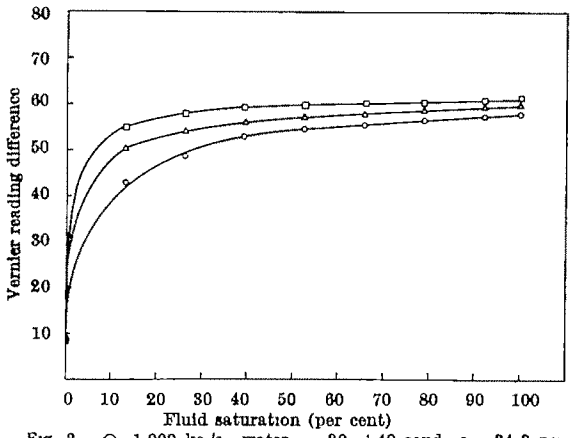

Fig. 3. ○, 1 000 kc./s., water, − 30 +40 sand, ε = 34 3 per cent; △, 500 kc/s, water, − 30 + 40 sand, ε = 34 3 per cent, □, 1,000 kc./s, 0 05 *N* sodium chloride solution, − 30 + 40 sand, ε = 34 3 per cent

increase of frequency appears to change the curvature, increasing the extent of the sensitive range. In the case of the 0·05 *N* sodium chloride solution the curve is displaced in such a manner as to decrease the sensitive range, and at any particular fluid saturation this is an analogous situation to a high-frequency titration, in that changes in concentration are being measured at constant saturation.

Further investigations of this method of measuring fluid saturation in porous media are continuing with the aim of increasing the range of sensitivity by the use of higher frequencies.

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GEOPHYSICS

Unidentified Earth Tremors in Dominica, West Indies

TREMORS the origin of which has not been identified were recorded by our seismograph station at Roseau in the volcanic island of Dominica during September 1959, and have been recorded at irregular intervals ever since.

Each tremor consists of an approximately sinusoidal ground motion of 0·3-sec. period. The first swing is always down, the first and eighth swings are maxima and there are about twelve swings in all. The ground amplitude of these maxima varies from about 0·1μ, which is the point at which the tremors become masked by the microseismic background, to 1 0μ. They are quite unlike the tremors produced by near earthquakes or by explosions on land or at sea. Factories, quarries and other possible artificial sources for the tremors in Dominica have been investigated and eliminated.

The tremors tend to occur in bursts, numbering from two or three to several hundred tremors, which may start at any hour of the day or night and continue for periods up to twelve hours. The average period between bursts has been seven days, but there is no evidence of periodicity.

We have operated three additional Willmore–Watts seismographs in Dominica for six weeks in January and February 1960 and have found that the tremors can be recorded only within a few kilometres of the town of Roseau. Because of long quiet periods between bursts of activity, useful recordings were obtained only of a burst of five tremors at one station 1 km. from the Roseau Station and at the Roseau Station itself. There is a possible correlation between the differences in arrival times and the ratios of the maximum amplitudes of the tremors at the two stations, which is consistent with each tremor having originated at a point source and having obeyed an inverse square law of attenuation. Assuming such an attenuation law the amplitudes at the two stations indicate that the sources lie close to a circle of about 5 km. diameter, the northern part of which passes through the town of Roseau. The differences in arrival times at the stations indicate a seismic velocity between 150 m./sec. and 740 m./sec. depending on the locations of the sources on the circle.

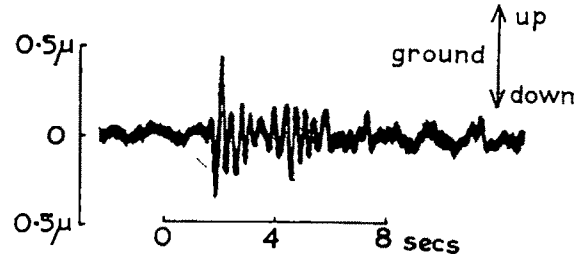

Fig. 1 Unidentified earth tremor recorded at the Seismic Research Unit's Seismograph Station at Roseau, Dominica, on September 11, 1959

The town of Roseau is situated on a delta of sand and gravel built by the Roseau River on the steeply shelving east coast of the island of Dominica. In such materials the velocity of longitudinal waves is about 750 m./sec. We have estimated the energy release at the source as about 10^{14} ergs for the largest tremor recorded. The island contains several active thermal areas and ancient centres of eruption, but none is near the apparent sources of the tremors. We can find no evidence that these are related in any way to the volcanic activity of the island; but we cannot put forward an alternative explanation for their origin. We should be grateful to hear from others who have had experience of similar tremors.

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CRYSTALLOGRAPHY

Crystal Structure of Orthorhombic Cobalt Molybdate

IN petroleum refinery practice de-sulphurization is carried out by catalysts consisting of an η- or γ-type alumina impregnated with cobalt and molybdenum oxides. However, the nature of the cobalt and molybdenum compound or compounds present on

the catalyst is quite unknown, and a search through the literature reveals that there is almost no information on the formula and crystal structure of cobalt molybdate. A mineral paterite is known which is quoted as having the formula $CoMoO_4$ [1].

A series of iso-structural normal tungstates of small cations is known[2] the general formula of which is RWO_4, where R = cobalt, iron, magnesium, manganese, nickel and zinc, and recently the structure of nickel tungstate has been investigated in detail[3]. Powder diffraction patterns of laboratory and commercially prepared cobalt molybdate, after heating to 700° C., show that the compound does not possess a structure isomorphous with the tungstate family. However, normal molybdates and tungstates of larger cations, for example, barium, calcium, cadmium, lead and tin, are known and form an iso-structural series, the parent structure being scheelite.

In order to provide fundamental information, attempts were made to grow single crystals of cobalt molybdate from a melt of normal sodium molybdate, anhydrous cobalt chloride and sodium chloride as a flux in the ratio of 1 : 2 : 2 by weight. The melt was kept at 750–800° C. for 2 hr. and allowed to cool slowly in the furnace. Small yields of crystals were obtained, but the quantities available were too small for accurate analysis. The percentages by weight from chemical and spectroscopic analyses are given in Table 1, leading to an empirical formula of $Co_2Mo_3O_{11}$.

Table 1

	Cobalt	Molybdenum
Chemical	21 1	45·8
Spectroscopic	20·1	51 2

Examination of the crystals in polarized light and subsequent X-ray photographs showed that monoclinic and orthorhombic crystals were present, both forms being deep blue in colour and possessing well-marked crystal faces. The monoclinic crystals will not be reported on here. The orthorhombic crystals possessed two well-formed crystal habits which were either long thin needles up to 2 mm. in length by 0·1 mm. × 0·1 mm. cross-section, or platelets with dimensions up to 1 mm. long × 0·3 mm. wide but only 0·01 mm. thick, with a pair of edges parallel to the long dimension. X-ray photographs showed that the shortest unit cell axis a was parallel to this dimension and to the needle axis, while the longest unit cell axis c was perpendicular to the plane of the platelet. The crystals showed straight extinction, and an acute interference figure was obtained on (001). The crystals are positive with α parallel to b, β parallel to a and γ parallel to c. No attempt was made to measure $2V$ or any of the refractive indices.

Laue and symmetrical oscillation photographs about all the axes confirmed the orthorhombic symmetry, and from rotation and zero layer Weissenberg photographs using copper $K\alpha$ radiation the unit cell dimensions were calculated: $a = 5{\cdot}245 \pm 0{\cdot}003$ Å., $b = 10{\cdot}778 \pm 0{\cdot}005$ Å., $c = 18{\cdot}017 \pm 0{\cdot}006$ Å., $V = 1018{\cdot}5 \pm 2$ Å.^{3}. The error is an estimated one.

The density was found to be $3{\cdot}79 \pm 0{\cdot}05$ gm./c.c. by flotation in a solution of thallous malonate and formate, leading to four formula units of $Co_2Mo_3O_{11}$ in the cell. Theoretical density = 3·80 gm./c.c.

Zero and upper-layer Weissenberg photographs about each axis showed that all hkl reflexions were present and that systematic absences were observed for $0kl$ with $(k+l)$ odd and for $hk0$ with h odd. The space group is therefore either $Pn2_1a$ or $Pnma$. A simple test for pyroelectricity was inconclusive, but the application of intensity statistics[4] to the principal zones $hk0$, $0kl$, $h0l$ and to all hkl reflexions showed that the distributions were centric. Space group $Pnma$ was therefore adopted.

A crystal fragment 0·3 mm. × 0·15 mm. × 0·2 mm. was cut from one of the largest needles, and zero-layer Weissenberg photographs about the three axes and equi-inclination photographs of layers h = 1 to 8 about the a axis were taken on molybdenum $K\alpha$ radiation using the multiple film technique. The intensities of all reflexions were measured out to the maximum limit of observation ($\theta \simeq 45°$). In all 103 $hk0$, 294 $h0l$, 314 $0kl$ and 2,412 hkl non-zero independent reflexions were measured by visual comparison with a calibrated strip. The intensities were corrected for the Lorentz and polarization factors to give a set of relative $|F|^2$. No absorption correction was applied as the crystal was of optimum size μ = 75 cm.$^{-1}$. Wilson's method was used for placing the relative $|F|^2$ on an absolute scale and for deriving the temperature factor. B = 1·29 Å.^{2}.

Patterson projections down the a and b axes, both sharpened and unsharpened, were calculated together with the complete three-dimensional Patterson function. The calculations were made on a *Deuce* computer using a programme written by Dr. J. S. Rollett (University of Oxford). The three-dimensional Patterson function was calculated over one-eighth of the unit cell at intervals of $u = 1/20$, $v = 1/80$, $w = 1/120$ and plotted in eleven sections parallel to the bc plane. Because of a limitation in the storage on *Deuce* the number of reflexions was restricted to about 2,350 and the calculation took 8½ hr.

The projection $P(u, w)$ showed special features in that nearly all the peaks were concentrated on the two lines $u = 0$ and $u = \frac{1}{2}$ with a very large peak, 75 per cent of the origin peak height, at $(0, \frac{1}{2})$. Some of the peaks were elongated in the u direction and only two shallow peaks existed elsewhere in the function. It was therefore clear that the cobalt and molybdenum atoms must all lie in or very close to the n glide plane. The projection $P(v, w)$ gave a well-resolved map, but no attempt was made to solve it directly and all the heavy atom co-ordinates were derived from $P(u, v, w)$.

Nearly all the peaks in $P(u, v, w)$ were concentrated in the sections $P(0, v, w)$ and $P(\frac{1}{2}, v, w)$, both of which showed apparent two-fold symmetry, about $(0, \frac{1}{4}, \frac{1}{4})$ and $(\frac{1}{2}, \frac{1}{4}, \frac{1}{4})$ respectively, of peak position but not peak height. The absence of peaks at $(0, \frac{1}{2}, 0)$, $(\frac{1}{2}, 0, \frac{1}{2})$ and $(\frac{1}{2}, \frac{1}{2}, \frac{1}{2})$ clearly indicated that no heavy atoms were sited on the centres of symmetry. They are therefore either in the general positions or on the mirror plane. Co–Co, Mo–Mo, Co–Mo, Mo–O and Co–O single interaction peaks were scaled in terms of the origin peak, and from a study of all the Harker symmetry vectors for the general and special positions it was possible to derive the co-ordinates of all the heavy atoms. Eight cobalt and eight of the molybdenum atoms were sited in the general positions and the remaining four molybdenum atoms on the mirror plane. The non-Harker vectors were calculated from these co-ordinates, which gave satisfactory agreement between peak heights and positions and accounted for all the major peaks in $P(u, v, w)$.

The co-ordinates are:

		x	y	z
General positions	8 cobalt	0 250	0 075	0·473
	8 molybdenum	0 278	0 017	0·155
Special positions	4 molybdenum	0·278	0·250	0·944

So far as could be detected the cobalt atoms were sited in the n glide planes with both sets of molybdenum atoms distributed a little to each side of it.

It was not possible to derive any information about the positions of the oxygen atoms as single Co–O or Mo–O peaks were not above the background of the function. Typical Mo–O distances vary between 1·75 and 2·2 Å. and Co–O distances are about 2·0 Å.; but there were no well-defined peaks around the origin peak and within these limits. A ring of high ground was present in the sections for which u = 3/20, 4/20 and 5/20. Buergers minimum function $M_2(yz)$ was applied twice to $P(v, w)$ using Co–Co and Mo–Mo rotation peaks, confirming the positions of all the heavy atoms, but the positions of the oxygen atoms were not resolved.

The unit cell projected on the 100 face is shown in Fig. 1, from which it is seen that the molybdenum atoms appear to lie at the corners of a puckered hexagon. The interatomic distances around the hexagon are almost equal at 4·3 Å. with somewhat larger distances between the hexagons of 4·5–5·0 Å. These distances are considerably larger than those found in the oxides Mo_4O_{11}, Mo_8O_{23}, Mo_9O_{26} and MoO_2, where the structure is composed of linked octahedra for which Mo–Mo = 3·25 Å. for octahedra sharing edges and 3·75–3·8 Å. for octahedra sharing corners. In unlinked octahedra Mo–Mo = 3·92–3·96 Å. It seems clear that octahedral co-ordination is not present in this structure but that free unlinked $(MoO_4)^{--}$ exist. If this is so, then there must be 48 oxygen atoms in the cell and the chemical formula must be revised to $Co_2Mo_3O_{12}$.

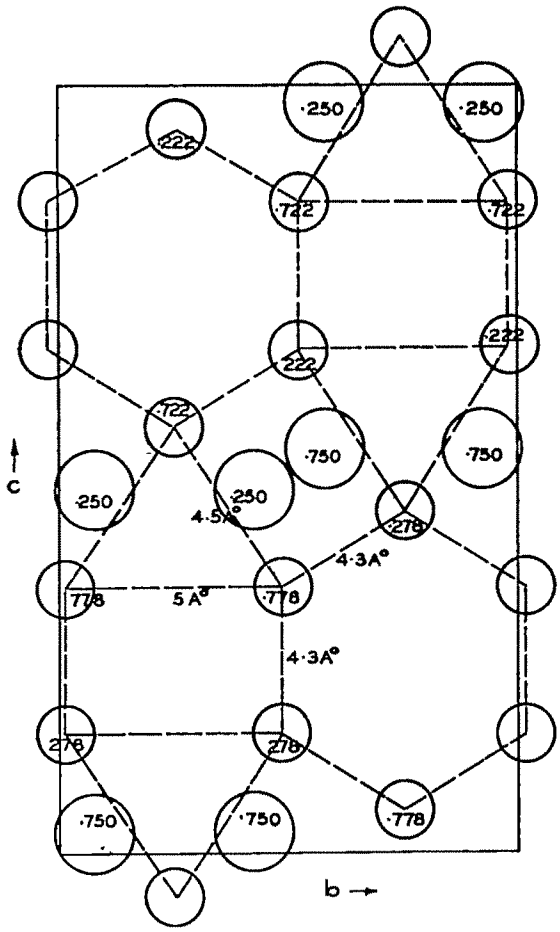

Fig. 1. Projection on bc plane. Large circles, cobalt; small circles, molybdenum

I wish to thank the Chairman and Directors of the British Petroleum Co., Ltd., for permission to publish this communication. Thanks are also due to Mr. L. A. Lloyd, who helped in the measurement and statistical analysis of the intensity data, and to Mr. D. Alderton, who made the calculations.

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METALLURGY

Frictional Properties of Molybdenum Disulphide Films containing Inorganic Sulphide Additives

SOLID lubricants are most useful as films which separate metal surfaces that slide against each other. To be effective, the films should be highly durable. Recently, we have observed that inorganic additives can greatly enhance the durability of such films.

During the course of some work on the frictional properties of lamellar sulphides which crystallize in the cadmium iodide system, it was observed that though stannic sulphide displayed relatively high friction, it formed excellent films when rubbed over a metal surface. In such an experiment good filming is an essential property which the inorganic solid must possess if it is to lubricate effectively. When an adherent film is formed on the metal, shearing is confined to the film and the sliding behaviour is that of the lubricant against itself. It was observed that the filming properties of molybdenum sulphide, which is an excellent lubricant, could be enhanced by adding 10 per cent by weight of stannic sulphide. However, a number of additional unexpected synergistic effects were also noted. The most important of these was an improved resistance of the films to penetration under highly loaded sliding conditions. An experimental programme was initiated to find other effective sulphide additives, and some of the results are briefly summarized here.

Rider samples were prepared from powders of high-purity molybdenum disulphide, and 10 per cent by weight of finely ground sulphide additives. The solids were mixed, passed through a 200-mesh screen and compressed into $\frac{5}{16}$-in. diameter pellets at a pressure of 20,000 p.s.i. without the use of added binder. The riders were rubbed against disks of degreased and de-oxidized mild steel which had been cut from rolled sheets.

The test procedure, which used a friction dynamometer designed by E. H. Hull[1], has been described in detail[2]. Briefly, lubricant riders were rubbed against the steel at a load of 2 kgm. and a speed of 70 cm./sec.

for several hours to establish a film. Then a $\frac{1}{8}$-in. diameter chrome alloy steel hemisphere was slid over the film at the same speed. Load was increased in 50-gm. increments according to a standard schedule until film failure (metal-to-metal contact or seizure) was indicated by a precipitous rise in friction. Observations were taken in room air at 25° C. within the relative humidity range of 30–40 per cent. The seizure loads attained with a number of additives together with the minimum values of coefficient of friction for the films are reported in Table 1.

Table 1

Additive	Coefficient of friction	Maximum load carried (kgm.)	Additive	Coefficient of friction	Maximum load carried (kgm.)
Sb_2S_3	0 057	5 8	ZrS_2	0·061	2 3
PtS	0 056	5·5	HgS (black)	0 048	1·8
TiS_2	0 04	5·4	Tl_2S_3	0·060	1 5
HgS (red)	0 038	5·3	Cr_2S_3	0·08	1·2
Ag_2S	0·06	5 3	BaS	0 07	1 0
PbS	0 038	5·2	Tl_2S	0 082	0·9
FeS	0·063	4·9	SnS	0·07	0 9
Tl_2S_3	0·065	4·9	CaS	0·15	0·9
Cu_2S	0 064	3·9	CdS	0 14	0·8
CuS	0·059	3·6	FeS_2	0·40	0·3
Au_2S	0·065	2·8	ZnS	—	0 3
Bi_2S_3	0·045	2 9	MoS_2	—	0 3
SnS_2	0·047	2 8			

For the most favourable case the additive increases the seizure load for the film by more than a factor of twenty over that for a pure molybdenum disulphide film. The low friction values indicate that molybdenum disulphide is the lubricant in all cases and that the additives probably take little part in any shearing phenomena. Similar results were obtained when tungsten disulphide was the lubricant in place of molybdenum disulphide. For substrates harder than mild steel (for example, 1090 steel, chromium plate) the seizure loads observed are even greater.

The action of these additives in solid lubricants resembles that of the extreme pressure additives for liquid lubricants. A chemical role is assigned to such additives, and a similar mechanism may explain the behaviour of additives in solid lubricant films. However, evidence to support this hypothesis is indirect. Where thermodynamic data are available, the most effective additives tend to have the lowest stability. Films of molybdenum disulphide have higher load-carrying ability if they are applied to mild steel surfaces on which a surface film of ferrous sulphide has been formed by chemical reaction. Chemical analyses indicate that an active additive tends to be more concentrated in a rubbed film than in the rider from which the film was rubbed.

Though the hypothesis of chemical attack by the additives is attractive, the results do not preclude the possibility that effects other than chemical are important in enhancing the adhesion of the film to the metal substrate.

It is planned to publish a more detailed account of this work elsewhere.

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RADIATION CHEMISTRY

Effect of X-Rays on Cytosine in Aerated Aqueous Solution

WHILE X-irradiation of aqueous solutions of thymine and uracil in an atmosphere of air gives rise to high yields of hydroperoxides[1-3], X-irradiation of cytosine under similar conditions does not give more than traces of hydroperoxides in our hands.

However, ion exchange chromatography of cytosine solutions irradiated with X-rays under air or oxygen (1 atm.) separates three degradation products, which are not detected when the solutions have been irradiated under nitrogen. A typical elution diagram is shown in Fig. 1, giving the positions of these three products, designated as *A*, *B* and *C*, and of unchanged cytosine. Product *C* and cytosine are detected by measuring the optical densities of the chromatographic fractions at 300 mμ and at 275 mμ, respectively. Products *A* and *B* are not detected under these conditions, since they do not absorb strongly at these wave-lengths; but if the fractions containing them are first boiled for 30 sec., their optical densities at 275 mμ increase to give the figures plotted in Fig. 1, products *A* and *B* being transformed by heating into compounds with high absorption coefficients at this wave-length.

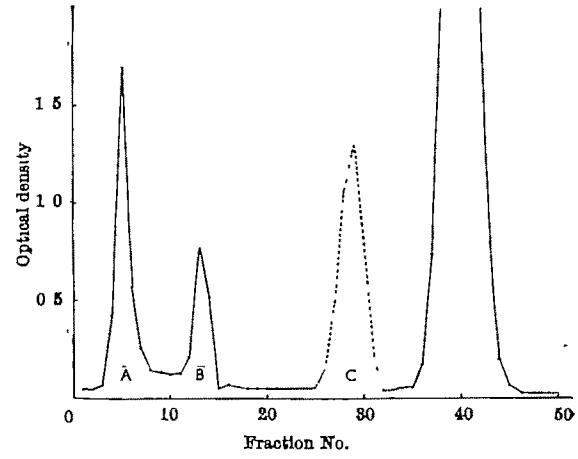

Fig. 1. Ion exchange chromatography of X-irradiated cytosine. Cytosine solution: 10^{-3} *M* in water, 40 ml., irradiated in the presence of air at room temperature. X-rays: 40 kV., filtered through 0 04 mm. aluminium; dose-rate: 25 kr./min.; dose = 150 kr. Chromatography on 'Dowex 50, H^+' (125 cm.), elution with 2 *N* hydrochloric acid at room temperature; fraction volume: 3 ml. ——, Optical density at 275 mμ; – – –, optical density at 300 mμ. Fractions 1–16 have been heated to boiling

Product *C* has been compared with synthetic 2,5-dioxo-6-aminopyrimidine (6-amino-*iso*-barbituric acid), prepared according to Johnson *et al.*[4]. The ultra-violet absorption characteristics of product *C* and of 6-amino-*iso*-barbituric acid are recorded in Table 1. The two compounds cannot be separated from each other by paper chromatography (Table 2) or by ion-exchange column chromatography. By heating product *C* in a sealed tube at 175° for 4 hr., a compound is formed having the absorption spectrum (Table 1) and the chromatographic behaviour (Table 2) of synthetic *iso*-barbituric acid, obtained by deamination of 6-amino-*iso*-barbituric acid under the same conditions[4]. All these results allow us to conclude that product *C* actually is identical with 6-amino-*iso*-barbituric acid. Under the conditions

of the experiment described in Fig. 1, the yield in product C is $G = 0{\cdot}34$.

When product A is heated to boiling in 2 N hydrochloric acid, the resulting compound has the same ultra-violet spectrum (Table 1) and the same chromatographic behaviour on paper chromatograms (Table 2) as *iso*-barbituric acid. The yield in product A, estimated after transformation to *iso*-barbituric acid, is $G = 0\ 20$. When product B is similarly heated, ion exchange chromatography of the resulting solution separates two products B_1 and B_2. Product B_1, which is much more abundant than B_2, has the same ultra-violet spectrum (Table 1) and the same chromatographic behaviour (Table 2) as *iso*-barbituric acid. B_2, on the other hand, has the same spectral and chromatographic properties as 6-amino-*iso*-barbituric acid. If product B is heated at a nearly neutral pH, the same compounds are also produced, but the yield in the 6-amino one is increased relatively to that of the free acid. Since products A and B have no absorption bands between 250 and 300 mμ, their 4,5 bond is presumably saturated. B differs from A by having a 6-amino group, which is more easily lost than the amino group of 6-amino-*iso*-barbituric acid. It can be recalled in this respect that Green and Cohen[5] have already shown that 4,5-dihydrocytosine is very easily deaminated.

When synthetic 6-amino-*iso*-barbituric acid itself is X-irradiated in the presence of air (10^{-3} M solution receiving 300 kr.), *iso*-barbituric acid is formed, but no product B.

We think that the preceding experimental results can best be explained by assuming that products A and B have the formula shown in Fig. 2, and are related to cytosine through a hypothetical highly unstable hydroperoxide, since they are not produced in the absence of oxygen.

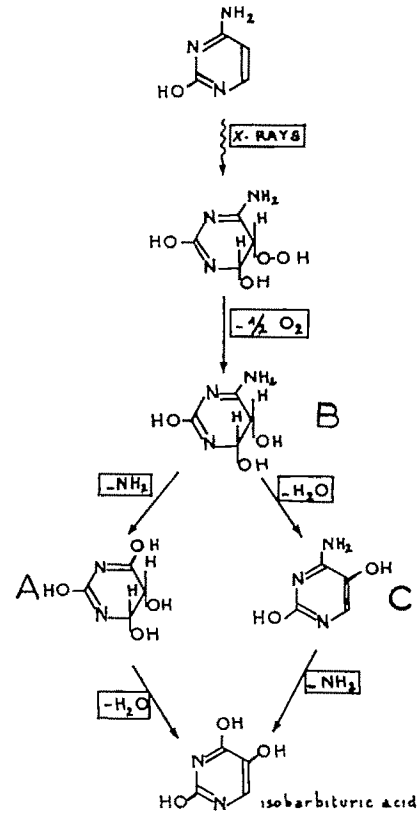

Fig. 2

Table 1. ULTRA-VIOLET ABSORPTION DATA

	pH 1			pH 11		
	Maximum (mμ)	Minimum (mμ)	$\epsilon_{max} \times 10^{-3}$	Maximum (mμ)	Minimum (mμ)	$\epsilon_{217\cdot5} \times 10^{-3}$
6-Amino-*iso*-barbituric acid	215 300	250	5 38	221 317 5	273	4·2
iso-Barbituric acid	276	246	—	307	272	—
C	215 299	250	—	221 317·5	272 5	—
C (heated at 175° for 4 hr.)	276	246	—	307	272	—
A (heated to boiling)	275	246	—	307	272·5	
B (heated to boiling) B_1	276	246	—	307	272·5	
B_2	215 300	250	—	221 317 5	272 5	

Table 2. R_F OF COMPOUNDS ON PAPER CHROMATOGRAMS*

	n-Propanol/water (10 : 3)	*iso*-Butyric acid/water/conc. ammonia (100 : 52 : 1 12)	*iso*-Propanol/water/conc. hydrochloric acid (65 : 18·3 : 16·7)
Uracil	0 53	0 62	—
Cytosine	0 42	0 73	0·55
6-Amino-*iso*-barbituric acid†	0 37	0 67	0 50
iso-Barbituric acid	0 43	0 43	—
6-Aminobarbituric acid	0 87	—	0 91
C	0·37	0 67	—
C (heated at 175° for 4 hr.)	0·43	—	—
A (heated to boiling)	0 43	0 41	—
B (heated to boiling) B_1	0 43	0 44	
B_2	0·37	0 73	—

* Development by gravity on Whatman No. 1 paper.
† Gives a blue fluorescence when irradiated with λ 2537 Å.

We wish to thank Dr. R. Latarget for his interest throughout this work.

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CHEMISTRY

Use of Chlorine in the Detection of Compounds on Paper Chromatograms

Rydon and Smith[1] described a sensitive method for the detection of amino- and imino-compounds on paper chromatograms: the method consisted of exposure of the dried chromatograms to an atmosphere of chlorine, followed by aeration to remove 'background' chlorine, and detection of the resultant chloramines by liberation of iodine from a starch/

potassium iodide reagent. In Reindel and Hoppe's modification[2] of the procedure, the chromatograms were moistened with an acetone/alcohol mixture and exposed to gaseous chlorine in a tank before detection of the chloramino derivatives with a tolidine/potassium iodide reagent. In a further modification[3], the chromatograms were moistened with steam, exposed to gaseous chlorine, heated briefly to 50° and developed with the tolidine/potassium iodide reagent.

In our hands, both the chlorination and aeration stages of the original procedure[1] proved difficult to standardize. Prolonged aeration, which had a variable effect on the chloramino derivatives, was sometimes required to remove background chlorine. It seemed that this was necessary when the tank atmosphere was particularly humid; on these occasions, and in Smith's procedure[3], the paper presumably retained a layer of chlorine water which had to be removed by aeration, or by heating to 50°, in order to obtain a satisfactory background. The need for water in the chlorination process was suggested by unsuccessful attempts to detect nitrogenous compounds using dry carbon tetrachloride saturated with chlorine as the chlorinating reagent (unpublished results).

In preliminary attempts to replace the inconvenient tank procedure by a reliable spray reagent, different effects were observed, which were used to advantage in the procedures to be described. The spray reagents were prepared by dilution of a sodium hypochlorite solution (10–14 per cent w/v) or a potassium chlorate/hydrochloric acid reagent[4], and were applied to dried chromatograms using about 1 ml./50 cm.^{2}. In procedure (*a*) the chromatogram was sprayed with sodium hypochlorite solution diluted 1 : 150, and then left for 45 min. at room temperature. In procedure (*b*) the chromatogram was sprayed with sodium hypochlorite solution diluted 1 : 25, left 45 min. at room temperature and heated for 5 min. at 55°. In procedure (*c*), the chlorate/hydrochloric acid reagent was diluted 1 : 10 and, after spraying, the chromatogram was left for 45 min. at room temperature before heating for 15 min. at 55°. Chromatograms treated in this way were developed by immersion in a tolidine/potassium iodide reagent[2].

The effect of these procedures on a variety of sugar derivatives is shown in Table 1. It can be seen that procedure (*a*) located only amino-compounds, whereas procedure (*b*) located both amino- and imino-compounds. This provided a convenient method for distinguishing amino- and imino-compounds which was particularly useful with compounds reacting poorly with ninhydrin (for example, the anomeric 1 : 3 : 4 : 6-tetra-O-acetyl-2-amino-2-deoxy-D-glucose hydrochlorides, unpublished results).

Table 1. DETECTION OF COMPOUNDS ON PAPER CHROMATOGRAMS USING VARIOUS CHLORINATION PROCEDURES AND A TOLIDINE/POTASSIUM IODIDE REAGENT (ref. 2)

Compound*	Colour of spot obtained from compounds by procedure. *a*	*b*	*c*
D-Glucose	—	—	white
Phenyl β-D-glucoside	—	—	white
2-Amino-2-deoxy-D-glucose hydrochloride	blue	blue	—
Phenyl 2-amino-2-deoxy-β-D-glucoside	blue	blue	white
2-Acetamido-2-deoxy-D-glucose	—	blue	—
Ethyl 2-acetamido-2-deoxy-β-D-glucoside	—	blue	—
Phenyl 2-acetamido-2-deoxy-β-D-glucoside	—	blue	white
Background colour	white	pale blue	blue

* 100 μgm. was used, but less is detectable in each case.

On chromatograms developed immediately after spraying with hypochlorite, the blue spots generated by the chloramino derivatives could be distinguished only with difficulty from the dark background. The success of procedures (*a*) and (*b*) depended on being able to reduce this background colour without affecting seriously the chloramino derivatives. Certain compounds, however, showed as white spots against a blue background, indicating the removal of hypochlorite and the formation of products unable to react with the tolidine reagent. It appeared that, in contrast to tank chlorinations, the amount of chlorinating agent in the spray reagents was the limiting factor. Procedure (*c*), which used the more easily controllable chlorate/hydrochloric acid reagent to generate the background colour, was based on this effect. Table 1 shows that whereas compounds with a benzene nucleus or a reducing group (for example, phenyl β-D-glucoside, glucose) were detected, the result given by compounds containing one of these groups together with an amino- or imino-group depended on the reactivity of the groups present: the results in Table 1 indicated reactivities in the order phenyl > amino > imino > reducing group. Procedure (*c*) was the most sensitive method for the detection of some compounds, particularly the anomeric phenyl 2-acetamido-2-deoxy-D-glucosides[5].

Other chlorinating agents (for example, 'Chloramine-*T*', chlorine water) and other indicator systems (for example, starch/potassium iodide, diphenylamine, *o*-phenanthroline) were tried, but none proved so satisfactory as those described. The three procedures are reproducible and can be used for the detection of a wide range of nitrogenous, aromatic and reducing compounds on paper chromatograms. However, care may be necessary in the selection and removal of chromatographic solvents, since some of these may interfere with the detection procedures (cf. Reindel and Hoppe[2]).

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A Split-Temperature Column System for Gas Chromatographic Analyses

THIS communication describes a simple but effective improvement on the speed and resolution in gas chromatographic analyses by means of a split-temperature column system which has provisions for two or more different temperature regions in the same unit and which provides a means of changing rapidly the temperature in these various regions (patent applied for). Such a system possesses the combined advantages of a single low-temperature system, a single high-temperature system, as well as a temperature-programmed system[1], and, usually,

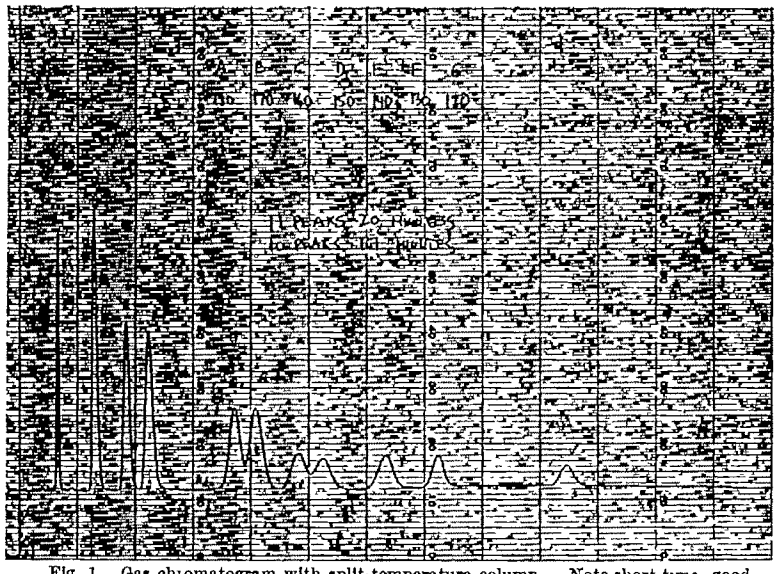

Fig. 1. Gas chromatogram with split-temperature column. Note short time, good resolution and well-defined peaks

can result in an appreciable reduction of the time required for each analysis.

Consider the analysis of a mixture containing both high- and low-boiling components. If a single low-temperature column is used, the time required to resolve the low-boiling components is sometimes unnecessarily long without any gain in resolution, whereas the high-boiling components are either held back even after a very long time, and thus cannot be detected at all, or are detected only as extremely broad peaks which cannot be accurately measured. If only a high-temperature column is used, the high-boiling components can form well-defined peaks; but the resolution of the low-boiling materials may become too poor and not useful. A manually temperature-programmed column requires considerable attention by the operator, and can give reproducible retention results only if the analysis is carried out with great care. A linear temperature-programmed system is, at least for the present, still rather expensive, and also requires longer time for analysis than the split-temperature system.

In our preliminary experiments, we used a steel enclosure consisting of seven sections individually heated by heating tapes and controlled by bimetallic thermo-regulators. These sections were partly insulated from each other by glass wool packings, and partly connected with each other by metal strips, providing thereby a sufficiently uniform temperature within each section, and a reasonably smooth temperature gradient between sections. A 10-ft. glass column, packed with 'Apiezon-*L*' on firebrick, and connected to a 'Burrell Kromotog-*K*-1', completed the chromatographic system. A mixture, consisting of (i) *n*-pentane, (ii) benzene, (iii) methyl *cyclo*hexane, (iv) toluene, (v) *o*-xylene, (vi) *m*- and *p*-xylene, (vii) ethyl benzene, (viii) *n*-propyl benzene, (ix) *i*-propyl benzene, (x) *t*-butyl benzene and (xi) *t*-butyl toluene, formed the analytical sample. In operation, portions of the column were kept initially at lower temperatures so that there would be adequate resolution for the low-boiling components, and the remainder of the column was kept at the higher ultimate temperature. After the lower-boiling components had been eluted, the whole column was brought to the ultimate temperature for the analysis of the higher-boiling substances.

A series of experiments with the various sections having different initial temperatures ranging from 120° to 180°, and an ultimate temperature of 180°, have been carried out. For the purpose of comparison, the column was also heated uniformly at 130° and at 180° only, and the corresponding chromatograms were also obtained. It was found that, for the case when the column was heated uniformly at 130° C., although the low-boiling components (i–vi) were satisfactorily resolved, the peaks for the higher-boiling components (vii–x) were ill-defined and that the peak for the highest boiling component (xi) was not detectable within a period of 1½ hr. For the case when the column was heated uniformly at 180° C., the total time required for the 11 components was 14 min.; but the resolution of components (v) and (vi) and components (vii) and (viii) was very poor and not useful. In contrast, the split-temperature column system permitted the separation of all eleven components in a time-period of 20 min. with the resolution of the low-boiling components comparing favourably with those obtained by the low-temperature column, and the resolution of the high-boiling components comparing favourably with those obtained by the high-temperature column. This is illustrated in Fig. 1, which shows clearly the satisfactory performance of the split-temperature system from the points of view of both the short time required for analysis and satisfactory resolution.

A split-temperature column system can be constructed easily and inexpensively with readily available components, and should be usable with most of the existing gas chromatographs. It permits the analysis of a larger number of samples per chromatograph, and also permits the use of one single long column for each type of packing since the effective length of a column now can be conveniently varied by changing the length of the lower-temperature portions of the column.

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Separation of Sphingosine and Dihydrosphingosine by Reversed Phase Paper Chromatography

THE isolation of dihydrosphingosine from cerebrosides of beef brain and spinal cord by Carter *et al.*[1] raised questions regarding its distribution in different sphingolipids and its metabolic relationships to sphingosine. However, no method for the routine

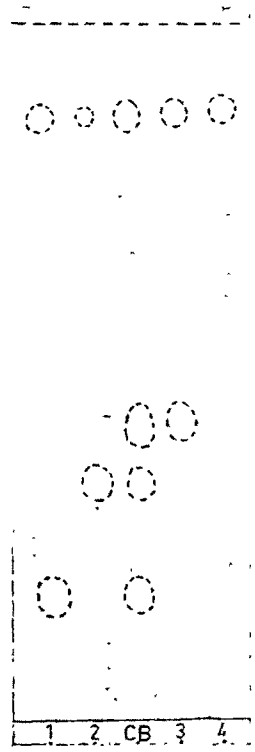

Fig. 1. Chromatogram showing the dinitrophenyl derivatives of O-methylsphingosine (1), dihydrosphingosine (2), sphingosine (3) and crude base fraction (*CB*). (4) is dinitrophenol

differentiation of sphingosine and dihydrosphingosine appeared until very recently with the gas chromatographic method of Sweeley and Moscatelli[2]. Wittenberg[3] separated the N-succinyl derivatives of sphingosine and related compounds by reversed phase chromatography on diatomaceous earth treated with dichlorodimethylsilane, but he was unable to separate sphingosine and dihydrosphingosine. This communication describes a reversed-phase paper chromatographic method for the separation of the dinitrophenyl derivatives of sphingosine and dihydrosphingosine.

A crude fraction of sphingolipid long-chain bases was prepared principally according to Carter *et al.*[1]. 1–5 mgm. of the bases were transferred to their dinitrophenyl derivatives by keeping them for 30 min. in 4 ml. of a potassium borate buffer, *p*H 10, containing 2 μl. fluorodinitrobenzene in 1 ml. ethanol at 60° C. The derivatives were extracted with diethylether and 5–15 μgm. were applied with a micropipette to Whatman paper 3*MM* on a line 2 cm. from the bottom of the paper. The paper was sprayed almost to transparency with the stationary phase of tetralin down to a line 1 cm. above the line of the derivatives. The paper was then immediately run in methanol/triethylamine/water (85 : 5 : 10 v/v) saturated with tetralin in the ascending direction for 17 hr. at room temperature. The spots were read under ultra-violet light and the R_F values obtained were for dinitrophenyl-O-methylsphingosine 0·20, dinitrophenyl-dihydrosphingosine 0·36, dinitrophenylsphingosine 0·44 and dinitrophenol 0·87 (Fig. 1). The R_F values of dinitrophenyl-O-methylsphingosine and dinitrophenyl-O-methyldihydrosphingosine differed only little and the spot of dinitrophenyl-O-methylsphingosine therefore also contained dinitrophenyl-O-methyldihydrosphingosine. Dinitroaniline, which was only just traceable, had an R_F value of 0·71. Authentic samples of triacetylsphingosine, tribenzoyldihydrosphingosine and O-methylsphingosine sulphate, which were gifts from Dr. Carter, University of Illinois, were after hydrolysis used as references for the identification of the bases. These were further indirectly identified by the following procedures. The dinitrophenyl-O-methylsphingosine spot disappeared after changing the hydrolysis in the isolation procedure from methanolic to aqueous sulphuric acid. Sphingosine and dihydrosphingosine were precipitated from the base fraction according to Carter *et al.*[4]. After hydrogenation of the bases with platinum oxide as catalyst the dinitrophenyl-sphingosine spot disappeared and the dinitrophenyl-dihydrosphingosine spot was correspondingly enlarged.

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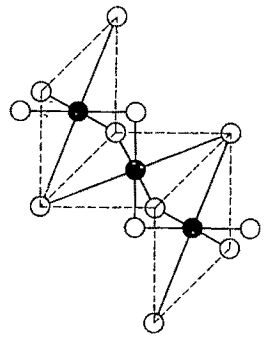
Structure of the Trinuclear Titanium (IV) Alkoxides

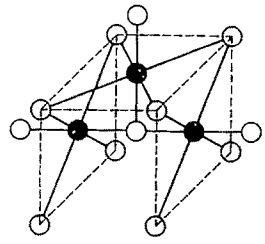
THE association of *n*-alkoxy derivatives of orthotitanic acid was first established as recently as December 1951 by Caughlan *et al.*[1]. Cryoscopic determinations of molecular weight in freezing benzene revealed that $Ti(OC_2H_5)_4$, $Ti(OC_3H_7)_4$ and $Ti(OC_4H_9)_4$ were all trimeric except at very high dilutions when dissociation to the monomer was observed. The association was ascribed to the strong tendency of quadrivalent titanium to attain a six-covalent oxygen environment, as, for example, in rutile or anatase. Caughlan *et al.* suggested that this could be achieved if each pair of titanium atoms was supported by three bridging alkoxy-groups giving two alternative structures I and II, which were based on the stacking of three TiO_6-octahedra face to face. Structure II necessitates a four-co-ordinated square planar oxygen atom attached to three titanium atoms and one alkyl group, and for this reason is considered by us to be untenable.

Structure I has been widely accepted[2] as the basis on which to interpret the chemistry of titanium (IV) alkoxides, and, in particular, the group working at Birkbeck College[3] have stressed this arrangement when discussing the hydrolysis of these compounds. In fact, they have claimed that the synthesis of polymeric oxide alkoxides (structure IV), built up by cross-linking trimer units with structure I through Ti-O-Ti bridges, "appears to be unique and justifies exclusive consideration".

The purpose of this communication is to indicate that at least two other stereochemical arrangements are possible, which we believe are in better agreement with the available experimental data. The first of these is again based on a six-covalent oxygen environment for titanium, but a trigonal prismatic rather than an octahedral arrangement of the TiO_6-group is envisaged. This leads to structure III in which two 'bridge' and two 'terminal' alkoxy-groups per

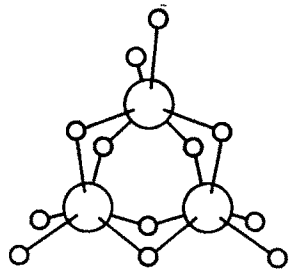


(I) $Ti_3(OR)_{12}$. ●, Ti; ○, O in OR

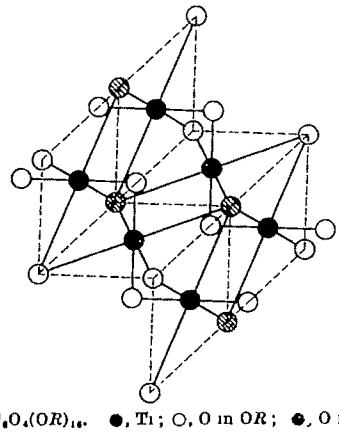


(II) $Ti_3(OR)_{12}$. ●, Ti; ○, O in OR

titanium atom are present. A geometrical model reveals that twelve n-alkyl groups can be nicely accommodated about the three titanium nuclei without steric hindrance. We believe that an important advantage of structure III lies in its natural symmetry, in contrast with structure I, in which the central titanium atom is surrounded by six alkoxy bridges with the other titanium atoms each carrying three terminal and three alkoxy bridges. The need for a high degree of symmetry in these compounds is reflected, for example, in the inter-



(III) Proposed cyclic structure for $Ti_3(OR)_{12}$ based on TiO_5-trigonal prisms



(IV) $Ti_6O_4(OR)_{16}$. ●, Ti; ○, O in OR; ⊗, O in Ti-O-Ti

pretation of the molecular complexity of chlorine-substituted alkoxides. Thus, in agreement with Caughlan *et al.*, we also find that monochloro-titanium (IV) butoxide is trimeric. A symmetrical structure for $Ti_3Cl_3(OC_4H_9)_9$ based on structure I is not possible, but follows naturally from structure III, which can accommodate one terminal chlorine atom per titanium. Similarly, the hydrolysis reactions of titanium (IV) alkoxides become much more amenable to a reasonable kinetic interpretation. For example, the careful studies of Bradley, Gaze and Wardlaw[4] have resulted in the isolation of $Ti_6O_4(OR)_{16}$ as the product of the first stage of hydrolytic polymerization of $Ti_3(OR)_{12}$, for which they propose structure IV. A polymerization of this kind would appear to require a statistically unfavourable mutual orientation of two $Ti_3(OR)_8(OH)_4$ units before effective collision and expulsion of four water molecules could occur, and would also require the preferential hydrolysis of two terminal and two bridging alkoxide groups from only one side of the trimer. Furthermore, it also involves an unknown four-covalent bonding arrangement between oxygen and its nearest four titanium neighbours.

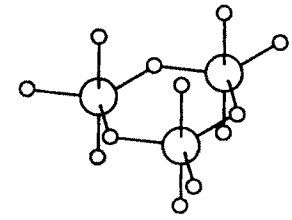
We suggest that the hydrolysis of $Ti_3(OR)_{12}$ with structure III can be formulated without raising the above difficulties, and yet can lead logically to oxide-alkoxide polymers of the type $Ti_6O_4(OR)_{16}$, $Ti_9O_6(OR)_{20}$ and $Ti_{12}O_{12}(OR)_{24}$ reported by the Birkbeck school. The hydrolysis of terminal alkoxy groups, the intermolecular elimination of alcohol, and the intramolecular elimination of water appear to be likely successive stages. Such a mechanism involves a kinetically simple two-point collision, and a possible scheme would be as follows (b = bridge; t = terminal group):

(i) $Ti_3(OR)_6{}^b(OR)_6{}^t + 6H_2O \rightarrow Ti_3(OR)_6{}^b(OH)_6{}^t + 6ROH$

(ii) $Ti_3(OR)_6{}^b(OH)_6{}^t + Ti_3(OR)_6{}^b(OR)_6{}^t \rightarrow (RO)_4{}^t(RO)_6{}^bTi_3(O)_2{}^bTi_3(OR)_6{}^b(OH)_4{}^t + 2ROH$

(iii) $(RO)_4{}^t(RO)_6{}^bTi_3(O)_2{}^bTi_3(OR)_6{}^b(OH)_4{}^t \rightarrow (RO)_4{}^t(RO)_6{}^bTi_3(O)_2{}^bTi_3(OR)_6{}^b(O)_2{}^t + 2H_2O$

The terminal Ti = O groups formed involve five-covalent titanium, and in this connexion the recent work of Andersson and Wadsley[5] is particularly relevant, since these workers have established that quadrivalent titanium in the mixed oxide $K_2Ti_3O_6$ is five-covalent. In a personal communication, they have suggested to us structure V, which is based on a trigonal bipyramidal TiO_5-grouping, as an alternative configuration for $Ti_3(OR)_{12}$. This differs from structure III, not only in the five-covalency of titanium, but also in that only one alkoxy-bridge per titanium atom is present.



(V) Alternative cyclic structure for $Ti_3(OR)_{12}$ based on TiO_5-trigonal bipyramids

We believe that the known behaviour of titanium (IV) alkoxides and the chloro-alkoxides is in better agreement with a cyclic than a linear arrangement of the three titanium atoms. Whether the titanium is five- or six-covalent must rest on a complete structure analysis. It is quite conceivable that in the pure state or in benzene solution, titanium exhibits five-covalency, but under the influence of a strong solvating medium such as butanol, expansion to six-covalency takes place.

A more detailed account of this work will be published elsewhere.

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Heat Treatment of Irradiated Polypropylene

It has been shown by Lawton[1,2] that during the high-energy irradiation of a polymer, the main effect produced is either intermolecular cross-linking or degradation of the molecular chain, and radicals produced during irradiation can be trapped in the crystalline regions. Crystalline 'Marlex-50', irradiated at 25° C. and then annealed at 150° C., gave more cross-links than 'Marlex-50' irradiated at 25° C. and not annealed, but less than that of the polymer irradiated at 150° C. for the same dose of irradiation. We have been able to demonstrate the delayed cross-linking effect by heat treatment of pre-irradiated isotactic polypropylene. We find that many trapped radicals produced during irradiation, which are stable at room temperature (as detected by electron spin resonance measurements), could contribute to delayed cross-linking on annealing the irradiated polymer after irradiation, and a big increase of gel content was observed. On the other hand, materials irradiated at 180° C. (molten state) gave no gel content for high dosage beyond 80 Mrads, indicating that in the molten state degradation of the molecular chain was predominant. The phenomenon is very different from the effect in polyethylene.

Isotactic polypropylene ('Moplen') powder was used. The molecular weight determined from viscosity was $2 \cdot 7 \times 10^5$. The degree of crystallinity is reported to be 75 per cent. Rods were prepared by melting the powder in the glass ampoule under high vacuum. The materials were irradiated at 25° C. (in the crystalline state) and at 180° C. (in the molten state) in glass ampoules under a vacuum of less than 10^{-5} mm. mercury with γ-rays from a 1,000-curie cobalt-60 source; the irradiation intensity was $3 \cdot 0 \times 10^5$ rads/hr.

In some experiments, polypropylene powder was irradiated in air. The polypropylene rods pre-irradiated *in vacuo* were annealed for an hour in a vacuum at the temperature-range 100–230° C. in an oil-bath soon after irradiation without exposing them to air. The powder irradiated in air was annealed at 150° C. for an hour in a vacuum.

Solubility measurement to determine gel content was used as a measure of the relative cross-linking effectiveness of the irradiation. The cross-linking gel fraction was determined by measuring the insoluble fraction extracted by suspending the irradiated samples (or samples annealed after irradiation) in a large volume of boiling tetraline at 207° C. for 48 hr. After extraction, the materials were immersed in hot methanol for different times, and traces of solvent in the materials were removed, vacuum dried and weighed.

In the case of isotactic polypropylene, the delayed cross-linking effect by heat treatment of pre-irradiated polymer is very conspicuous (Table 1).

Table 1. GEL CONTENT (PER CENT) OF IRRADIATED POLYMERS

Irradiation dosage	13 Mrads	83 Mrads
Irradiation at 25° C. *in vacuo*	0	47
Irradiation at 180° C. *in vacuo*	0	0
Irradiation at 25° C. in air	0	0
Irradiation at 25° C. *in vacuo*, and then annealed at 180° C. *in vacuo*	34	72

The gel content of irradiated polymers under various conditions is shown in Table 1. Irradiation dosages were 13 Mrads or 83 Mrads. The gel content of the specimen annealed at 180° C. after irradiation was much higher than that of unannealed.

The observations indicate that trapped radicals in the crystal could move to form intermolecular cross-links. When irradiated at 180° C. (amorphous molten state), the specimen gave no gel content with even 83 Mrads, indicating that scission of the main chain is more important here than cross-linking.

In Fig. 1 the relations of the delayed cross-linking effect to annealing temperature in the case of pre-irradiation dosages of 13 Mrads and 83 Mrads are shown. In both cases, gel content increases rapidly in the temperature range of the melting point, due to the mobility of the trapped radicals in the crystal. The relation of the sol fraction S of specimen irradiated at 25° C. in vacuum, and of the specimen irradiated at 25° C. in vacuum and then annealed at 150° or 180° C. *in vacuo*, to irradiation dosages is shown in Fig. 2.

Charlesby's formula[3] can be applied to the results:

$$S + \sqrt{S} = p_0/q_0 + 1/q_0 U_1 R$$

in which p_0 is the probability of degradation of a molecular chain by unit irradiation, q_0 is the probability of cross-linking by unit irradiation, U_1 is number average degree of polymerization, and R is irradiation dosage (in megarads). Assuming the initial

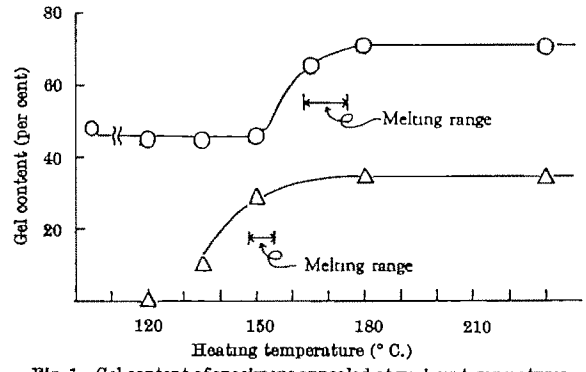

Fig. 1. Gel content of specimens annealed at various temperatures. Dosage: ○, $8 \cdot 7 \times 10^7$ rads; △, $1 \cdot 3 \times 10^7$ rads

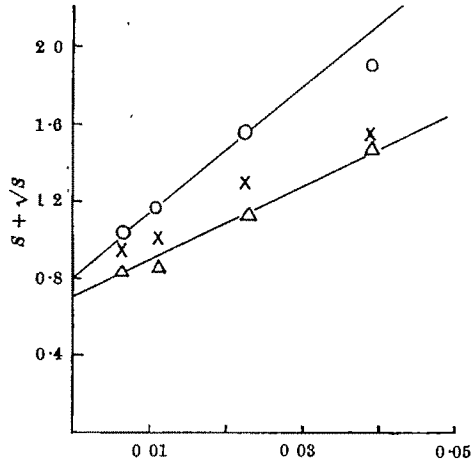

Fig. 2. ○, Irradiated at 25° C.; ×, irradiated at 25° C. then annealed at 150° C.; △, irradiated at 25° C. then annealed at 180° C.

distribution is random, the ratio p_0/q_0 and cross-linking efficiency G_c (number of cross-linking per 100 eV. absorbed) could be calculated from the results.

In the case of irradiation at 25° C., p_0/q_0 was 0·8, and G_c was 0 1, and in the case of annealing at 180° C. after irradiation, p_0/q_0 was 0 7 and G_c was 0·16. During pre-irradiation in the air, a considerable amount of peroxide[3] might be formed in the polymers. By annealing the pre-irradiated materials at 150° C., these peroxides are decomposed into the radicals which produce intermolecular cross-linking.

Table 2. GEL CONTENT OF THE MATERIALS PRE-IRRADIATED IN THE AIR AND THEN ANNEALED AT 150° C. *in vacuo*

Irradiation dosage (Mrads)	Gel content (per cent)
18	6 0
29	12 1
52	10 2
102	0

In Table 2 the gel content of annealed material pre-irradiated in the air for various dosage is shown. The gel content decreases beyond 50 Mrads because of rapid decrease of molecular weight during pre-irradiation in the air.

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BIOCHEMISTRY

Oxidation of Human Hæmoglobin by Vitamin K_3

PREVIOUS work in this laboratory has given support to the conclusion that the brain lesion in neonatal bilirubin encephalopathy or kernicterus is primarily due to a toxic effect of free bilirubin on cellular energy metabolism[1]. Hæmolytic diseases in new-born children, resulting in severe hyperbilirubinæmia, may therefore lead to the development of kernicterus, regardless of the cause of the hæmolysis.

Among exogenous factors inducing hæmolysis in new-born babies, vitamin K_3 or menadione (2-methyl-1,4-naphthoquinone), and some of its water-soluble derivatives (for example, synkavit), have recently been paid particular attention. These compounds are widely given to new-born children, and especially to premature infants, in order to improve their capacity to maintain adequate prothrombin titres. Zbinden *et al.*[2], who have recently reviewed the pertinent literature, have shown that injection of sublethal doses of vitamin K_3 into dogs leads to severe hæmolysis, accompanied by hæmoglobinuria and hæmoglobinæmia. No such effects were obtained with vitamin K_1.

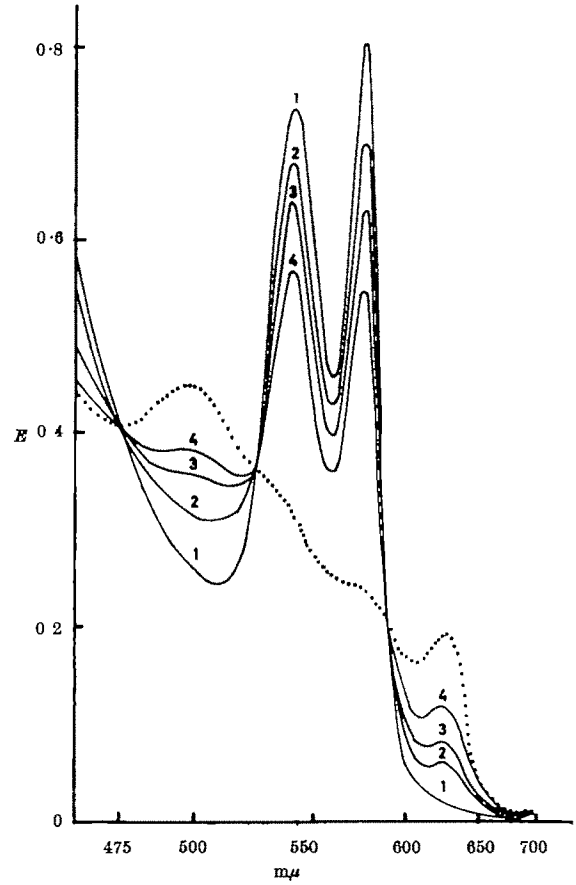

Fig. 1 Oxidation of human hæmoglobin by vitamin K_3
0 05 m*M* hæmoglobin in 0 05 *M* potassium phosphate buffer, *p*H 7 5
Curve 1, before addition of vitamin K_3;
Curve 2, 5 min. after addition of 1·3 m*M* vitamin K_3;
Curve 3, 10 min. after addition of 1 3 m*M* vitamin K_3;
Curve 4, 42 min. after addition of 1 3 m*M* vitamin K_3;
Dotted curve, after addition of an excess of potassium ferricyanide.
Vitamin K_3 was dissolved in ethanol and added in a volume of 0 1 ml. to a final volume of 3 ml
The measurements were carried out in a Beckman *DK*2 recording spectrophotometer, using glass cuvettes of 1 cm. light-path

In the present communication it is shown that vitamin K_3, but not vitamin K_1, oxidizes human hæmoglobin to methæmoglobin *in vitro*. It was observed that samples of whole blood, suspensions of washed erythrocytes, or erythrocyte-hæmolysates, when incubated in the presence of moderate concentrations of vitamin K_3, soon turned dark-brown, whereas vitamin K_1 induced no similar shift in colour. The phenomenon was afterwards investigated by adding vitamin K_3 to a solution of crystalline human hæmoglobin prepared according to Drabkin[3], and following the colour-shift with repeated scanning in a Beckman *DK*2 recording spectrophotometer. As shown in Fig. 1, the spectral change consisted of the

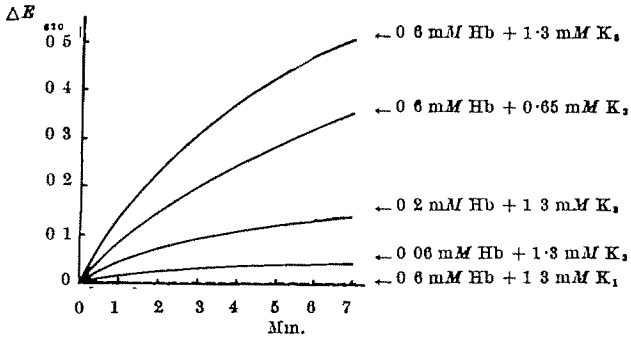

Fig. 2. Time-course of oxidation of hæmoglobin by vitamin K_3. Comparison of effects of vitamin K_3 and vitamin K_1. Hæmoglobin (Hb) and vitamin K_3 or K_1 were added in concentrations as indicated Other experimental conditions as in Fig. 1. Vitamin K_1 was dissolved in ethanol and the solution was mixed with a small amount of 'Tween-20' to prevent separation of the vitamin K_1 on addition to the test system

appearance of an absorption maximum at 630 mμ, a decrease of the two maxima at 577 and 541 mμ, and a shift of the absorption minimum at 510 mμ toward a maximum at 500 mμ, all these changes being typical of the transition of oxyhæmoglobin into methæmoglobin[4]. The dotted line in the figure shows the spectrum of 100 per cent methæmoglobin, obtained by adding an excess of potassium ferricyanide to the cuvette.

As is already seen from Fig. 1, the reaction was not linear with time, the rate of methæmoglobin formation decreasing on prolonged incubation. The kinetics of the reaction were studied in more detail by measuring the increase in optical density at 630 mμ as a function of time. Fig. 2 shows that the rate of reaction is dependent on both the concentration of hæmoglobin and the concentration of vitamin K_3. From the curves in Fig. 2 it can be estimated that $1{\cdot}3 \times 10^{-3}$ *M* vitamin K_3 oxidizes roughly 25 per cent of the hæmoglobin present in 7 min. A more detailed study of the kinetics of the reaction was complicated by the reoxidation of the reduced vitamin K_3 by molecular oxygen, with the formation of hydrogen peroxide. Addition of substantial amounts of reduced vitamin K_3 to oxyhæmoglobin caused an immediate colour-shift due to the removal of oxygen, followed by a gradual oxidation of the hæmoglobin to methæmoglobin largely according to the kinetics shown in Figs. 1 and 2. Synkavit, the diphosphate ester of reduced vitamin K_3, had no effect on hæmoglobin under the present experimental conditions. However, this does not exclude a possible effect *in vivo*, where synkavit may undergo enzymic dephosphorylation.

It is also shown in Fig. 2 that vitamin K_1 caused no oxidation of hæmoglobin, even when added in a concentration that in the case of vitamin K_3 gave a relatively rapid oxidation.

Although the relevance of these findings to the problem of the hæmolytic effect of vitamin K_3 may not be obvious, there might exist some relation between the two phenomena. It is generally considered that hæmolysis is in some way related to a deficient ability of the erythrocyte to maintain its normal level of reduced glutathione[5]. Methæmoglobin has been reported to oxidize reduced glutathione non-enzymically[6]. Furthermore, the reduction of glutathione in the erythrocyte is mediated by glutathione reductase, with reduced triphosphopyridine nucleotide as the specific hydrogen donor[7]. This latter compound is also utilized in the erythrocyte for the reduction of methæmoglobin, by way of a reduced triphosphopyridine nucleotide-specific methæmoglobin reductase[8]. An increased rate of formation of methæmoglobin, for example, due to vitamin K_3, may therefore constitute an increased competition for reduced triphosphopyridine nucleotide, thus rendering difficult the maintenance of glutathione in the reduced form. In fact, Zinkham and Childs have reported that incubation of neonatal and of primaquine-sensitive erythrocytes with vitamin K_3 resulted in a serious decrease of the level of reduced glutathione[9].

The above hypothesis is not in conflict with the often-emphasized fact that hæmolysis and methæmoglobinæmia do not necessarily go hand-in-hand[10], since the capacity of the methæmoglobin reductase system may be sufficient for maintaining a normal level of hæmoglobin even at an enhanced rate of hæmoglobin oxidation; besides, this reaction seems not to be fully dependent on reduced triphosphopyridine nucleotide, there being also a diphosphopyridine nucleotide-specific methæmoglobin reductase[11]. Glutathione reduction, on the other hand, may seriously suffer in capacity when methæmoglobin formation, and thus the drainage of reduced triphosphopyridine nucleotide, is increased, especially in cases, as in new-born children or in primaquine-sensitive patients, where the capacity to maintain the level of reduced glutathione seems to be insufficient.

We wish to thank Dr. Andrew Sass-Kortsak, Toronto, for stimulating discussions, and the F. Hoffmann-La Roche and Co., A.-G., Basel, for the preparations of vitamin K used in this work.

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2-Hydroxyœstrogens

RECENT work in several laboratories indicates that 2-hydroxylated œstrogens may be important metabolites of these naturally occurring steroid hormones. Thus King[1,2] has shown that œstriol is converted into 2-hydroxyœstriol and 2-methoxyœstriol by incubation with rat liver preparations in the presence of molecular oxygen. Work on the oxidation of di- and triphosphopyridine nucleotides by phenolases with oxygen, induced by natural and synthetic phenolic

œstrogens[3], clearly demonstrates that *o*-diphenols are involved in this system. Mueller[4] has claimed that formate incorporation into uterine tissue is increased by the addition of *o*-hydroxylated derivatives of œstradiol *in vitro*. Finally, 2-methoxyœstrone[5,6] and 2-methoxyœstriol[7] have been isolated from human urine. It is therefore of importance to devise practical syntheses of the 2-hydroxyœstrogens, in order to facilitate further biochemical and biological investigations.

Mueller has outlined a procedure for the preparation of 2- and 4-hydroxyœstradiol via 2- and 4-nitroœstrone, but has given no experimental details or physical constants for the intermediate or final compounds. Recently the partial synthesis of 2-hydroxyœstradiol, starting from 19-nortestosterone-17β acetate, has been described by Axelrod and Rao[8]. A method for *o*-hydroxylation of phenols due to Loudon and Scott[9] has been employed by Fishman[10] to convert œstradiol-17β into 2-methoxyœstradiol-17β and 2-methoxyœstrone. This method has now been adapted to the partial synthesis of 2-hydroxyœstradiol 17β and 2-hydroxyœstrone from œstradiol-17β, and to 2-hydroxyœstriol from œstriol.

Œstradiol-17β was converted into 2-hydroxy-17β-acetoxyœstradiol-3-(2-benzoyl-4-nitrophenyl) ether by Fishman's method, and this ether was cleaved with boiling piperidine. The reaction mixture, after separation by chromatography on silica gel, afforded 2-hydroxyœstradiol-17β acetate, m.p. 181°. Hydrolysis with cold *N* sodium hydroxide in nitrogen gave 2-hydroxyœstradiol - 17β, m.p. 161–162°, λ_{max}^{EtOH} 289 mμ (ϵ, 4,187), λ_{min}^{EtOH} 254 mμ (ϵ, 543), $[\alpha]_D^{19°}$ + 89° (ethanol), $\nu_{max.}^{Nujol}$ 3,350 (broad), 1,600, 1,510 cm^{-1}. (Found: C, 75·15; H, 8·3. Calculated for $C_{18}H_{24}O_3$: C, 75·0; H, 8·4 per cent.)

Treatment of 2-hydroxyœstradiol-17β with exactly 2 moles of acetic anhydride in dilute pyridine solution at 0° gave predominantly the 2,3-diacetate, m.p. 106–107°, isolated by chromatography on alumina. The infra-red spectrum showed a single, intense, ester band at 1,760 cm.$^{-1}$. Chromium trioxide in acetone-sulphuric acid smoothly oxidized this secondary alcohol to 2,3-diacetoxyœstrone, m.p. 170–171°. Hydrolysis as before yielded 2-hydroxyœstrone, m.p. 193–194°, λ_{max}^{EtOH} 289 mμ (ϵ, 4,296), λ_{min}^{EtOH} 255 mμ (ϵ, 527), $[\alpha]_D^{19°}$ + 160° (ethanol), $\nu_{max}^{CHCl_3}$ 3,550 (sharp) and 3,250 (broad), 1,635, 1,600 cm.$^{-1}$. (Found: C, 75·55; H, 7·9. Calculated for $C_{18}H_{22}O_3$: C, 75·5; H, 7·75 per cent.)

Œstriol was condensed with 2-chloro-5-nitrobenzophenone to give the 3-(2-benzoyl-4-nitrophenyl) ether, m.p. 130°, which yielded the 16,17-diacetate, m.p. 84–85°, with acetic anhydride in boiling pyridine. Cyclization of the diacetate with cold, concentrated sulphuric acid, followed by oxidation with hydrogen peroxide in acetic acid, gave the 2-hydroxy-3-ether. The latter was cleaved with boiling piperidine, and after chromatography on silica gel, 2-hydroxyœstriol-16,17-diacetate, m.p. 176–178°, was isolated. Alkaline hydrolysis, in the absence of oxygen, yielded 2-hydroxyœstriol, m.p. 267° (sealed, evacuated capillary tube), $\lambda_{max.}^{EtOH}$ 289 mμ (ϵ, 3,656), λ_{min}^{EtOH} 254·5 mμ (ϵ, 562), $[\alpha]_D^{19°}$ + 44° (ethanol), ν_{max}^{Nujol} 3,420 and 3,190 (broad band), 1,600, 1,500 cm.$^{-1}$.

All the above intermediates for which a melting point is quoted were obtained in the pure crystalline form and show satisfactory analytical figures. The yields were generally good, and these routes therefore provide practical partial syntheses of these suspected metabolites from the available natural hormones.

The 2-hydroxyœstrogens are colourless, crystalline substances which dissolve freely in aqueous alkali, and may be recovered unchanged from their colourless solutions provided oxygen is excluded. In air or oxygen, rapid autoxidation occurs; approximately five atoms of oxygen per molecule of œstrogen are absorbed in a few minutes, with the production of an orange coloration, and the destruction of the aromatic *A* ring. Strong reducing properties are demonstrated by the ability of these compounds, as spots on paper, to give a blue coloration with the Folin–Ciocalteu reagent before exposure to ammonia vapour. The R_F values for paper chromatograms run with the system acetic acid (70) – water (30) – methylenedichloride are: 2-hydroxyœstrone, 0·73; 2-hydroxyœstradiol-17β, 0·59; 2-hydroxyœstriol, 0·23 (œstradiol-17β, 0·78; œstriol, 0·54).

Further work on the chemistry of these compounds is in progress, and the results of this, together with details of the syntheses outlined above, will be reported elsewhere.

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Lysosomal-like Particles in the Rat Mammary Gland

DE DUVE *et al.*[1] have described the occurrence in rat liver of a new type of cytoplasmic particle, the lysosome, which was characterized by the following properties: (1) A distinct enzymic composition, containing a number of hydrolytic enzymes (acid phosphatase, β-glucuronidase, acid ribonuclease and acid deoxyribonuclease). (2) They can be isolated as a distinct intermediate fraction, between the mitochondria and microsomes, by differential centrifugation. (3) When isolated undamaged, the lysosomes show a low level of enzyme activity, but when the membrane is ruptured by freezing, and thawing, or by the addition of non-ionic detergents such as 'Triton-*X*-100', there is a considerable increase in the activity of the enzymes.

Recently, several other hydrolytic enzymes (aryl sulphatase, phosphoprotein phosphatase and β-glucosidases) have been reported to show properties similar to those outlined above (for references see ref. 1), and lysosomal-like particles have been reported to occur in a variety of tissues including rat brain, mouse liver, kidney and *S*.37 tumour[2].

We have investigated the possibility that similar particles exist in rat mammary gland by studying the effects of freezing and thawing and of 'Triton-*X*-100' on enzyme activation, and by comparing the sedimentation properties of these enzymes with mitochondrial and microsomal components.

The rats used were adult females weighing about 200 gm. The litters of lactating mothers were restricted to 6–10 pups. Animals were killed by cervical dislocation, and the abdominal and upper inguinal glands were quickly dissected and placed into ice-cold aqueous 0·25 *M* sucrose. The tissue was homogenized in an Emanuel and Chaikoff homogenizer[3]. The tissue was first forced through the homogenizer using a clearance of 64μ and the intractable connective tissue was removed by straining through cheese-cloth. The suspension was then finally forced through using the rod giving a clearance of 17μ. The whole operation was done in a cold room at 4°. Enzyme assays on such suspensions were carried out as follows: cathepsin by the method of Greenbaum and Greenwood[4] using hæmoglobin as substrate; phosphoprotein phosphatase by the method of Paigen[5]; acid ribonuclease as described by Slater[6]; β-glucuronidase as outlined by Greenbaum and Greenwood[4]; acid deoxyribonuclease by the method of de Duve *et al.*[7] and acid phosphatase by the method of Berthet and de Duve[8]. The activities found for both phosphoprotein phosphatase and acid phosphatase during lactation were very low and no activation studies could be performed with these enzymes. Mammary gland acid deoxyribonuclease, although showing activation on the addition of high final concentrations of 'Triton-*X*-100', appears to differ from that of liver in that it did not seem to be associated with particles in mammary suspensions; little of the activity could be sedimented by centrifuging for 16,000*g* for 20 min. Other work suggests that this enzyme is largely found in the milk retained in the ducts and alveoli of the gland[9].

Cathepsin, acid ribonuclease and β-glucuronidase were, however, present in amounts suitable for activation studies. It was found that the activities of β-glucuronidase and acid ribonuclease were greatly increased by freezing and thawing the mammary suspensions or by the addition of 'Triton-*X*-100' as described by de Duve *et al.*[10]. Experimental results are shown in Fig. 1. Cathepsin, however, showed only a slight activation on the addition of 'Triton-*X*-100'. The activity in particle preparations from lactating mammary gland suspensions was generally increased by about 30 per cent on the addition of 'Triton-*X*-100' in a final concentration of 0·2 per cent. This behaviour is analogous to the results of Beaufay and de Duve[1] on liver cathepsin.

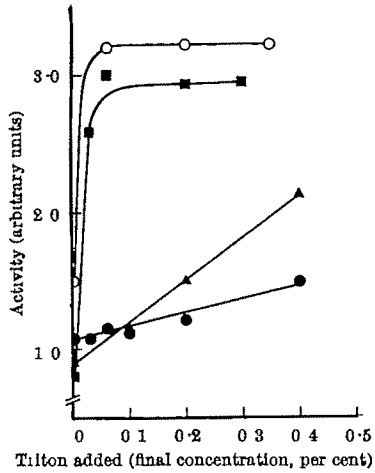

Fig. 1. Activation of acid ribonuclease (■), acid deoxyribonuclease (▲), cathepsin (●) and β-glucuronidase (○) by the addition of 'Triton-*X*-100' to the incubating medium. Enzyme activities are in arbitrary units and the procedures used for the assays are given in the text. All incubations were at 37° using mammary suspensions from rats in late lactation; the suspensions were prepared in 0·25 *M* sucrose using an Emanuel–Chaikoff type homogenizer[3]. The incubation times were 10 min. for acid ribonuclease and acid deoxyribonuclease, 20 min. for β-glucuronidase and 15 min. for cathepsin. The incubation medium was adjusted to a final concentration of 0·25 *M* sucrose with 1·7 *M* sucrose.

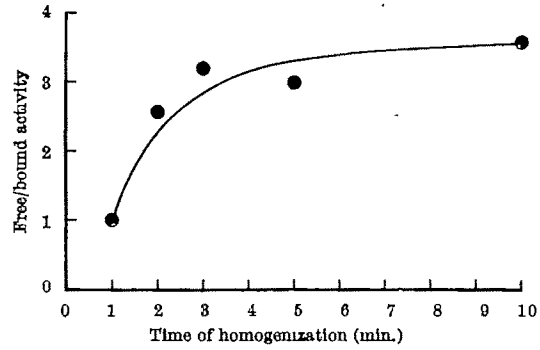

Fig. 2. Effect of increasing the time of homogenizing in a Potter–Elvehjem type homogenizer on the ratio of free/bound acid ribonuclease activity in rat mammary tissue suspensions taken from an animal in late lactation. The assay procedure for acid ribonuclease was as described by Slater[6] and consisted of 1 ml of ribonucleic acid in acetate buffer (0·1 *M*, pH 5·8, 4 mgm. ribonucleic acid per ml. buffer) + 0·2 ml. tissue suspension + 0·3 ml. 1·7 *M* sucrose. For total ribonuclease activity 0·1 ml. 1 per cent 'Triton-*X*-100' was added to the incubation mixture. The difference total activity minus free activity is the bound activity, that is, the activation produced by 'Triton-*X*-100'.

When tissue suspensions of mammary gland in 0·25 *M* sucrose were centrifuged at 16,000*g* for 20 min. at 0° in an Angle 13 M.S.E. centrifuge, 70–80 per cent of the total activity of acid ribonuclease, β-glucuronidase and cathepsin was sedimented. On the other hand, if homogenization was carried out using a conventional Potter–Elvehjem type homogenizer with a plastic pestle (clearance 0·01 in.) for 2 min., more than 70 per cent of the total enzyme activity was in a non-sedimentable form and little activation by 'Triton-*X*-100' could be demonstrated. Thus it appears that homogenizing of mammary tissue with the Potter–Elvehjem technique causes damage to the particles containing these three enzymes; the damage caused was proportional to the time of homogenizing at 0° as shown in Fig. 2 for acid ribonuclease. Times of homogenizing up to 2 min. in the Potter–Elvehjem instrument, however, had no detectable influence on the sedimentation properties of mitochondrial enzymes cytochrome oxidase and succinate neotetrazolium reductase. Breakage of the particles containing cathepsin, β-glucuronidase and acid ribonuclease, with consequent lack of further activation by 'Triton-*X*-100', was also achieved by high-speed blending, and by incubating in hypotonic sucrose solutions.

It would appear that acid ribonuclease and β-glucuronidase behave similarly in mammary suspensions in response to osmotic activation, to freezing and thawing and to the addition of 'Triton-*X*-100'; on centrifuging in 0·25 *M* sucrose the two enzymes sediment in the same fraction as cathepsin. Their behaviour therefore closely parallels the properties reported by de Duve *et al.*[7] for liver lysosomes. One point of great interest arising out of this work on mammary tissue suspensions concerns the variation in total enzyme activities over the lactation-cycle. Fig. 3 shows the variations in the total activities of cathepsin[4], β-glucuronidase[4] and acid ribonuclease[6] as reported previously. It can be seen that these three enzymes, which show very similar properties with respect to activation and centrifuging, have very different patterns of change over the lactation-cycle. It would seem that if these three enzymes are located

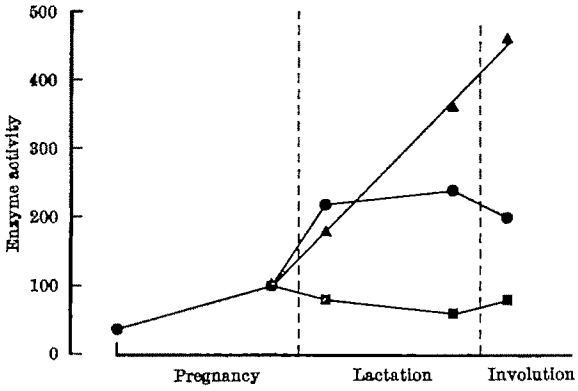

Fig. 3. Variation in β-glucuronidase (■), acid ribonuclease (●) and cathepsin (▲) in rat mammary gland suspensions over the lactation cycle. Figures taken from the literature: for β-glucuronidase and cathepsin from Greenbaum and Greenwood[4], for acid ribonuclease from Slater[6]

within a similar type of lysosomal particle in rat mammary tissue, either independent variations in enzymic activities can occur at different physiological states or there is a variety of lysosomal particles each with specific enzymic constitutions. This latter possibility has been mentioned by Conchie and Levvy[2] and by Beaufay and de Duve[1].

It seems of interest to follow the ratio of bound/free lysosomal enzyme activity over the lactation cycle particularly in mammary involution where the tissue is degenerating rapidly. This is under investigation.

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Base Composition of Ribonucleic Acid from Rat Mammary Gland during Pregnancy and Late Lactation

Ribonucleic acid has become increasingly associated with pathways of protein biosynthesis in many different types of tissue and there is a widely held belief that the sequential order of nucleotide bases in a particular ribonucleic acid molecule governs the amino-acid order of protein synthesized in its vicinity[1]. Incorporation of amino-acid, which has been equated with protein synthesis under certain conditions, has been shown to occur under these conditions in the intracellular fractions from many tissues. Differences in the ribonucleic acid base composition of mitochondrial, microsomal and supernatant fractions have been found for rat liver[2,3].

The rat mammary gland undergoes a rapid change in physiological activity at parturition. The rate of protein synthesis increases rapidly, and concomitant with this there is a rapid increase in the gland's content of ribonucleic acid; this increase is largely centred in the particulate fractions of mammary suspensions[4].

We have investigated the possibility that the sudden increase in both ribonucleic acid and protein synthesis occurring over parturition is accompanied by an alteration in the base composition of the newly synthesized ribonucleic acid. It was thought possible that the increase in the synthetic rate of the specific milk protein, casein, occurring over parturition might be sufficiently drastic to produce detectable alterations in the overall ribonucleic acid base composition. It was also of interest to study the base composition of lactating mammary gland ribonucleic acid to compare the acid-base composition of such an active protein secretory tissue with other tissues previously investigated.

The rats used were primiparous adult females the litters of which were restricted to 6–10 pups. All animals in the early pregnancy group were between 14–15 days pregnant; animals in the late-pregnancy groups were 17–20 days pregnant; the late-lactating groups were made up from animals 17–19 days lactating. Animals were killed by cervical dislocation and the abdominal and inguinal glands were quickly dissected and placed into ice-cold water. Tissue homogenates were prepared using a M.S.E. top-drive blendor and the cold suspension strained through muslin to remove intractable connective tissue. For the experiments involving separations of intracellular fractions, homogenates were prepared in ice-cold 0·25 *M* sucrose using an Emanuel–Chaikoff homogenizer[5]; cell debris and nuclei were removed by preliminary centrifuging at 600*g* for 10 min. and the supernatant from this was then centrifuged at 105,000*g* for 20 min. at 0°. The sediment was resuspended in water to give the original concentration.

Ribonucleic acid was extracted from homogenates or tissue fractions essentially by the phenol method of Kirby[6]. The nucleotide base composition of ribonucleic acid samples was determined by the method of Herbert, Potter and Hecht[7] using 'Dowex-1' resin in the formate form. The column size was 5 cm. × 0·72 cm.[2]; the rate of flow was approximately two 15 ml. fractions per hour.

The results for the base composition of mammary gland ribonucleic acid at three stages of the lactation-cycle are shown in Table 1. It can be seen that there is no significant alteration in the ratio of purine to pyrimidine bases at the three stages of the lactation-cycle studied. Thus, although the mammary gland changes very rapidly in protein synthetic ability during lactation, no significant alterations in the gross base composition of whole homogenate ribonucleic acid could be detected. Whereas in late pregnancy the protein synthetic machinery of the gland is concerned largely with the maintenance of the tissue protein itself, in lactation the emphasis is largely on the production of a very different protein, casein. Assuming that a close inter-relationship exists between ribonucleic acid and protein synthesis, it may be concluded that if differences in ribonucleic acid occur concomitant with a change over to the synthesis of a new protein, the differences are subtle and are not detectable by the type of overall base composition

Table 1. NUCLEOTIDE BASE COMPOSITION OF RIBONUCLEIC ACID SAMPLES EXTRACTED FROM MAMMARY GLAND TISSUE SUSPENSIONS AT THREE STAGES OF THE LACTATION CYCLE

The results are given as moles of nucleotide per 100 moles ribonucleic acid. A 12 per cent correction has been applied for the deamination of cytidylic to uridylic acid

Stage of lactation cycle	No of animals	CMP†	AMP	UMP	GMP
Early pregnancy	4	28	20	16	36
	4	27	22	15	36
Mean		27 5	21	15·5	36
Late pregnancy	3	29	21	14	36
	3	28	20	14	37
	2	29	20	14	37
	2	26	20	18	35
Mean*		28 ± 0 7	20 ± 0 3	15 ± 1 0	36 ± 0·5
Late lactation	1	27	16	17	40
	1	26	21	16	38
	1	28	21	15	36
	1	27	22	15	35
	1	29	15	16	37
	1	27	19	17	37
	1	27	22	15	37
	1	27	18	15	40
Mean*		27 ± 0 3	19 ± 0 8	16 ± 0 3	37 ± 0 7

* ± *S.E M.*
† Abbreviations: CMP, cytidine monophosphate; AMP, adenosine monophosphate; UMP, uridine monophosphate; GMP, guanosine monophosphate.

determinations reported in Table 1 for whole homogenate ribonucleic acid.

The base composition of mammary gland ribonucleic acid appears to be somewhat different from the base composition of rat liver acid. Rat liver (and rat kidney) ribonucleic acid has been shown to have a purine/pyrimidine ratio of unity[2,3,9]. Rat mammary gland acid, however, has a ratio of 1·34 but the ratio of 6-keto groups to 6-amino groups is 1·10 which is close to the corresponding value (1·08) given by Elson and Chargaff[8] for rat liver ribonucleic acid. It would thus appear that rat mammary gland ribonucleic acid has approximately equal numbers of 6-keto and 6-amino groups but that the added regularity of a purine/pyrimidine ratio of unity is not present.

The results for the base composition of ribonucleic acid from intracellular fractions of rat mammary tissue taken from animals in late lactation are shown in Table 2. A major role in protein biosynthesis has been ascribed to the microsomal fraction of many tissues. However, it can be seen from Table 2 that in late lactation, when casein synthesis is at its peak, the particulate fraction of mammary tissue suspensions shows no significant differences in ribonucleic acid base composition from the soluble fraction remaining after approximately 3×10^6 g.min. There are indications that the nuclear fraction from mammary suspensions has a lower purine/pyrimidine ratio than the other fractions; a similar low ratio for liver nuclei has been previously reported[2].

Table 2. BASE COMPOSITION OF RIBONUCLEIC ACID SAMPLES EXTRACTED FROM INTRACELLULAR FRACTIONS OF RAT MAMMARY GLAND SUSPENSIONS TAKEN FROM ANIMALS IN LATE LACTATION

For details of the centrifugings see the text. The results are expressed as percentages of the corresponding whole homogenate value for each base ratio (that is, the whole homogenate value for all ratios is 100)

Fraction	No. of experiments*	Molar ratios compared to whole homogenate value of 100			Purine/pyrimidine compared to whole homogenate value of 100
		AMP/CMP	UMP/CMP	GMP/CMP	
Nuclear	2	93	173	118	77
Particles	4	100±5	87±5	97±4	105±3
Supernatant	6	116±14	100±7	105±7	110±8

* Two animals used per experiment

Total ribonucleic acid estimations were performed on the intracellular fractions, and the results were in agreement with earlier work on the distribution of ribonucleic acid in mammary tissue[4]. The bulk of the homogenate ribonucleic acid is associated with the particulate fraction (70–80 per cent); only some 10–20 per cent of the total suspension ribonucleic acid was found in the soluble fraction with the centrifuging procedure used. Thus the purine/pyrimidine ratio of the whole homogenate ribonucleic acid is largely determined by the purine/pyrimidine ratio of the particulate fraction. This is shown in Table 2, where it can be seen that the purine/pyrimidine ratio for the particulate fraction is not statistically different from the whole homogenate value.

Ribonuclease did not have any appreciable effect on the bulk of the ribonucleic acid since in experiments where homogenates were allowed to stand for 2 hr. at 0° no differences in the purine/pyrimidine ratios were observed compared with similar homogenates placed in phenol immediately after homogenization (2 hr. was approximately the time taken to prepare the intracellular fractions before phenol extraction). It has been shown that ribonuclease is associated with lysosomal-like particles in rat mammary tissue[10] and that when a mammary suspension is prepared using an Emanuel–Chaikoff type homogenizer, only some 10 per cent of the total ribonuclease is in a free and non-sedimentable form.

It would thus appear from the results obtained in this investigation that there is no gross alteration in the base composition of mammary gland ribonucleic acid at the three stages of the lactation-cycle studied. Further, during late lactation, there are only small differences between the base compositions of ribonucleic acid extracted from intracellular fractions Since the differences in composition of ribonucleic acid, which almost certainly occur in the mammary gland in response to the stress of lactation, cannot be detected by overall base composition analyses a study has been initiated on the composition of ribonucleic acid species isolated by chromatographic techniques similar to those used in the studies of Goldthwaite[11] on liver.

This work was done during the tenure of a Beit Memorial Fellowship held by one of us (T. F. S.) and of a Medical Research Council Studentship held by D. Y. W.

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Binding of Zinc in Carboxypeptidase

CARBOXYPEPTIDASE is a metallo-enzyme which contains zinc. It has been reported by Coleman and Vallee[1] that the enzyme can be de-activated by removal of zinc and that activity can be restored by the addition of zinc, cobaltous, ferrous, nickel and manganous ions but not by addition of cadmium, magnesium or calcium ions. This metallo-enzyme therefore falls in the group of enzymes which have no specific metal requirement for activity[2]. In biological systems, however, a particular metal, zinc, is associated with the enzyme presumably because complex ion equilibria favour this particular association over all others. The situation is not very different from that found in the case of the enzyme enolase, where magnesium and manganous are the particular ions associated with activity in the biological system, but where other cations such as zinc can activate the enzyme *in vitro*[3]. The apparent stability constants for the association of zinc and cobaltous ions with carboxypeptidase are 2×10^8 and 1×10^6 respectively[1]. The *p*H range of activation by the different cations indicates that association with the active centre is in the order zinc(II) > nickel(II) and cobalt (II). The study of complexes of a wide variety of simple organic ligands has shown[2] that this stability sequence is observed only when one of the co-ordinating centres is sulphide, R—S^-. I conclude that zinc is bound by a sulphide group in carboxypeptidase and give the following additional evidence in support of this binding.

The cobaltous carboxypeptidase complex is highly coloured. The molar extinction coefficient at 530 mμ is 150[1]. The usual value of the extinction coefficient of cobaltous complexes is <10, except when the cobalt ion is bound to large, polarizable ligand atoms such as chloride and sulphide[4]. Thus both cobaltous thiocyanate and thiosulphate have extinction coefficients of the order of 10^2, and cobaltous cysteine and thioglycollate complexes are highly coloured. In the complex with carboxypeptidase, the binding of the cobaltous ion is probably restricted to oxygen, nitrogen or sulphur centres, and it would appear that only in the case of binding to sulphur is the colour of the complex explicable from the known properties of model complexes. The shift of the absorption band from 512 mμ in the hydrate to 530 mμ in the carboxypeptidase complex, that is, a shift to longer wavelengths, is in the expected direction if binding to cobalt is through a mixture of oxygen and sulphur co-ordinating centres, but is in the opposite sense from the shift produced by extensive co-ordination to nitrogen.

In the metallo-enzyme enolase I have postulated that the binding of the cations is largely through oxygen atoms[2]. In this enzyme magnesium is active. Magnesium cannot activate carboxypeptidase. It is not known to bind to sulphide groups. On the other hand, cations such as lead(II), cadmium, mercuric, silver, and cupric which bind sulphur groups more strongly than zinc may be expected to be powerful inhibitors.

If cobalt is bound to sulphur in carboxypeptidase, it is possible to predict that there will be a further new absorption band absent in the complexes of the other cation complexes of this enzyme. The new band will be at about 285–300 mμ and will have an extinction coefficient greater than 10^3. Both this strong band and the band in the visible of extinction coefficient 10^2 are present in model cobalt complexes containing Co—S—R links[4]. Neither of these bands is observed in cobaltous insulin, and we can predict that in this complex the binding of zinc is to a mixture of oxygen and nitrogen groups. Both insulin and carboxypeptidase contain sulphur groups.

Note added in proof. Since this communication was submitted I have heard from B. L. Vallee and his associates that they have demonstrated Zn—S binding independently.

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A Plate Assay for Elastase

SINCE Balo and Banga[1] described the pancreatic enzyme elastase, its dissolving effect on elastin, and its possible implications in atherosclerosis, a considerable amount of interest has been focused on the quantitative measurement of its enzymatic activity.

Two methods most commonly used for the assay of elastase are based on gravimetric measurements and nephelometry. Much has been learned in regard to the interaction of elastin and elastase and its inhibitor, serum, by these two methods. However, both methods suffer from the fact that they require much time and special equipment and skilled personnel.

If a programme designed to establish and follow elastase-inhibitor levels in sera from a variety of sources, including human sera, is anticipated, a relatively easy and rapid assay for elastase and its inhibitor is essential. Such a programme is in progress in this laboratory, and an assay fulfilling these requirements has been developed.

Table 1. WATER-SODIUM HYDROXIDE ELASTIN IS USED. IT IS AUTOCLAVED FOR 10 MIN. AT 10 LB. PRESSURE. THE RESULTING *p*H IS 7

Components	Composition of elastin medium: Amount of components in stock solution	Volume of stock solutions for 100 ml. of complete medium
Inorganic salts		
K_2HPO_4	25 gm.	
KH_2PO_4	25 gm.	
Distilled water	250 ml.	0 5 ml.
Inorganic salts *B*		
$MgSO_4 7H_2O$	10 gm	
NaCl, $FeSO_4 7H_2O$	0 5 gm.	
$MnSO_4 4H_2O$	of each	
Distilled water	250 ml	0 5 ml.
Elastin	10 gm.	
Distilled water	100 ml.	10 ml.
Distilled water		87·5 ml.
Agar		1·5 gm.

Table 1 shows the composition of elastin agar. 20 ml. of this medium is poured into a sterile 15 × 150 mm. Petri dish. The non-transparent medium (due to the presence of elastin) is allowed to harden. Six wells are made in the medium by either allowing the medium to harden in the presence of plastic molds which can then be easily removed after hardening, or the medium is allowed to harden and the molds are pushed through the agar. The resulting cylinder of agar can be teased away with an inoculating needle. The wells serve as reservoirs for elastase and its inhibitor serum. The diffusion of elastase from the wells and its subsequent dissolution of elastin result in clear zones around the wells, the zones varying in diameter with the concentration of elastase used. The resulting clear zones can be seen

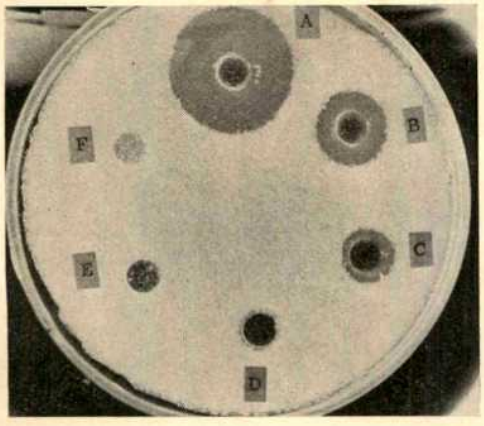

Fig. 1. Photograph of an elastin agar plate showing solubilization (clear zone) of elastin around the wells containing decreasing concentration of elastase, wells *A–E* (5, 4, 3, 1, 0·5 mgm.); *F* is a buffer control. 0·06 ml. of bovine pancreatic elastase in the desired concentration is placed in each well. An equal amount of buffer (not containing elastin) is placed in well *F*. The plates are allowed to incubate right side up for 72 hr. at room temperature. The zone of solubilization can be read at each 24-hr. interval. Bovine pancreatic elastase was prepared according to the method of Lewis (ref. 3). Water–sodium hydroxide elastin was prepared by the method described by Gilfillan *et al.* (ref. 4)

in Fig. 1. Inhibition of elastase can be easily demonstrated by the addition of serum to the reaction well. The results obtained when a constant amount of elastase is placed in each of five different wells along with decreasing concentrations of serum are illustrated in Fig. 2. The inhibitory effect of serum is obvious. Partridge and Davis[2] have shown that elastin degradation is accompanied by the liberation of N-terminal substances. Ninhydrin added to the well surrounded by the clear area shows a bluish-purple area indicating the liberation of free amino groups.

Preliminary work indicates that this plate assay correlates well with the nephelometric–ninhydrin method used by Gilfillan *et al.*[4].

We believe that the elastase plate assay described is less time-consuming, requires less special equipment, does not require skilled personnel, and most important is readily adaptable to assaying large numbers of sera for elastase inhibitor or tissue, bacterial, and fungal extracts for elastase.

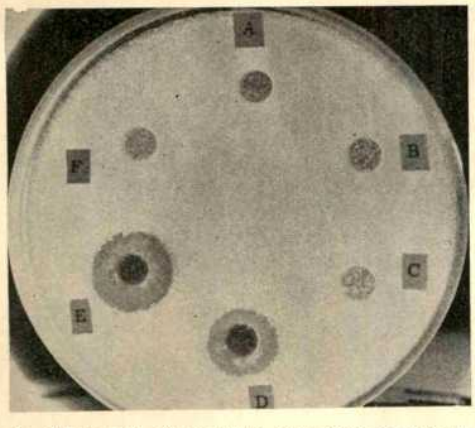

Fig. 2. Photograph of an elastin agar plate showing the inhibitory effect of third trimester pregnancy serum on elastase. The elastase concentration (5 mgm./well) was constant in wells *A–E*. Serum concentrations decreased from *A* to *E* (1/20, 1/40, 1/60, 1/80, 1/160). Well *F* contained an equal amount of serum and served as a control. Plates are incubated and read as in Fig. 1. (Photographs taken by George Daynes)

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PHYSIOLOGY

Specific Activities of Acid-soluble Nucleotides in Hind-Leg Muscles of Mice with Dystrophia Muscularis

IN an earlier paper[1], we showed that the concentrations of adenosine monophosphate, guanosine triphosphate and guanosine diphosphate were significantly higher in the hind limb muscles of dystrophic mice than those obtained for normal mouse muscles, while for adenosine triphosphate the reverse was found. Although the concentration of the adenosine diphosphate component was the same for both normal and dystrophic tissue, radioautographs of nucleotides containing radioactive phosphorus seemed to show an area of higher radioactivity for the adenosine diphosphate derived from the dystrophic muscle. The present work was designed to examine the turn-over rates of the acid-soluble nucleotides in the skeletal muscle of normal mice and mice afflicted with a hereditary myopathy (dystrophia muscularis).

Both dystrophic mice and their normal litter mates (obtained from the Roscoe B. Jackson Memorial Laboratories, Maine) were injected subcutaneously with carrier-free radioactive phosphorus (20 μc./gm. body-weight). Two hours later, the animals were anæsthetized and the hind leg musculature was excised. In order to minimize the enzymatic degradation of the nucleotides, the muscle was handled at temperatures of 0° C. or below[1].

After weighing the frozen tissue on a torsion balance, the muscle was transferred to a homogenizing flask containing 10 ml. of 0·25 *M* perchloric acid (1–2° C.) per gm. of tissue[2]. 0·5–1·0 gm. of muscle tissue was available for each analysis. The sample was homogenized for 10–20 sec. at 40,000 r.p.m. and then centrifuged (3,000 r.p.m.) for 15 min. at 0° C. A 10 per cent suspension of acid-washed 'Norite' (0·4 ml./gm. of extracted muscle tissue) was added to the supernatant and the emulsion was agitated for 30 min. in the cold[3–5]. The 'Norite' was separated by centrifugation, washed with water and recentrifuged. 10 per cent pyridine in 60 per cent ethanol (8 ml./gm. extracted muscle tissue) was added to the 'Norite'. The contents of the tubes were mixed, and elution was allowed to proceed over a 2-hr. period at 37° C. with occasional mixing[5]. The charcoal was removed by centrifugation, and the eluate containing the acid-soluble nucleotides was measured. Aliquots were taken for the measurement of radioactivity present in the total extracted nucleotides, and the remaining eluate was concentrated to a small volume.

The concentrated nucleotides were quantitatively transferred to Whatman No. 1 filter paper and re-

Table 1. SPECIFIC ACTIVITIES* OF ACID-SOLUBLE NUCLEOTIDES FOUND IN MUSCULAR TISSUE (HIND LEGS) OF NORMAL AND DYSTROPHIC MICE†

Cases	Adenosine monophosphate	Adenosine diphosphate	Adenosine triphosphate	Diphosphopyridine nucleotide	Guanosine triphosphate‡	Guanosine diphosphate‡
4 Normal	67,900	149,400	477,700	12,000	408,800	310,000
S.D.	±15,400	±26,200	±88,800	±2,200	±84,600	±62,000
5 Dystrophic	50,900	226,700	552,300	24,500	493,400	478,600
S.D.	±9,100	±24,500	±39,800	±4,900	±45,300	±32,300
P	<0·05	<0·001	<0·05	<0·001	0·05	<0·001

* Specific activity = $\frac{\text{counts per min.}}{\mu\text{mol. of nucleotide (average of 18 determinations)}}$

† Animals killed 2 hr. after the subcutaneous injection of radioactive phosphorus.

‡ Guanosine tri- and di-phosphate contain other nucleotides (ref. 1).

solved by descending chromatography for 40 hr. using the *iso*butyric acid–ammonium *iso*butyrate solvent system of Magasanik[6]. Following resolution of the unknown mixture, 6 spots corresponding to adenosine monophosphate, diphosphopyridine nucleotide, adenosine diphosphate, adenosine triphosphate, guanosine di- and tri-phosphate were made visible with ultra-violet light. However, radioautographs prepared from the chromatogram indicated the presence of an unidentified radioactive phosphorus-containing substance in the adenosine monophosphate–diphosphopyridine nucleotide area, which did not absorb ultra-violet light. Since we were interested in the specific activity of each component, and this non-nucleotide substance might contribute to the specific activity of either adenosine monophosphate or diphosphopyridine nucleotide, it was necessary to remove this compound before eluting the adenosine monophosphate and diphosphopyridine nucleotide. This was accomplished by ascending chromatography in the second dimension for 5 hr. at 20° C. using the *n*-butanol/*n*-propanol/formic acid (10 : 40 : 30) solvent of Venkstern and Baev[7]. With this solvent, the unidentified component as well as orthophosphate were resolved away from the nucleotides, which remained at the origin.

Quantitative elution and estimation techniques for the separated nucleotides were the same as described in the previous publication[1]. After determining the optical densities of the various eluates, aliquots were pipetted into metal planchets. The counting samples were dried and radioactivity measurements were determined with a Nuclear Chicago gas-flow counter.

The specific activities calculated for the acid-soluble nucleotides obtained from the hind-leg musculature of 5 dystrophic and 4 normal mice run by the above procedure are tabulated in Table 1. Significantly higher specific activities were found for the adenosine diphosphate (226,700), diphosphopyridine nucleotide (24,500), and guanosine diphosphate (478,600), from the dystrophic mouse muscle, as compared to normal values of 149,400 for adenosine diphosphate, 12,100 for diphosphopyridine nucleotide, and 310,000 for guanosine diphosphate. On the other hand, little or no differences existed in the specific activities of the adenosine mono- and tri-phosphate, and guanosine triphosphate derived from the two types of tissue.

Although the concentration of adenosine triphosphate from the dystrophic tissue is 30–40 per cent lower than that found in normal tissue, the specific activities for adenosine triphosphate from both types of tissue are not significantly different. While it has been postulated that adenosine triphosphate plays a significant part in all phases of muscle metabolism, the roles of the other acid-soluble nucleotides cannot be dismissed[8]. In view of the significantly higher specific activities of adenosine diphosphate, guanosine diphosphate and diphosphopyridine nucleotide, it is possible that they contribute through secondary pathways to make up for the deficiency in adenosine triphosphate.

A more comprehensive study of the turn-over rates of the various acid-soluble nucleotides is in progress.

We wish to express our gratitude to Dr. Solomon A. Berson and to Dr. Stanley M. Aronson for their helpful advice throughout the course of this work.

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Storage and Release of Catecholamines, and the Occurrence of a Specific Submicroscopic Granulation in Hearts of Cyclostomes

THE relatively large amounts of catecholamines found in the hearts of cyclostomes[1,2] suggest that these substances may be stored in specific cells or cellular structures. Preliminary examination with the light microscope of specimens from the hearts of the lamprey (*Petromyzon fluviatilis*) and the hagfish (*Myxine glutinosa*) indicated the presence of a specific cell type possibly serving as store. It was therefore considered of interest to analyse different cardiac structures of these two cyclostomes with regard to their content of catecholamines and to make a parallel study of the morphology of this unknown cell with the aid of the electron microscope.

Adrenaline and noradrenaline were determined fluorimetrically by the method of Euler and Lishajko[3] after extraction of the hearts with 5 per cent trichloracetic acid, adsorption on alumina and elution

with acetic acid. Column chromatography of an eluate obtained with sulphuric acid was used for the determination of catechol compounds in general. A granular fraction was also isolated by high-speed centrifugation of press juice from the hearts according to the method described by Euler[4], using 0·3 *M* and 0·075 *M* potassium phosphate as medium for *Myxine* and *Petromyzon* hearts, respectively.

For histological examination specimens were freeze-dried or fixed in various fixatives and were studied under light and fluorescence microscopes. For electron microscopy specimens were fixed in buffered osmic acid and embedded in methacrylate; sections were examined in an R.C.A. type *EMU 2 B* electron microscope.

Table 1. ADRENALINE (A) AND NORADRENALINE (NA) IN HEARTS OF *Petromyzon fluviatilis* (LAMPREY) AND *Myxine glutinosa* (HAGFISH) IN μGM PER GM.

	Auricle		Ventricle		Portal heart	
	A	NA	A	NA	A	NA
Lamprey	140	3·4	25	0	—	—
	118	7·6	24	0	—	—
	132	7·9	35	0	—	—
Hagfish	15	40	40	5·6	3·1	53
	11	54	49	6·4	0·3	59
	—	—	—	—	4·5	44

Table 1 shows the amounts of adrenaline and noradrenaline in the auricle and the ventricle of lamprey and hagfish and also in the portal heart of hagfish. It can be seen that the lamprey heart contains chiefly adrenaline which is present in large amounts in the auricle as well as in the ventricles. In the hagfish a peculiar distribution of the two amines is noted in that the portal heart and the auricle contain mainly noradrenaline, while adrenaline is the dominating amine in the ventricle.

By column chromatography of heart extracts of hagfish and lamprey it could be shown that adrenaline and noradrenaline were the predominant catechol compounds and that dopamine and dihydroxyphenylacetic acid were present only in very small amounts. In fractions of isolated granules the proportion of the two amines was approximately the same as that found in total extracts.

It has recently been shown that reserpine causes a release of noradrenaline from isolated transmitter granules from mammalian splenic nerves[5]. Incubation of isolated granules from *Petromyzon* and *Myxine* hearts with reserpine (0·1 mgm./ml. for 30 min. at 20° C. and *p*H 6·1) increased the release of catecholamines from the granules by about 30 per cent as compared with the controls.

After 6 daily injections of 0·1–0·2 mgm. reserpine subcutaneously the amounts of adrenaline and noradrenaline in the hearts of *Myxine* and *Petromyzon* were reduced to 15–30 per cent of the control values.

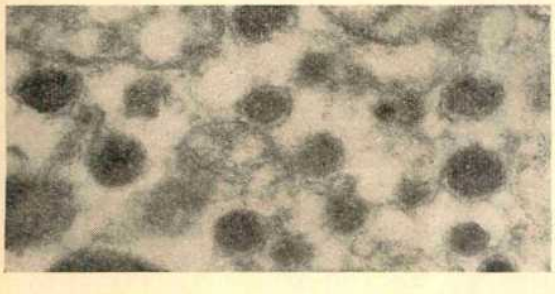

Fig. 1. Electron micrograph showing a detail of a specific granular cell from heart ventricle of *Myxine*

Electron micrographs of specimens of hearts from both species have revealed the occurrence of numerous cells containing large numbers of dense, osmiophilic granules, round in shape and measuring in diameter about 0·1μ. The granules generally show a distinct border surrounded by a lighter space which in turn is encircled by a limiting membranous structure (Fig. 1). With regard to the localization of these granules, this varies in a somewhat puzzling way. In the hagfish auricle, accumulations of granules have been observed in what appears to be ordinary heart muscle cells. However, in both species there appear to be present specific cells, extremely rich in granules of the type described. Hitherto two types of such cells have been observed, one characterized by a dark-staining cytoplasm which is completely packed with granules, and the other showing a light, almost empty-looking cytoplasm with only few granules. It is at present not possible to state if two different cell types really exist or if the varying appearance may be due to different functional stages of one and the same cell type.

The granular structures found in the hearts of these two fish species show a striking morphological resemblance to the granules found in cells of the adrenal medulla of the rat[6] and of the mouse, guinea pig and cat[7]. Furthermore, the varying appearance of the cells is very similar to that described by Lever[6] in adrenal medullary cells of the rat. He describes: "a dark cell in which abundant osmiophilic adrenaline granules are contained in a relatively opaque background cytoplasm and a light cell containing fewer secretory granules".

It is at present not possible to draw definite conclusions as to the true nature of the granular cells encountered in hearts of the cyclostomes *Myxine* and *Petromyzon*. However, taking into consideration the large amounts of catecholamines present in heart tissues of these fishes and the interesting observation that characteristic nervous elements seem to be lacking in *Myxine*[2] it seems possible that we are here dealing with a cell type belonging to the chromaffin system.

This investigation is being continued, and a full report will be presented elsewhere.

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Cannulation of Minute Mesenteric Veins for Continuous Portal Perfusion of Rats

THE introduction of a cannula into a very small vein (< 1 mm.) is almost impossible because of collapse and cohesion of the vessel walls. Any looping or clamping of the vein beyond the incision in order to avoid bleeding and to maintain a clear visual field causes spasm which will not permit further passage of the tubing into the vascular lumen. If the cannula is forced, it will perforate the thin vessel. We have, therefore, constructed a cannulating device which permits the introduction of a fine plastic tubing into a small vessel without visual control.

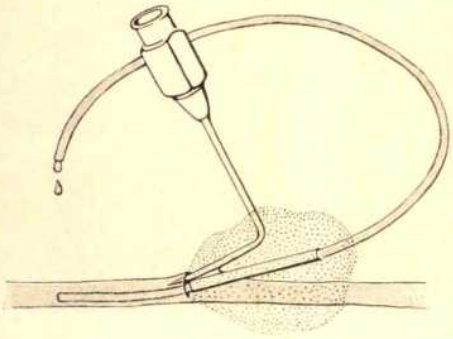

Fig. 1

The device consists of a No. 22 injection needle, 1½ in. long, the distal ½ in. of which is bent to a right angle so as to form a trough terminating at the needle point. To this trough, and just at the base of the needle point, is soldered a straight 1 in. long metal cannula, which forms an angle of about 15° with the base of the needle trough (Fig. 1). A polyethylene tubing (No. 10 Clay-Adams) with a square end is introduced into the metal cannula which will guide the plastic tubing exactly to where the point of the angled needle has punctured the vessel. When the plastic tubing is now pushed forward, it passes close to and beneath the needle point into the vascular lumen (Fig. 1). In spite of lack of visibility due to the bleeding from the punctured vessel, successful cannulation is evident from the flow of blood into the tubing. Threads which have been previously passed under the vessel and looped are tied after the point of the cannulating device has been pulled back about 3 mm. The plastic cannula is now firmly grasped with a thumb forceps in front of the needle point and held in position while the cannulating device is slipped off the tubing. The polyethylene tubing is filled with a 1:10,000 heparin–saline solution and stoppered. Eighty-eight female rats weighing 220–260 gm. were anæsthetized with intraperitoneal 'Nembutal' (6 mgm./100 gm. body-weight) and a laparotomy with exposure of the ileocæcum was carried out. The ileocæcal loop and its mesentery containing the exposed vein were spread on a thin cork plate covered with moist gauze. The mesentery was pinned down to the cork plate in order to permit the smooth sliding of the cannula into the stretched vein. The cannulating device containing the plastic tubing was attached to the barrel of a 2 c.c. syringe, thus providing a steady grip of the instrument. The cannulation of the ileocæcal vein by this technique is done close to the intestinal border of the mesentery. The abdomen is closed in two layers and the cannula brought out through the most cephalad part of the mid-line incision to prevent the rats from catching their hind-feet in the cannula. A small glass bead is slipped over and glued to the cannula at its point of exit from the abdominal wall. The cannula is fixed by putting a suture through the skin and tying it in front of the glass bead. The animals are then restrained[1] and continuously perfused with various solutions.

Of the 88 rats, 26 have been perfused for less than 3 days, 41 have been perfused for 4–10 days, and 21 have been perfused for more than 10 days.

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ANATOMY

Histochemical Demonstration of Aromatic Monoamine in the Locus Cœruleus of the Mammalian Brain

SHIMIZU *et al.* have reported several interesting histochemical results of the locus cœruleus of the mammalian brain—the strong activity of acid phosphatase[1] and cholinesterase[2] but rather poor action of respiratory enzymes[3,4], and further, characteristically strong monoamine oxidase activity[5]. The last finding led us to suppose that some aromatic monoamines such as catechol amines and serotonin would be concentrated in the locus. Although Falck and Hillarp[6] recently reported that no chromaffin reaction could be observed in the hypothalamus and the caudate nucleus, and concluded that noradrenalin and dopamine are not stored in a small number of nerve cells of these regions, they did not examine the locus cœruleus. In the present investigation several histochemical reactions including argentaffin, Schmorl's, chromaffin, azo-coupling and Gibbs's reaction were carried out in mammalian brain tissues containing the locus cœruleus.

The materials used were taken from the healthy adult rabbit, rat, mouse, guinea pig, dog and cat and also from the scorbutic guinea pig and animals treated with marsilid or catron. All tissue slices were fixed in 10 per cent neutral formalin or 5 per cent potassium bichromate–chromate solution with or without formalin[7]. The specimens were quickly embedded in paraffin, since a yellow compound due to an oxidation of chromaffin substances might be dissolved in hot paraffin[8]. The sections (7–10μ) were subjected to the following histochemical reactions: the argentaffin reaction (Gomori's methenamine silver or Fontana's ammoniacal silver solution, cf. Pearse[9]) for 24 hr. without pretreatment with Gram's iodine solution, Schmorl's ferricyanide reaction (Lillie and Burtner[10]), azo-coupling reaction (diazo blue *B* in alkaline solution, cf. Pearse[9]) and Gibbs's reaction (cf. Gomori[11]). The results are summarized in Table 1.

The silver or Prussian blue granules due to the presence of a reducing substance occurred almost exclusively in the locus cœruleus of all animals hitherto studied except for rats and mice, where the

Table 1. HISTOCHEMICAL REACTIONS OF THE REDUCING GRANULES OF THE LOCUS CŒRULEUS OF GUINEA PIGS

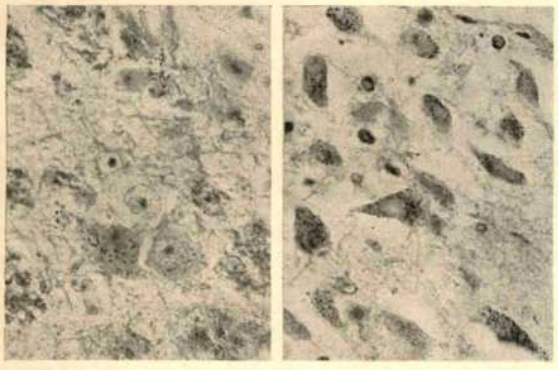
Fixation	Argent-affin reaction	Schmorl's reaction	Chrom-affin reaction	Azo-coupling reaction	Gibbs's reaction
Formalin	++	++	−	±	−
Bichromate-formalin	+	±	−	−	−

−, No reaction; ±, slightly positive reaction; +, weak reaction; ++, moderate reaction.

granules were always recognized within the nerve cell bodies and their processes but not in the neurophil. It should be mentioned, however, that the granules did not occur equally in all specimens tested, and they were not always demonstrated in all nerve cell bodies of the nucleus, but their quantity and distribution varied according to the animal species used. The granules, for example, were observed most abundantly in the dog, cat and guinea pig (Fig. 1*a*) but slightly in the rabbit and were absent in the rat and mouse. Similar but less amounts of these granules were further revealed in the dorsal nucleus of the raphe of the rabbit, dog and cat. These granules positive for argentaffin or Schmorl's reaction were further tested with chromaffin, Gibbs's and azo-coupling reactions. Although the former two were negative, the last gave slightly positive reaction.

This substance was still capable of reducing ammoniacal silver or ferricyanide after the sections had been exposed to some of the blocking agents for SH groups and aldehydes. Shimizu *et al.*[12] recently showed histochemically the characteristic deposition of ascorbic acid in the locus cœruleus, which completely disappeared in the scorbutic guinea pigs. These granules were demonstrated with the argentaffin and Schmorl's reactions even in the scorbutic guinea pig's brain. These results seem to indicate that the reducing capacity of the granules is not ascribed to the presence of SH, aldehyde and ascorbic acid.

Furthermore, administration of a specific inhibitor of monoamine oxidase (1-phenyl-2-hydrazinopropane, catron, *JB*-516), 200 mgm./kgm., to normal rats, in which the granules could not be demonstrated, produced the appearance of abundant reducing granules in the locus cœruleus (Fig. 1*b*). This experiment indicates that this reducing substance might be the physiological substrate of monoamine oxidase in this locus.



(*a*) (*b*)

Fig. 1. *a*, Locus cœruleus of the guinea pig. Moderate amounts of argentaffin granules are seen within nerve cell bodies. Fixation with formalin. Fontana's argentaffin reaction. (× *c.* 450) *b*, Locus cœruleus of the catron-administered rat. Showing the appearance of abundant granules. The animal was killed 4 hr. after subcutaneous administration of catron (200 mgm./kgm.). Fixation with formalin. Gomori's methenamine silver reaction. (× *c.* 450)

The present observations, together with the previous result of the pronounced monoamine oxidase activity in the locus[5], suggest that the reducing granules occurring in the locus cœruleus might consist of aromatic monoamine. It is likely that they could not be demonstrated by the chromaffin and Gibbs's reactions, because they occurred in low concentration and were scarcely recognizable.

The possibility that the locus cœruleus probably contains aromatic monoamine might also be supported by the recent physiological investigation by Megawa[13], which showed that the electrical stimulation of the locus has displayed the characteristic parasympathetic reactions. Brodie and Shore[14] suggested that serotonin acted as the chemical transmitter of the central parasympathetic system. This substance in the locus cœruleus seems to be easily demonstrable with fixation of formaldehyde and its reducing capacity seems to be weakened or abolished after fixation without formalin, a fact which resembles the enterochromaffin substance, serotonin. From our histochemical results and the physiological data of other investigators[13,14] it may be supposed that the locus cœruleus contains aromatic monoamine acting as parasympathetic transmitter.

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RADIOBIOLOGY

Reaction of Formaldehyde with Deoxyribonucleic Acid in Phage *T1*

IN viruses the formaldehyde reaction takes place not only with the protein but also with the ribonucleic acid, as has been shown by Fraenkel-Conrat[1]. According to Staehelin[2] the binding of formaldehyde by ribonucleic acid appears to be a specific function of the amino-groups of the bases. Yet there is no formaldehyde reaction with amino-groups involved in hydrogen bondings, as is the case in the double-stranded deoxyribonucleic acid[2]. If this acid is subjected to dialysis with distilled water for several days in the cold (a procedure which is believed to break hydrogen bonds) it is rendered more reactive

towards formaldehyde[2]. This increased reactivity is reversible by addition of a buffer[2].

In concentrations lower than 1 per cent, formaldehyde is supposed to react with nucleic acid by forming monomethylol groups (—NH—CH_2OH), which can afterwards form methylene bridges by condensation[2]. The formaldehyde reactions in proteins have been discussed by Fraenkel-Conrat[3]. Heicken and Spicher[4] studied the inactivation and reactivation phenomena in phage *T*1 after formaldehyde treatment. Since amino-methylol groups are unstable[2], inactivated phages can be reactivated by storage in the presence of formaldehyde-binding media[4]. The reactivation-rate is low and does not disturb inactivation experiments if constant conditions for phage growth are used.

The following experiments were performed to decide whether the formaldehyde inactivation of *T*1 is caused by protein damage or by reaction with the deoxyribonucleic acid.

It is known that the ultra-violet survival curve of *T*1 is made up of two components of different ultra-violet sensitivities, where the lower sensitivity results from a reactivation of a certain fraction of inactivated phages, probably by the genome of the host bacterium[5,6]. This host cell reactivation requires an injection of the phage genome and can therefore be used to indicate that an inactivated phage still injects its deoxyribonucleic acid. It is further known that doses of ultra-violet light commonly used for inactivation experiments do not affect the adsorption and injection mechanisms of bacteriophages to an appreciable extent. If other inactivating agents permit a host cell reactivation at least involving the same number of inactivated phages as does ultra-violet light, it may be concluded that the inactivation results from damage in the phage genome and that the adsorption and injection mechanisms are not disturbed to any greater extent than after ultra-violet irradiation. If *T*1 is inactivated by a solution of formaldehyde in distilled water (*p*H 5·6), the survival follows an exponential function of the formaldehyde dose (Fig. 1, curve *A*). But if *T*1, inactivated under the same conditions, is pre-adsorbed on bacteria irradiated with ultra-violet light (*E. coli B*), the number of plaque-forming *T*1 is markedly decreased, since the reactivating mechanism within the bacteria is destroyed by the irradiation (Fig. 1, curve *B*); whereas the capacity of irradiated cells to yield progeny from untreated *T*1 is unchanged. This indicates that a great number of inactivated phages are reactivated by the host bacterium and that the formaldehyde reaction takes place in the genome. A comparison was made between the sensitivity of *T*1 towards formaldehyde and ultra-violet light, when in both cases the phage is propagated in bacteria irradiated with ultra-violet light, and the sensitivity towards formaldehyde and ultra-violet light when phages are grown in bacteria that perform a reactivation. After ultra-violet irradiation as well as after inactivation by formaldehyde, and within the experimental error, the ratio of total hits to those that cannot be reactivated is about 7 : 2 (Fig. 1, curves *B* and *C*). The similarity of the ratios makes it probable that the inactivation occurs in the same structure in the case of ultra-violet and formaldehyde treatment. As the reactivation is believed to be a result of recombination between homologous parts of phage and bacterial genome, equal ratios would be expected, if the protein damage after treatment with formaldehyde is negligible.

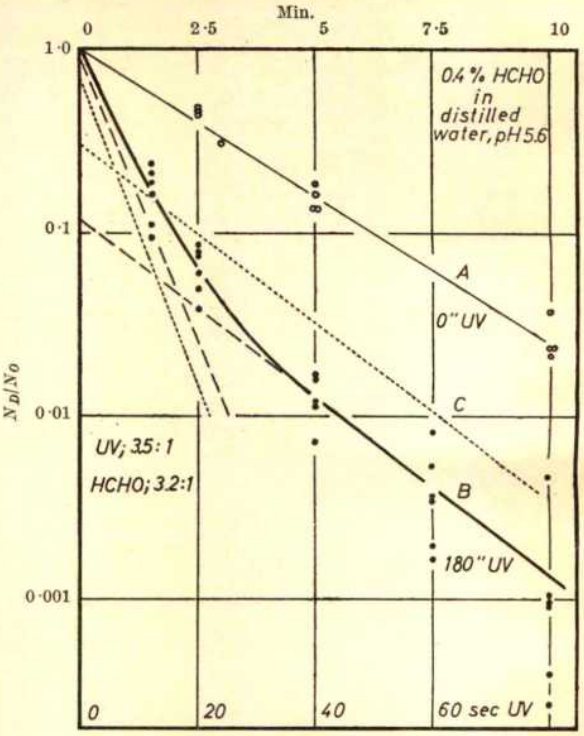

Fig. 1. Survival of formaldehyde-inactivated *T*1 in normal and ultra-violet irradiated *E. coli B*. Curve *A*, survival after pre-adsorption to unirradiated bacteria. Curve *B*, after pre-adsorption to bacteria irradiated by ultra-violet light, 180 sec. (a dose reducing the colony-forming ability of *E. coli B* by a factor of 10^4). Broken lines, decline and size of the two components of the survival curve *B*; ratio of declines 3·2 : 1. Curve *C*, dotted lines, decline and size of the two components of the *T*1-surviving curve after ultra-violet irradiation and propagation in untreated *E. coli B*; ratio of declines 3·5 : 1. Abscissa, time of incubation with formaldehyde and of ultra-violet irradiation respectively. Ordinate, relative number of surviving *T*1

But there exists still another possible explanation for the results in curve *A* and curve *B* of Fig. 1. In the case of inactivation by formaldehyde each phage which is injected survives by reactivation independently of the number of formaldehyde hits in its genome. Then, the inactivation measured in curve *A* must prevent the injection of the genome. By ultra-violet irradiation of the host bacteria, the ability for phage reactivation is lost in a certain number of cells and the damage by formaldehyde can be expressed (curve *B*). The ratio 3·2 : 1 would give the sensitivity of the total phage to the sensitivity of absorption and injection mechanisms. This explanation is very improbable, as it demands a survival of each injected phage independently of the number of formaldehyde hits in its genome.

According to the results of Fig. 1, formaldehyde hits and ultra-violet hits show the same relations concerning inactivation and host cell reactivation. Therefore, after inactivation by formaldehyde of *T*1 to 10 per cent or less survivors, the ultra-violet-surviving curve of the phages after subsequent irradiation should be an exponential function of the ultra-violet dose with the same slope as that of the 30 per cent fraction in the ultra-violet curve of untreated *T*1 (Fig. 2, curves *A*, *B* and *C*). (The steeper decline of the curves *B*, *C* and *D* in Fig. 2 is caused by the formaldehyde which has been present during irradiation in different concentrations[7].) Inactivation by formaldehyde to about 60 per cent survivors must yield an ultra-violet curve at subse-

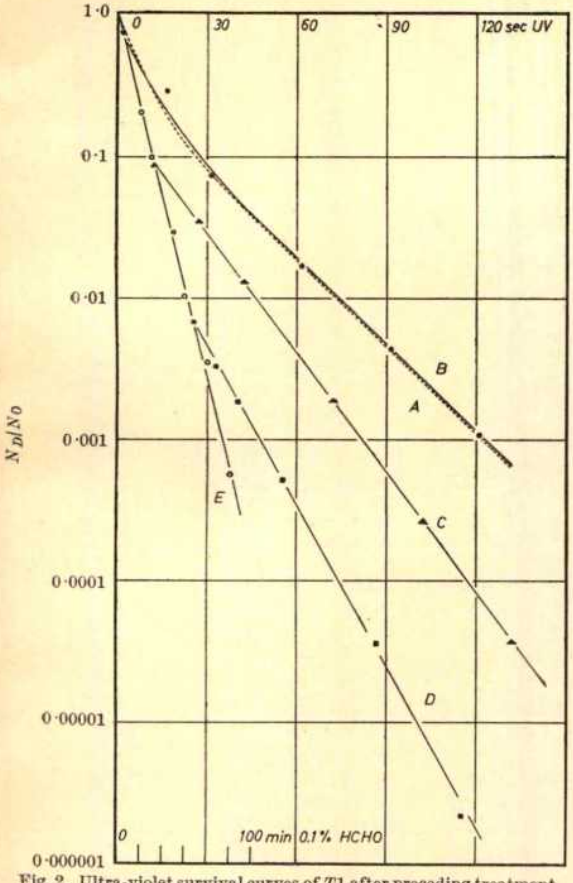

Fig. 2. Ultra-violet survival curves of $T1$ after preceding treatment with formaldehyde. Curve A, dotted line, ultra-violet survival curve of normal $T1$. Curve B, inactivation by formaldehyde to 65 per cent survivors and subsequent ultra-violet irradiation. Curves C and D, inactivation by formaldehyde to 9 per cent, respectively, 0·7 per cent survivors and subsequent ultra-violet irradiation. (The steeper decline of curves C and D results from an increased reaction-rate of formaldehyde with ultra-violet irradiated $T1$, ref. 7.) Curve E gives the survival of $T1$ after incubation with a 0·1 per cent formaldehyde solution in distilled water (pH 5·6) at 37° C. Abscissa, time of ultra-violet irradiation (for curves B, C and D the scale begins with the first point on the formaldehyde-inactivation curve); and time of treatment with formaldehyde respectively. Ordinate, relative number of surviving $T1$

quent irradiation, which is still composed of two fractions of different ultra-violet sensitivities (Fig. 2, curve B).

The results in Figs. 1 and 2 indicate that the inactivation of $T1$ by formaldehyde is mainly caused by a reaction with the phage genome. The fact that the ratio of reactivable to non-reactivable hits is the same in the case of formaldehyde and ultra-violet inactivation makes a formaldehyde reaction with the deoxyribonucleic acid most probable. The reaction has to occur with free amino-groups, which shows that not all possible hydrogen bonds are established in the deoxyribonucleic acid of $T1$.

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Effects of Ultra-Violet Light on Hydrogen Bonds in Deoxyribonucleic Acid of Phage *T1*

PHAGE $T1$, inactivated by formaldehyde, still injects its deoxyribonucleic acid, as can be shown by the degree of reactivation of 'formaldehyde-hits'[1]. The formaldehyde inactivation of $T1$ is believed to result from a reaction with the amino-groups of the bases in the deoxyribonucleic acid[1]. As Staehelin[2] has shown, formaldehyde in concentrations lower than 1 per cent reacts with free amino-groups of nucleic acids, but it does not react if these groups are involved in hydrogen bondings. Furthermore, the experiments of Nitschmann and Hadorn[3] make a formaldehyde reaction with the free imino-groups of the bases improbable.

Ultra-violet irradiation might cause a break of purine–pyrimidine hydrogen bonds in deoxyribonucleic acid. This break could be a non-lethal effect either in that it is reversible or in that it does not influence the viability of the phage. If ultra-violet light breaks hydrogen bonds in deoxyribonucleic acid, this would lead to an increased reaction-rate of formaldehyde with the amino-groups of the nucleic acid; but there should be no increase in phages with single stranded nucleic acid, if the reaction with the protein is not increased after ultra-violet irradiation. Presuming that a break of a hydrogen bond in the deoxyribonucleic acid is not necessarily lethal, the increased reaction-rate of formaldehyde with ultra-violet-irradiated phage deoxyribonucleic acid must lead to an increased inactivation-rate of irradiated

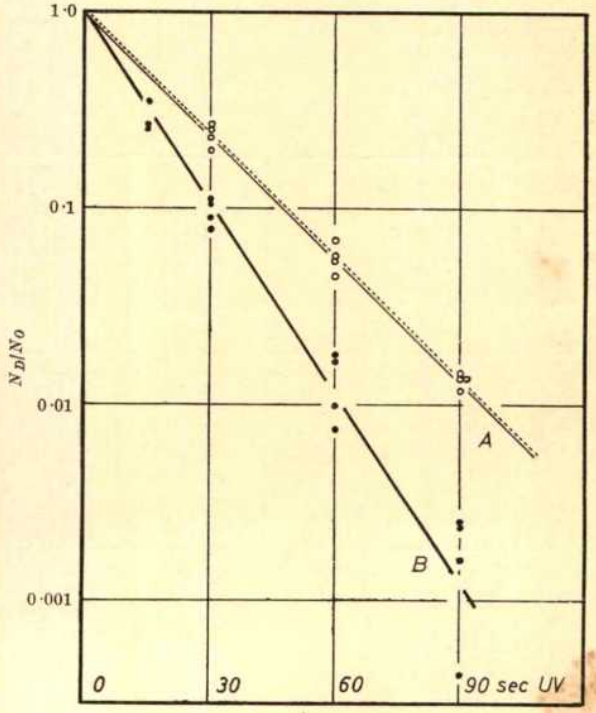

Fig. 1. Survival of $T1$ after irradiation with ultra-violet light. Dotted line, untreated $T1$, fraction which performs host–cell reactivation. Curve A, survival of $T1$ after pretreatment with formaldehyde and subsequent irradiation in buffer. Curve B, survival after irradiation in a 0·9 per cent formaldehyde solution in buffer. The steeper decline in the curve B does not result from an increased ultra-violet sensitivity, but shows the increased reaction-rate of $T1$ with formaldehyde after irradiation. Abscissa, time of irradiation; ordinate, relative number of surviving $T1$

$T1$ by formaldehyde ; and this increased inactivation-rate can easily be measured.

As a restitution of the hydrogen bonds might occur immediately after the break by ultra-violet light, the incubation with formaldehyde was performed during irradiation. In a first set of experiments, $T1$ was irradiated by ultra-violet light of wave-length 2537 Å. in the presence of 0·9 per cent formaldehyde in a phosphate buffer (pH 6·7, 0·02 M disodium hydrogen phosphate + 0·02 M potassium dihydrogen phosphate + 0·06 M sodium chloride). In these experiments the incubation times with formaldehyde were exactly the same for each sample of the different points in curve B (Fig. 1). In a second set of experiments, $T1$ was incubated at room temperature with 0·9 per cent formaldehyde in a phosphate buffer for the same time as the samples of the first experiments. Formaldehyde was then removed by a hundred-fold dilution in buffer, and the phages were afterwards irradiated (Fig. 1, curve A). These experiments were performed to show that formaldehyde given before irradiation does not alter the ultra-violet sensitivity of the surviving $T1$. The difference between curve A and curve B shows the increased inactivation-rate of irradiated $T1$ by formaldehyde. The number of amino-groups accessible for formaldehyde increases with greater doses of ultra-violet light, which indicates that hydrogen bonds are broken by the irradiation and that not each break leads to an inactivation of the phage.

The second aim was to determine whether the increased sensitivity to formaldehyde after ultra-violet irradiation is reversible, that is, whether the broken hydrogen bonds in the deoxyribonucleic acid rejoin. In these experiments, the phages were incubated for a given time with formaldehyde, at different times after ultra-violet irradiation. The curves drawn in Fig. 2 indicate that even after 24-hr.

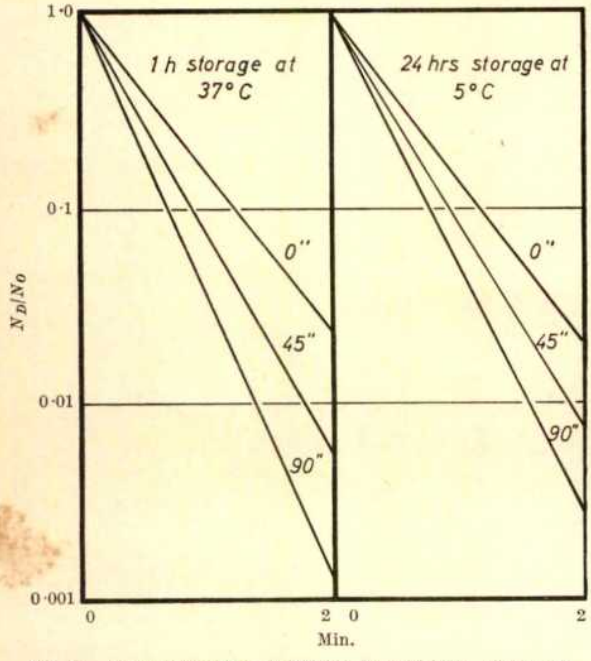

Fig. 2. Inactivation-rate of $T1$ by formaldehyde at several times after irradiation with ultra-violet light. Abscissa, time of incubation with formaldehyde; ordinate, relative number of surviving $T1$. Curve parameters, doses of ultra-violet light on $T1$

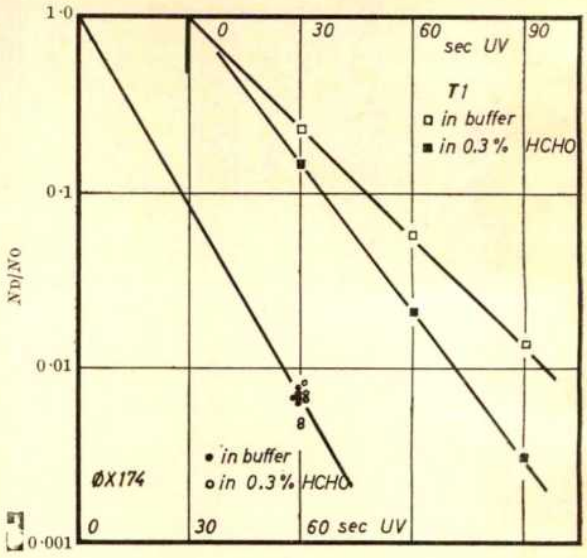

Fig. 3. Survival of φX 174 and $T1$ after irradiation in buffer and in a 0·3 per cent formaldehyde solution in buffer. Abscissa, time of irradiation; ordinate, relative number of surviving phages

storage in a phosphate buffer at 5° C. the increased formaldehyde-inactivation-rate of ultra-violet irradiated phages is still observed. (An increase of the reactivity of formaldehyde by the applied ultra-violet irradiation can be excluded.)

If the presumption should be correct that the rise in formaldehyde reaction-rate after ultra-violet irradiation is caused by a break of hydrogen bonds in the double-stranded deoxyribonucleic acid of $T1$, there should be no increase in the single-stranded deoxyribonucleic acid of φX 174. Therefore, $T1$ and φX 174 were irradiated in a buffer and, for comparison, in a 0·3 per cent formaldehyde solution. Fig. 3 shows an unchanged sensitivity in φX 174 but a significant increase in $T1$. This gives the additional result that there also is no increased inactivation from the formaldehyde reaction with the phage protein after ultra-violet irradiation, at least in φX 174.

As has been shown in Fig. 2, the hydrogen bonds broken by ultra-violet irradiation do not rejoin during a storage time of 24 hr. As it is improbable that a break of a single hydrogen bond alters the steric configuration of the deoxyribonucleic acid at this spot in such a way that the increased distance between the amino-group of one base and the ketone group of the complementary one does not allow a restitution of the hydrogen bond, a chemical change in the bases will be the cause. A possible mechanism might be the transition from the ketone- to a stable enole-configuration in the thymine, cytosine or guanine, since the enole-configuration prevents a rejoining of hydrogen bonds between the bases.

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BACTERIOLOGY

'Oxidosomes' in Bacterial Anatomy

When bacterial cells are disrupted by any of the methods now in use, a considerable amount of ultramicroscopic particles is released from them, and these can be isolated by ultracentrifugation, usually for 1–2 hr. at 100,000*g*. This fraction is quite heterogeneous. The function and localization in the cell of its different components are not yet clearly known. This is probably the reason why the nomenclature of these particles is still in a rather confused state. According to different authors they have been called 'mitochondria', 'microsomes', 'particles', 'small particles', 'particulate fraction', '*ETP*', etc.

It seems to me that up to now two different groups of particles have been adequately characterized: the 'ribosomes' and fragments of the cytoplasmic membrane with high enzymatic activity which I propose calling 'oxidosomes'. It is hoped that a sharp delineation of both concepts will promote the eventual discovery of other types of particulate subunits of the bacterial cell.

Ribosomes[1] or ribonucleoprotein particles contain 40 or more per cent ribonucleic acid, and they appear to have little enzymic activity, except perhaps in protein synthesis. Their size ranges from 20 to 100 *S*. They are probably free-floating in the cytoplasm of the bacterial cell[2–5] and possibly identical to the granules seen with the electron microscope in ultra-thin sections[6]. A single cell of *Escherichia coli* is supposed to contain about 10^5 ribosomes.

The second group of particles, which has been studied to some extent, represents the small fragments from the solid cell envelope (probably the cytoplasmic membrane), and arises artificially during the disruption of the cells. They are enzymatically very active and contain, for example, many dehydrogenases and often the complete electron transport system (flavins, cytochromes, cytochrome oxidase) to oxygen. The latter particles are still designated by a variety of vague and often incorrect names, as mentioned above, and deserve an appropriate nomenclature. Since the main enzymatic function of the cytoplasmic membrane appears to consist in the oxidation of a large variety of substrates, I propose the name 'oxidosomes' for the particles derived from it. This name has been coined in analogy with other subcellular units, such as microsomes, lysosomes[7], sarcosomes, episomes[8], protosomes[9], chromosomes, ultramicrosomes, centrosomes and kinetosomes.

These oxidosomes have been studied in several bacteria. Mitchell and Moyle[10–12] showed that the cytochrome- and dehydrogenase-bearing oxidosomes from *Staphylococcus aureus* are derived from the protoplast membrane. The 'hulls' of *Azotobacter vinelandii* are fragmented into oxidosomes, containing cytochromes, hydrogenase and the oxidases for reduced triphosphopyridine nucleotide, reduced diphosphopyridine nucleotide, succinate and malate[3,4]. The particulate L-mandelic acid dehydrogenase of *Pseudomonas fluorescens*[13] is linked to oxidosomes, since Nakada and Nozu[14] recovered this enzyme in the 'ghost' fraction. The oxidosomes of *Acetobacter* have recently been studied extensively in this laboratory[15–19]. It was shown that 'protoplast' membranes contained the same enzymes as the particulate fraction[15] and that intermittent ultrasonic disruption fragmented the 'hull' of intact cells into the oxidosomes[16]. The latter contain the cytochrome system, several peroxidases[17], catalase[17], pyruvate decarboxylase, the oxidases for D- and L-lactate, acetaldehyde, ethanol and several other alcohols[18], glucose, gluconate, 2-ketogluconate, galactose, xylose, glycerol, several polyalcohols, reduced diphosphopyridine nucleotide, malate and succinate.

Except for the fact that oxidosomes can be isolated by ultracentrifugation at 100,000*g* for 1–2 hr. and look like small roughly spherical granules of a few hundred Å. in diameter[17] under the electron microscope, little is known of their physical properties. In view of their origin and formation, it seems possible that it is a group of particles with dimensions ranging from a few hundred Å. to the visible fragments of the 'protoplast' ghost.

Ultra-microscopic particles, containing cytochromes and other enzymes, have been isolated from several bacteria (for a review, see Alexander[20]). However, for most of them, their localization in the bacterial cell has not yet been established, and this problem needs re-investigation in view of the properties and the origin of the oxidosomes. It can be postulated, though, that most of them will be oxidosomes. It would furthermore not be surprising that it is a general rule that most, if not all, of the aerobic bacteria would contain nearly all their cytochromes and cytochrome-linked oxidase systems on the cytoplasmic membrane.

Work along this line with the strictly aerobic chemi-autotrophic micro-organisms is in progress in our laboratory.

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Interconnexion between the Protective Antigen and the Histamine-sensitizing Factor of *Bordetella pertussis*

The interconnexion between the protective antigen and the histamine-sensitizing factor of *B. pertussis* forms the subject of earlier reports[1–11]. Results agree in that the two factors, if not identical, are in any event closely related as regards both their site in the

bacterial cell[11] and their activity. We have studied the behaviour of the protective antigen and the histamine-sensitizing factor under conditions which may impair *pertussis* vaccines in the course of preparation. We produced 3-day-old cultures of each of six *B. pertussis* strains of phase I on solid semi-synthetic medium. After centrifuging them, the sediment was resuspended in buffered saline so as to obtain suspensions containing 500×10^9 cells/ml. The suspensions were divided in two parts: the first was treated with 0·3 per cent formalin and kept at 37° C. for 24 hr., the second with merthiolate (1 : 5,000) and heated to 56° C. for 30 min. Both kinds of suspensions were then stored at + 4° C. We prepared, moreover, suspensions from a mixture which contained all the six strains in equal proportions. These too were divided into formalin and merthiolate fractions (7 formalin, 7 merthiolate; 8 formalin, 8 merthiolate). Seven and 8 merthiolate seemed to be especially satisfactory in respect of protective potency and histamine-sensitizing activity: we prepared two precipitated vaccines from each of them. One contained 7 mgm./ml. of preformed aluminium phosphate gel (Holt[12]); a solution of trisodium phosphate was first added to the suspension in the case of the other vaccine and followed immediately by the admixture of a solution of aluminium chloride producing aluminium phosphate gel *in statu nascendi*. This vaccine contained likewise 7 mgm. of aluminium phosphate/ml. The addition of trisodium phosphate was observed to have raised the *p*H value of the mixture to 14. We determined the mouse-protection value of the suspensions and precipitated vaccines according to the prescriptions of the National Institutes of Health, Bethesda[13], and their histamine-sensitizing activity by the method of Preston[14]. It is evident from Table 1 that suspensions treated with merthiolate were significantly superior to those treated with formalin as regards both mouse-protective potency and histamine-sensitizing activity. The respective values of the two factors thus ran along parallel courses, and this close correlation was independent of whether old or fresh vaccines were employed. As regards precipitated vaccines, it is shown by our results that, however short their duration, strong alkalinity considerably impairs mouse-protective potency and histamine-sensitizing activity, while they are not affected by the preformed gel of Holt. Repeated tests confirmed these results in every respect.

Table 1. MOUSE PROTECTIVE POTENCY AND HISTAMINE-SENSITIZING ACTIVITY OF DIFFERENT *Pertussis* VACCINES

Strain and lot	Mouse protection test		Test of the histamine-sensitizing factor	
	ED_{50}	*RP**	SD_{50}	*RP*†
324*E* (1F)	4,278	0·14	54	0·11
324*E* (1M)	305·4	1·90	17	0·36
358*E* (2F)	6,390	0·09	25	0·25
358*E* (2M)	1,454·4	0·41	6·25	1·00
41405 (3F)	3,148·8	0·18	30	0·20
41405 (3M)	388·8	1·50	5·38	1·16
*CN*2894 (4F)	>3,000		21·6	0·28
*CN*2894 (4M)	926·4	0·64	5·4	1·15
*CN*2896 (5F)	2,319	0·25	45·5	0·14
*CN*2896 (5M)	401·4	1·50	2·5	2·50
*CN*2897 (6F)	2,319	0·25	21·6	0·28
*CN*2897 (6M)	179·4	3·30	4·2	1·45
546/4 (7F)	3,639	0·37	>50	<0·10
546/3 (7M)	1,054	1·30	6·25	1·00
*K*701*A* (8F)	3,524·4	0·38	20	0·31
*K*701*B* (8M)	519	2·60	2·2	2·88
546/3/1 St. n.	>3,000		>45	
546/3/2 Holt	228·3	2·60	11·25	
*K*64 St. n.	2,949	0·46	28	
*K*65 Holt	382	3·50	11·6	

Date of preparation of the vaccines. 1–6: VI (1959). 7: VI (1956). 8: X (1959). 546/3/1–2: V (1958). *K*64–65: XII (1959).
ED_{50} in million germs. Testing, I–II (1960).
SD_{50} in 1,000 million germs. Testing, II–III (1960).
* *RP*, relative potency referred to a lyophilized reference vaccine.
† *RP*, relative potency referred to the most frequently tested suspension 546/3, used also for the preparation of the lyophilized reference vaccine.
F, Formalin; M, merthiolate.

It was shown in earlier experiments[1,3] that *B. pertussis* of phase IV displays no histamine-sensitizing activity, and it is known to have no protective potency. We examined some factors which our experiments had shown to influence the protective antigen and histamine-sensitizing factor of *B. pertussis* in a similar manner. Similarity in their sensitivity to heat and in their response to different chemical agents and to variations in the phase of the bacterium has convinced us that the two factors, if not identical, are closely related and of a similar chemical structure; it is possible that they form a common antigen-complex. Since the mouse-protective potency and the histamine-sensitizing factor are affected in exactly the same manner by practically all factors which influence the efficacy of *pertussis* vaccines, it seems that—with the application of an adequate (perhaps lyophilized) standard vaccine—determination of the histamine-sensitizing factor might enable us to ascertain the real value of *pertussis* vaccines.

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BIOLOGY

Embryonic Mortality induced Experimentally in the Rabbit

SYSTEMIC treatment of the pregnant doe with suitable preparations, for example stilbœstrol, results in the destruction of the entire litter[1]. However, a surgical approach is required in order to destroy selected embryos. Huggett and Pritchard[2] induced prenatal mortality in rats by crushing the fœtuses with toothed forceps through the intact uterine wall at laparotomy. Later, Frazer[3] employed this technique to produce a standard number of implantations by destroying any in excess of the desired number. In rabbits, Brambell *et al.*[1] also used a surgical technique to kill embryos on the 16th or 19–20th days of pregnancy; in some animals attempts were made to kill the entire complement of embryos while in others only some of the embryos were treated. The technique

consisted of perforating the uterine swellings through the antimesometrial wall of the uterus and stabbing at the embryos with a fine suture needle. Rather surprisingly several of the embryos survived this treatment. During experiments on rabbits[1] concerning the distribution of embryonic death after implantation, it became necessary to ascertain the effect of the stage of pregnancy when death occurred on the resorption of dead embryos and their placentæ in litters that survived to term. Accordingly, a technique was developed whereby embryos could be killed selectively between the 7th and 17th days of pregnancy. It is the purpose of this communication to describe the application of this technique, which proved to be highly successful.

In 14 does laparotomy was performed under 'Nembutal' and ether anæsthesia, and the uterine horns were exposed. Then an incision about 4 mm. long was made through the antimesometrial wall of the selected uterine swellings, and the underlying membrane was also incised so that fluid would escape from the conceptus. In some cases very gentle digital pressure was applied to assist the escape of fluid, care being taken to avoid exteriorizing the embryo. In each animal, alternate uterine swellings were treated, but any sites that were considered to be undergoing resorption were not included. Altogether, 71 sites were treated in this manner either on the 7, 8, 10, 12, 15 or 17th day of pregnancy. Autopsy was performed on the 28th day of pregnancy, when the uterine contents were examined and weighed. Apart from one doe which was treated on the 15th day of pregnancy but aborted 7 days later, the remaining 13 does maintained the pregnancy. None of the sites which had been treated surgically contained a live fœtus at autopsy and with one exception death of the embryos appeared to have occurred shortly after the operation. When the operation was performed on or before day 15, the 62 treated sites were all represented by atrophic placentæ at autopsy. However, of the 9 sites treated at 17 days, only 2 were represented by atrophic placentæ, whereas the other 7 contained dead fœtuses. Six of these fœtuses were quite small and necrotic (crown rump length approximately 15 mm.) but the remaining one, which weighed 24 gm., probably survived the operation for at least 8 days. The weights of placentæ corresponding with treated sites are given in Table 1. Control placentæ associated with live fœtuses weighed 5–8 gm. on the 28th day of pregnancy.

It is thus apparent that the removal of fluid from the conceptus between days 7 and 17 prevents embryonic development in the rabbit. It would appear that during this period of pregnancy, when there is normally a peak of mortality[1], the embryo is more sensitive to environmental disturbances than at slightly later stages when it may continue to grow even after such severe operational procedures as decapitation[5]. No exact information is available on the interval elapsing between treatment and death of the embryo, but in one doe examined 2 days after the operation, which was performed on the 12th day of pregnancy, the treated embryos were no longer visible. This suggests that death and resorption take place very rapidly. However, judging from the amounts of placental tissues still present at the end of pregnancy it seems that the placenta may survive for some time after the embryo dies.

Table 1. EFFECT OF EMBRYONIC DEATH, INDUCED SURGICALLY BETWEEN SEVENTH AND SEVENTEENTH DAY AFTER MATING, ON THE WEIGHTS OF PLACENTÆ RECOVERED ON THE TWENTY-EIGHTH DAY OF PREGNANCY. (MEANS ± *S.E.*; RANGES IN PARENTHESES)

Stage of pregnancy at operation (days)	Does No.	Uterine swellings		Weight (gm.) of placentæ corresponding to treated sites
		Total	Treated surgically	
7	2	23	11	0·7 ± 0·1 (0·3–0·9)
8	2	17	9	0·6 ± 0·1 (0·3–0·8)
10	3	28	15	1·1 ± 0·2* (0·3–1·7)
12	2	22	11	1·0 ± 0·1 (0·6–1·6)
15	3	37	16	2·6 ± 0·4† (1·5–4·4)
17	2	18	9	3·6 ± 0·2 (2·6–4·4)

* Based on 10 placentæ in 2 does; † based on 11 placentæ in 2 does.

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Photographic Studies of Fish Populations

FOLLOWING the work of Veevers at Plymouth, we have been using cameras for some years for studies of sea-bed and mid-water life. These electronic flash cameras are suspended from a stationary or drifting research vessel, and operated either from the ship or by triggering at a set distance from the bottom. Our frogmen have also made studies of fishing gear and fish behaviour, though their work is limited to water of less than 10 fathoms depth and to conditions of full daylight.

We wished to extend our observations of fishing gear to deep water and to night, as well as daylight, conditions. We also felt it would be useful to take repeated photographs on one spot to study changing conditions.

We have therefore developed a simple self-contained camera and flash unit, using dry batteries and operated by a clockwork timer, which can take about 200 exposures at pre-set intervals—actually 1-min. and 3-min. intervals have been used up to the present.

This camera has been used in two ways:

(*a*) Attached near the headline of a trawl, so as to photograph the groundrope, or the zone immediately in front of it. The first sets of results, in depths up to 65 fathoms, confirm our frogmen's observations that fish in this region are normally swimming away from the groundrope and are therefore aware of the fishing gear. These observations will be continued to determine more exactly the influence of depth and light.

(*b*) Placed on a heavy tripod and left on the sea-bed for subsequent recovery by means of a buoy rope. When used in this way there is less chance of fish being disturbed from their normal behaviour than when the camera is swinging below a ship. A first set of experiments was made using this technique in March on Ballantrae Bank, in the Firth of Clyde. This showed that most of the fish then present near the bottom were herring, that their numbers and shoaling pattern on that occasion did not vary with the time of day

or night, and that the fish were present in small shoals of twelve to twenty fish. A local population density of about 2,000,000 fish per square mile was estimated from the known lens angle and limits of visibility.

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Influence of the Organic Matrix on Crystal Type in Molluscs

THE calcium carbonate of mollusc shells occurs as calcite in some species, as aragonite in others, and certain species deposit calcite in one portion of the shell and aragonite in another portion. Various explanations have been suggested for the formation of aragonite, which is significantly less stable. Participation of the enzyme carbonic anhydrase and the influence of the protein matrix on which the crystals are deposited have both been suggested[1]. We have investigated the capacity of pieces of decalcified matrix to induce aragonite formation when inserted into a mollusc which normally forms only calcite, and also under *in vitro* conditions in which calcium carbonate is normally precipitated as calcite.

Protein matrix was prepared from shells of the fresh-water clam *Elliptio complanatus*, from the marine fan shell *Atrina rigida*, and from the nacreous layer of the Japanese pearl oyster *Pinctada martensii* by decalcifying with 1 per cent sodium ethylenediamine tetraacetate at *p*H 5·0. In each case the shell from which the matrix was taken was aragonite. Microscopic examination of each piece of matrix showed that all crystalline material had been removed. To make certain that submicroscopic crystals did not remain, some pieces of matrix were treated further with 0·01 *N* hydrochloric acid. For *in vivo* studies a single piece of decalcified matrix was wrapped around a fragment of glass cover-slip and inserted between the mantle and shell of the oyster *Crassostrea virginica*, which deposits a calcite shell. The temperature of the water was 19–25° C. The inserted pieces of matrix were removed after various intervals, usually 24 hr., washed thoroughly in deionized water, and the crystals identified under the polarizing microscope. *In vitro* calcification of matrix was carried out at 25 ± 2° C. in 100 ml. of a calcium bicarbonate solution prepared from reagent grade calcium carbonate in deionized water[2]. Pieces of decalcified matrix were placed in this solution for 25–44 hr., during which time the *p*H rose from 6·4 to 8·3.

Both *in vivo* and *in vitro*, aragonite crystals formed on protein matrix from aragonite shells (Table 1). Calcite crystals were also deposited on the matrix in both cases. The forms of calcite and aragonite crystals were distinct, the former being rhombic or rosette-shaped, and the latter irregular, spherulitic or hexagonal elongate. Aragonite was never found on substrates other than aragonite matrix. Tested substrates and conditions included: (1) glass cover-slip fragments inserted in *Crassostrea* (25 cases); (2) 'Formvar' plastic inserted in *Crassostrea* (4 cases); (3) decalcified calcite matrix from prismatic layer of *Pinctada* inserted in *Crassostrea* (3 cases); and (4) decalcified calcite matrix from prismatic layer of *Pinctada* tested *in vitro* (10 cases). Calcite crystals only were deposited in each of these instances.

Table 1

Test system	Source of protein matrix	Total No. of matrix pieces analysed	No. of matrix pieces with aragonite crystals
In vivo	*Pinctada martensii*	4	2
	Elliptio complanatus	8	1
	Atrina rigida	5	1* (?)
In vitro	*Pinctada martensii*	5	2†
	Elliptio complanatus	3	1‡
	Total	25	6 or 7

* The crystals were clustered and could not be analysed. Their form was irregular and different from calcite crystals.
† Final *p*H 8·3.
‡ Final *p*H 7·3.

Even though freshly secreted matrix might normally induce aragonite formation in aragonite-forming molluscs, aragonite induction might well have been prevented in the present experiments by at least three conditions: (1) alteration of the original state of the aragonite matrix; (2) conversion of small aragonite crystals to calcite after deposition; (3) presence of freshly secreted matrix by the calcite-forming host mollusc. The finding of aragonite in approximately one-quarter of the cases (Table 1) is accordingly of a higher frequency than might have been anticipated.

The results point to the protein matrix as a factor determining the crystal type in molluscs. At present we have no information on molecular spacing of protein matrix of calcite and aragonite shells which might permit profitable speculation as to possible mechanisms.

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The Skipper (*Scomberesox saurus*) in the Southern North Sea and the Thames Estuary

THE skipper or saury pike is a pelagic fish of the open Atlantic and Mediterranean, ranging from Tristan da Cunha[1] northwards to the Gulf of Maine and the Bay of Fundy[2] in the western Atlantic, and to Christiana Fjord and Gjesvaer, near the North Cape, in the European Atlantic[3]. On the southern and south-western British coast it is of frequent, if not annual, occurrence, and catches of up to 100,000 have been reported at Mevagissey, Cornwall[4]. Farther north it has often been recorded from the Hebrides, the western Scottish coast and the Shetland and Orkney Islands[5], but the number of records decreases noticeably on the eastern coast of Scotland. Rae (personal communication) has found a specimen off Buchan Ness, Aberdeenshire (November 21, 1957); one in the Moray Firth (December 18, 1958); a shoal at Saltburn, Cromarty Firth (December 21, 1958); one at May Island, Firth of Forth (December 1, 1958); and one from a cod stomach 12′ N. St. Abbs, Berwick (February 18, 1959).

Farther south in the North Sea, records are still fewer. It has been noted from Scarborough[4] prior to 1884, and again in 1932[6], off Norfolk (October 1843)[4], and at Yarmouth[7], although it is probably more common than these few records suggest. In 1958 more than fifty were washed up at Southwold, Suffolk, and not less than twenty near Lowestoft (January 4–6, 1958); one at Corton (January 1); and one at Lowestoft (January 14) (R. W. Blacker, personal communication). In the Thames estuary, the skipper seems to have been recorded only once before, when one was found on the shore of West Mersea, Essex (December 20, 1907), as reported by Murie[8]. Writing of the occurrence of this fish on the Belgian coast, Poll[9] regarded it as rare, and in fact cited only two records, of a number on the coast in December 1854, and of one at Ostend in 1933. Kristensen[10] has, however, recorded more than a hundred in December 1955, stranded between Egmond and Texel (Holland), and three in January 1956 stranded at Den Helder, Egmond and Zandvoor. He also gives details of ten other records from the Dutch coast during the years 1909–52.

Records from various sources during the winter of 1959–60 indicate that the skipper entered the southern North Sea in larger numbers than previous records would suggest is usual. The following records have been made available to us by R. W. Blacker; two of a large number seen were caught (November 26) near Boston in the mouth of the River Witham; one alive at Corton (December 11); one alive on Lowestoft beach (December 28); two dead at Corton (December 29); a heavy stranding at Hemsby (December 31); one alive at Corton (January 1, 1960); two at Lowestoft, one at Gorleston (January 2); seventeen records between Walberswick and Yarmouth, mostly live strandings (January 2 to 12). Also during this period one of us (M. N. M.) obtained single live specimens from the River Crouch, Essex, on December 4 and 8, and a third one was found dead in the river on December 31. We have been informed by W. H. Harvey, fishery officer for the Kent and Essex Sea Fisheries Committee, that a number of skippers were caught in December by Southend and Leigh-on-Sea fishermen, while catching sprats near the East Cant Buoy, River Thames.

It seems likely from the records given here, and from those published by other authors, that in the late summer and early autumn there is often an invasion of the North Sea by shoals of *Scomberesox* through its northern entrance. Some, at least, of these fish turn southwards and may be caught later off the east coasts of Scotland and England. Others, reported in the Kattegat and the Oresund[11], probably represent a contingent entering the Baltic. Apparently only exceptionally do they move southwards as far as the Thames estuary. It is interesting that most of the skippers reported here were stranded, or were swimming in shallow water in the winter months of November, December and January, which seems to us to suggest that the winter cooling of the North Sea is associated with these strandings. A similar explanation has been advanced by Kristensen, who also considers that violent disturbance of the sea by storms may have some effect. In addition, he pointed out that exposure to low temperatures can result in disorientation in fish accustomed to warmer water.

We thank B. B. Rae, R. W. Blacker, W. H. Harvey and H. E. Jenner (through R. W. Blacker) for their co-operation in reporting catches of *Scomberesox*.

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Influence of Light Intensity on the Redox Potential in Leaves in cases of Iron-induced Chlorosis

AN investigation of the variation of the oxidation-reduction potential in cases of iron deficiency or calcareous chlorosis has been made in an attempt to find a relation between the redox general condition, the formation of the chlorophyll complex and its stability.

The phenomenon of iron-induced deficiency and its consequence, the low chlorophyll content, is thought to be the result of two effects[1]: (1) the low content of soluble iron; (2) the influence of light. The correction of the deficiency, that is, increasing the amount of chlorophyll present, can be obtained by injecting iron or by lowering light intensity[1]. After correcting the deficiency by one of the two processes, the green area of the leaf shows a redox potential higher than the normal characteristic of chlorotic material. However, the oxidation-reduction stage reached after the first process is permanent while that achieved by lowering light intensity is only temporary, since the potential returns again to that of the chlorotic conditions when a return to intense sunlight is made[2].

The existence of a higher redox stage after correcting the deficiency suggests the problem of discerning whether the increase of potential is a consequence or rather the cause of the formation of chlorophyll. The results obtained[2] have supported the second hypothesis, that is, that for raising the chlorophyll content a certain redox-level is needed below which the actual amount cannot be increased.

Study of variation in the redox potential when light intensity is changed is one of the points considered of main interest for the interpretation of iron-induced chlorosis.

The photolability of the chlorophyll complex formed with low light intensities has been ascribed[3] to the high amount of chlorophyll *b* formed, that is, to the different relation between the *a* and *b* forms of chlorophyll. But if the decomposition observed when reversing the conditions of light were only due to the different composition of the chlorophyll complex, it could be expected to stop such a decomposition as soon as the corresponding value for the green material had been reached. However, my results[2] do not con-

firm such assumption, since when the change from low to intense sunlight is made the decomposition continues, yet the relation between the two forms of chlorophyll shows a similar value to that of the green leaves. It means that the decomposition of the chlorophyll complex ought to be independent of the proportion of the *a* and *b* components.

Therefore it can be deduced that while the mechanism of chlorophyll formation is actually working in the chlorotic material, its protective mechanism on the contrary fails. The protection has been ascribed to reducing substances like polyphenols[3] since iron deficiency is reflected in the contents[1]. Now, if such interpretation were correct it is obvious that the formation of polyphenols ought to be prior to the formation of chlorophyll ; but my results show that when iron is injected into the system following the diagnostic biological method[4] the formation of polyphenols occurs subsequent to the formation of chlorophyll.

According to this, the phenomenon of iron-induced deficiency and the protective effect of iron may be explained in the following way :

The chlorophyll present in chlorotic leaves is activated under the action of light, but only a small fraction will be stabilized while the rest decomposes. The reason is that in chlorotic conditions, ferric compound (protective agent) is present in small amounts, relative to the large number of electrons to be trapped. Then the iron will be mainly present in the ferrous form, and thence the redox potential will be low. If light intensity is lowered, only a small amount of chlorophyll will be activated and the small amount of ferric compound already present may not have at its disposal a sufficient number of electrons to pass to the ferrous form. In consequence, only very little ferrous compound will be present, and the redox potential will be higher than before. It can be easily realized that this stage cannot be permanent, because when restoring the high light intensity the conditions will be as in the beginning, namely, limited amount of ferric compound and high amount of activated chlorophyll will be present again. The only way to normalize the process is, therefore, by directly increasing the amount of ferric compound, for example, by injecting iron into the system.

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ENTOMOLOGY

A Fly Larva that tolerates Dehydration and Temperatures of −270° to +102° C.

THE chironomid, *Polypedilum vanderplanki* Hint., breeds in small pools formed in shallow hollows on unshaded rocks in Northern Nigeria and Uganda. The hollows are often only 5–9 in. deep, and during the rainy season they may fill and dry several times. When the pools dry up the larvæ also dry up and remain in this condition until it rains again, when in about 1 hr. or so they resume feeding. The degree to which the larvæ dry up depends upon the relative humidity of the air. When moisture content was plotted against relative humidity, it was found that at 0 per cent relative humidity it was less than 3 per cent, at 60 per cent relative humidity it was 8 per cent, and at higher humidities the curve rose more steeply. In saturated air the moisture content altered from 3 to 33 per cent within 6 hr. at 25° C. The figures for moisture content are based on the assumption that the larva contains no water when its weight is constant at 106° C. The capacity to tolerate repeated dehydration is clearly of selective value to this species, and in the laboratory larvæ have survived as many as 10 dehydrations to a moisture content below 8 per cent. Between dehydrations they were allowed to feed in water, usually for 1–4 days.

Larvæ remain viable for long periods in the dry state. Larvæ kept at room temperatures and humidities for 39 months produced normal adults when allowed to grow in water[1]. For most of this period their moisture content was probably about 8 per cent ; but in damp weather it may have risen to as much as 20 per cent. Recent attempts to activate 130 larvæ stored for 7 years and 127 larvæ stored for 10 years at room humidities were not successful. However, a high percentage of larvæ stored for 3 years at room humidities and then over calcium chloride for a further 7 years recovered temporarily when placed in water : hearts beat for several hours and the larvæ would respond to tactile stimuli.

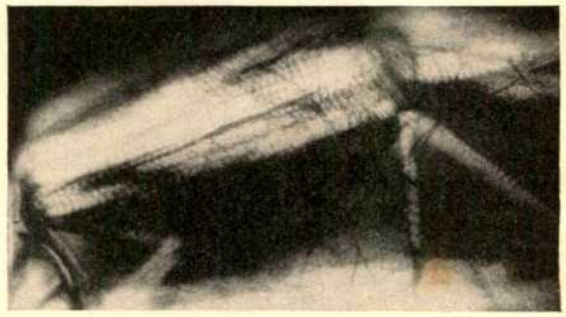

Fig. 1. Skeletal muscles and tracheæ of the thorax of a living larva of *Polypedilum vanderplanki* that had been stored dry for ten years : three years at room humidities and a further seven over calcium chloride

It has been shown[2] that active larvæ tolerate water temperatures up to 41° C. for continuous periods longer than any they encounter under natural conditions. They do not survive exposure to temperatures of more than 43° C. for more than about 1 hr. The temporary pools in which the larvæ live have a bottom layer of mud in which the larvæ tunnel. When the pools dry, the larvæ remain in their tunnels and dry out with the mud. In the dry season the shade temperatures of some of the localities in which the species is found rise to a little above 40° C. The surface temperatures of fine soils may be 20–30° C. above shade temperatures. During the hottest part of the day temperatures at the surface of the dry mud may therefore be as high as 70° C., or perhaps a little higher owing to radiation from the rock sides of the hollows. However, the larvæ are probably rarely exposed to such temperatures because the surface of the mud is usually protected by some plant debris and most larvæ are 4–8 mm. below the surface. There is a steep fall in temperature away from the surface : even assuming a surface temperature of 80° C., the temperature at 4 mm. is 70° C. and at 8 mm. it is 60° C.[3]. When dried larvæ

were exposed to similar temperatures, it was found that 93 per cent survived exposure to 61° C. for 14 hr. and 26 per cent survived exposure to 68° C. for 11 hr.[2].

It has recently been found that some larvæ will grow and successfully metamorphose after exposure to 102–104° C. for 1 min. when dry. The moisture content of such larvæ was first reduced to less than 3 per cent with phosphorus pentoxide or other dehydrating agents. They were then placed in an electric oven at 53–55° C., and the temperature raised in 10 min. to 70° C. The larvæ were then dropped on to a watch-glass in another oven at 102–104° C. The temperature of the watch-glass in the second oven had reached equilibrium with the air temperature, so that no heat was lost from the larvæ by conduction. Larvæ exposed to temperatures of over 100° C. for as much as 5 min. did not live for more than 41 hr. when afterwards placed in water, but they will recover for a short time after exposure to 106° C. for 3 hr. or to 200° C. for 5 min.

Larvæ with a moisture content of about 8 per cent survive being dropped from room temperatures into liquid air (− 190° C.) or liquid helium (− 270° C.). Two lots of 5 larvæ each were dropped directly into liquid air and kept there for 2 and 77 hr. respectively. All the larvæ grew normally when afterwards placed in water. Larvæ were immersed in liquid helium in a glass tube inside a metal container. Five larvæ were exposed for 3 min. and six for 5 min. All eleven grew normally when placed in water. Some of the larvæ treated with liquid air and with liquid helium were kept and in due course metamorphosed.

Active larvæ die in less than 1 min. when immersed in absolute alcohol, but when their moisture content is reduced to about 3 per cent most recover. After 24 hr. in absolute ethanol, 27 of 33 larvæ recovered. Of these all but three died within 27 hr. One died after 24 days without feeding, one that was active but not feeding was fixed after 16 days, and one metamorphosed. Ten larvæ in absolute ethanol for 7 days all recovered, and the heart of one beat for more than 55 hr. Larvæ recovered for very short periods when kept in 95 per cent ethanol for 24 hr., but none recovered when the percentage of ethanol was as low as 90. Attempts to keep dry larvæ in pure glycerol were slightly more successful: three of four larvæ in glycerol for 24 hr. survived, as did two of six in glycerol for 67 hr. and one of twelve in glycerol for 7 days.

I am grateful to Mr. R. G. Bennett, Dr. T. M. Leach, and Dr. F. L. Vanderplank for supplies of larvæ.

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Effect of amputating Stylets of Mature Apterous Viviparæ of *Myzus persicae*

WHILE investigating the transmission of viruses by aphids, I observed that amputating the stylets of mature apterous viviparæ of *Myzus persicae* (Sulz.) caused them to give birth to an unusually large number of larvæ for aphids that could not feed. Indeed, for about a day the aphids produced as many larvæ as if they were feeding. To appreciate the unusualness of this response, it should be understood that, as a rule, keeping *M. persicae* without food almost completely inhibits the birth of larvæ. For example, when 25 mature adults were kept singly in small vials at about 20° C., the number alive after 1, 2 and 3 days was 25, 22 and 0 respectively; and during this time 14 of the aphids produced no larvæ, 9 produced one each, and 2 produced two each (13 larvæ in all). In comparison, the same number of aphids on a host plant produced more than 100 larvæ each day; and when 25 aphids were kept in vials after amputation of their stylets, each one produced from two to several larvæ (a total of 133 larvæ the first day); the bodies of these aphids became greatly distended, and all of them died on the second day, which was about a day earlier than the controls in vials died. The larvæ born in vials were nearly all alive at the end of the day when they were counted, and those transferred to host plants developed into adults within two weeks. Thus they appeared to be normal.

Afterwards it was found that certain other treatments of the mouth parts of *M. persicae* also caused mature aphids to deposit numerous larvæ when kept without food in vials. For example, cutting off about 25μ from the distal end of one of the mandibular stylets or from the interlocked maxillary stylets caused as marked a larviposition response as did removing all four stylets (Table 1). These operations also inhibited feeding, for aphids died within 2–3 days whether kept in vials or on a host plant. Those on plants sometimes made what looked like feeble attempts to probe, but they never had their stylets inserted when they were anæsthetized with the tip of the labium affixed to the plant. Thus they seemed to be unable to insert their stylets. The mandibular stylets were separated from the maxillæ by first sliding the labium towards the head to bare the stylets[1], then supporting the bared stylets on a microrod and gently pressing across them with a single hair. This operation by itself did not cause a larviposition response (Table 1); and since this method leaves the basal part of the stylets within the labial groove, the aphid can get its stylets back together simply by sliding the labium outwards as when it withdraws from feeding. But if the stylets are taken right out of the labial groove and then separated, *M. persicae* cannot get the mandibles back alongside the maxillæ and therefore cannot reinsert all the stylets into the labial groove. This operation therefore prevents further feeding, and interestingly enough it also causes the larviposition response. The same is true if the stylets are taken out of the labial groove and the labium mutilated. It is also interesting to note here that Johnson[2] obtained a larviposition response after decapitation of mature adults of *Aphis fabae* Scop. These various treatments that cause larviposition in the absence of feeding may not all do so in the same way, but it is noteworthy that they have at least one other thing in common in that they also permanently inhibit feeding. When an animal carrying fully developed young can no longer feed, there are obvious evolutionary advantages to a mechanism that allows the young to be born instead of perishing within the mother.

Table 1 also presents results to show that the larviposition response following amputation of the ends of the stylets was not simply a general response to wounding. Thus there was no such response after amputation of the antennæ, their tips, a tarsus, or a leg. Cutting off the antennæ so affected *M. persicae*

Table 1. NUMBERS OF LARVÆ PRODUCED BY MATURE APTEROUS VIVIPARÆ OF *M. persicae* KEPT OVERNIGHT IN GLASS VIALS AFTER AMPUTATION OF CERTAIN PARTS

Part amputated	Larvæ from ten aphids	
	Treated	Controls
All four stylets	44	0
End of one mandible (about 25μ)	47	0*
End of maxillæ (about 25μ)	38	0*
Both antennæ	1	0
Tips of antennæ	4	2
One tarsus	0	2
One leg	0	2

* Controls anæsthetized and mandibular stylets separated from maxillary stylets.

that those kept in vials died more than a day earlier than the controls in vials, and though the other operations did not affect the mortality of aphids kept in vials, presumably they caused as serious wounding as the removal of the ends of the stylets, which are believed to be non-living structures.

Cutting off the ends of the stylets has also caused a marked larviposition response by non-feeding aphids of all other species thus far tested. These were mature apterous viviparæ of: *Aphis fabae* Scop., *Macrosiphum granarium* (Kirby) (= *M. avenae* Fabr.), *Macrosiphum euphorbiae* (Thom.), *Myzus ascalonicus* Doncaster, and *Myzus certus* (Wlk.). This larviposition response suggests that the functions of the stylets are more complex than is generally thought, but any discussion of its significance at this time would be rather speculative. Further studies of this response are in progress and will be published elsewhere.

That cutting off the stylets of mature aphids causes them to produce young without feeding has been overlooked in earlier work. Thus Miller[3] claimed that cutting off the ends of the stylets did not prevent feeding by *Macrosiphum ambrosiae* (Thom.) or *M. granarium*. Apparently he concluded that the aphids fed because they reproduced and appeared to be feeding when viewed with a lens. In tests with *M. granarium* I found that amputating the ends of the stylets of mature apteræ caused a marked larviposition response by aphids kept in vials or on host plants. It is true that those on plants appeared to be feeding, but none could be found to have its stylets inserted; and furthermore, whether on plants or in vials the aphids died within two to three days. A second case in point is the following statement by Johnson[4], who was discussing the colonization of plants by alatæ. "It is interesting to observe that insertion of the stylets into plant tissues is not essential for either host selection or reproduction, and aphids with their stylets cut off will settle down and reproduce on suitable hosts just as aphids with intact stylets." Although this statement is quite true, it seems likely that after removal of the stylets the aphids would have settled down and reproduced on unsuitable plants and even on a non-plant surface.

I am indebted to Mr. C. V. Wade for technical assistance.

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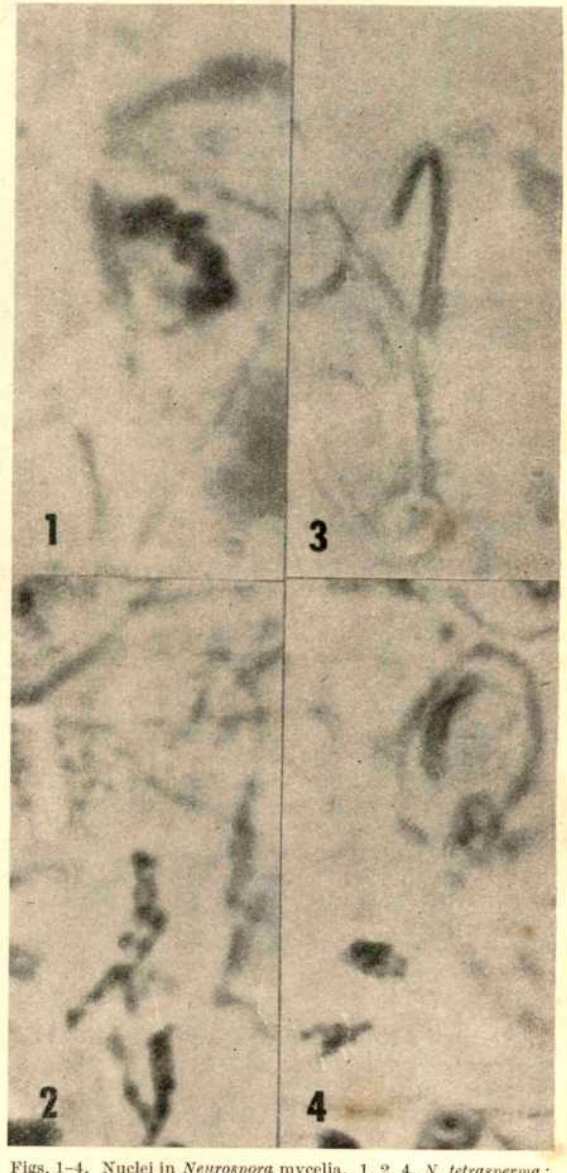
CYTOLOGY

Mitosis in *Neurospora*

IN the ascus of *Neurospora*, meiosis and mitosis appear to resemble those in higher plants[1-4]. However, within the mycelium of *Neurospora* and of a number of other fungi, some observers report that the conventional stages of nuclear division are lacking, that the spindle is absent, and that the nuclei divide by becoming constricted and pulling in two[5-8]. We too have found that mitosis in *Neurospora* mycelium is unlike that in higher plants and animals and that there is no spindle; but we have observed also that the nuclei are filamentous (Figs. 1–4) and that they divide by splitting longitudinally.

The mycelium of three species of *Neurospora* Shear and Dodge was grown on a cover-slip, fixed,



Figs. 1–4. Nuclei in *Neurospora* mycelia. 1, 2, 4, *N. tetrasperma*; 3, *N. crassa*. 1, post-divisional nucleus with seven chromosomes; 2, above, post-divisional nuclei; below, dividing nucleus; 3, longitudinally dividing nucleus; 4, a loop and a spiral-shaped nucleus in the conidium before dividing, three V-shaped nuclei in the hypha. (× 1,750)

hydrolysed, stained in Giemsa and examined with a Zeiss microscope with 'Optovar' to give an initial magnification of 2,500. By this method, the chromosomes in the mycelium of *Neurospora tetrasperma*, *N. crassa* and *N. sitophila* were revealed. As in the ascus there are seven chromosomes in each species.

The chromosome groups most suitable for counting appear at first glance to be at metaphase, but in reality there are no such stages of mitosis in these nuclei. The chromosomes are arranged in linear series upon a filament (Fig. 1). McGinnis[9] has previously observed similar nuclei in the basidium of *Puccinia graminis*. In *Neurospora* the chromosomes are most easily counted when the filament is coiled within the nuclear membrane.

We have observed the following types of nuclei which we believe to be consecutive stages in mitosis: (1) a network within a spherical membrane; (2) an elongated network free of the membrane; (3) a narrow thread; (4) a thread longitudinally split (Fig. 3); (5) two separate daughter threads; (6) a shortened and thickened filament with distinct chromosomes; (7) a similar filament coiled within a membrane.

Masses of nuclear strands may occur in the lumen of hyphæ and also passing through their transverse septa. The identity of the individual nuclei is lost in the tangle (Fig. 2). In such masses, nuclear components may become interchanged, and hyphæ may become unlike genetically.

A detailed report of this work will be published elsewhere.

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Amphiplasty in *Ribes*

SEVERAL authors have reported that in *Ribes nigrum* L. (black currant) and *R. grossularia* L. (gooseberry), as in all other *Ribes* species so far investigated, a pair of satellited chromosomes is constantly present[1–3]. However, in 1957 it was noticed that only one satellite could be seen at metaphase in root tip cells of a black currant × gooseberry hybrid. Two further black currant × gooseberry hybrids have since become available for study and in both of these only one satellite is visible in root tip cells. The presence of two satellited chromosomes in two black currant and two gooseberry varieties (Baldwin and Boskoop Giant black currants, Broom Girl and Green Ocean gooseberries), parents of two of the hybrids mentioned above, has been confirmed. Evidently, in the hybrid, one of the parental satellites disappears. This phenomenon has been described in interspecific hybrids of *Crepis* by Navashin[4], who includes this and other chromosome changes due to hybridization under the term amphiplasty[4,5].

Further work in progress on amphiplasty in *Ribes* species hybrids will be reported elsewhere.

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GENETICS

A Screening Technique for Photosynthetic Mutants in Unicellular Algæ

IN conjunction with experiments concerned with the genetics of photosynthesis in the sexually reproducing, unicellular, green alga, *Chlamydomonas reinhardi*[1] it became necessary to devise a technique to screen for mutants which were blocked in some phase of their photosynthesis. In the technique to be described here the inability to fix carbon dioxide in the light was taken as a requirement of a non-photosynthetic mutant.

There are forty-two mutants of *C. reinhardi* which cannot grow in the light unless the minimal medium[2] is supplemented with sodium acetate, and it was considered that certain of these mutants might not be able to fix carbon dioxide in the light. Rather than measuring carbon dioxide fixation individually for each mutant by the usual method[3] it was possible to assay for their ability to fix carbon dioxide while they were growing in colonies on agar medium contained in Petri dishes.

Petri dishes containing colonies of wild-type and several acetate mutants were inverted over a small watch-glass. Acetic acid (0·1 ml. of a 1 *N* solution) was pipetted into each watch-glass followed by the addition of 0·3 ml. of carbon-14 labelled sodium bicarbonate (2·5 μc./ml.). The operations were carried out in a hood. After the addition of the sodium bicarbonate the light from two 150-watt reflector floodlights was directed toward the Petri dishes. The light was allowed to remain on for 5 min. during which time a comparable set of colonies was exposed to carbon-14 labelled carbon dioxide in the dark as a control.

At the end of 5 min. the lights were turned off, and the colonies were replicated to filter paper. Each of the filter papers was exposed to the fumes of concentrated hydrochloric acid for 3 min. in order to drive off any unfixed carbon dioxide. Radioautographs were made of the replicated colonies using Kodak No-Screen X-ray film and were developed after exposure for one week. The ab lity of wild-type or a mutant to fix carbon dioxide was seen by the darkening of the emulsion of the film at a position which coincided with the position of the colony on the filter paper. The controls run in the dark gave negative radioautographs.

In this manner it was possible to screen rapidly the forty-two acetate-requiring mutants of *C. reinhardi* for their ability to fix carbon dioxide. Fig. 1*A* shows the filter paper replica of colonies of wild-type and seven different acetate mutants. Fig. 1*B* shows the radioautograph of the colonies. It appears from

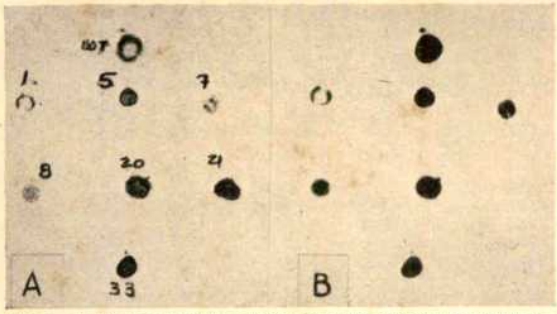

Fig. 1. Radioautographic technique used in screening for mutants which do not fix carbon dioxide. *A*, Filter paper replica of colonies which were exposed to $^{14}CO_2$ in the light; *B*, the radioautograph of the colonies. The wild type (*WT*) and seven acetate-requiring mutants are shown here. It is seen that *ac*-21 gives a negative radioautograph

the radioautograph that *ac*-21 does not fix carbon dioxide. Subsequent, more direct tests have revealed that the rate of carbon dioxide fixation in this mutant is some ten-fold less than that of wild-type and that the genetic block to photosynthesis lies in the process of photosynthetic phosphorylation[1].

Additional photosynthetic mutants have been obtained in the manner described here by screening colonies which had been derived from cells irradiated with ultra-violet light. Cells of wild-type were plated ($1 \cdot 5 \times 10^4$ cells per plate) to minimal agar which had been supplemented with sodium acetate. The cells were then irradiated with a dose which permitted 1 per cent survival. Following irradiation, the Petri dishes were placed in the dark for 12 hr., after which the colonies were allowed to develop at 25° C. and at a light intensity of 250-foot-candles from daylight fluorescent lamps. After 72 hr. the colonies were replica-plated to minimal agar supplemented with sodium acetate and to minimal agar supplemented with sodium acetate and yeast extract. When colonies had formed on these plates (usually within 72 hr. after replication) those growing on the medium supplemented with sodium acetate alone were tested for carbon dioxide fixation according to the method described above, while those growing on the medium supplemented with both sodium acetate and yeast extract were placed in the dark to await the results of the radioautographs. Those colonies giving a negative radioautograph were picked from the doubly supplemented medium in order to establish stock cultures. These in turn were tested for their inability to grow on minimal medium and to fix carbon dioxide as determined by more usual means.

The advantage of the technique described here lies in the rapidity and economy with which it is possible to screen large numbers of colonies for their ability to fix carbon dioxide. The technique should be feasible in any alga which can be handled in a manner similar to that of *C. reinhardi*. In addition, it should be possible to adapt the technique for most micro-organisms which can fix carbon dioxide when it is provided in the way described here.

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Elective Production of Thymine-less Mutants

THYMINE-LESS (*thy*⁻) mutants of micro-organisms have not been easy to obtain. They die rapidly in the absence of thymine[1] so that, when penicillin is used to concentrate them, none survives the treatment. To discover them after mutagenic treatment requires direct detection methods and this, in turn, either good fortune[2,3] or a very high frequency of *thy*⁻ mutants among the survivors[4]. We have recently discovered a method whereby *thy*⁻ mutants of some strains of *Escherichia coli* 15 and K 12 can be produced in frequencies of the order of 50 per cent. Although no success was obtained with *Salmonella typhimurium*, the method seems to involve the general principle of differential growth-rates. With *E. coli* both the *thy*⁻ and *thy*⁺ strains are inhibited by aminopterin, but it seems that only in the *thy*⁻ can thymidine completely overcome that inhibition.

The strains used were *E. coli* 15 *h*⁻ (histidine-less), its colicine-resistant T-phage-sensitive derivative (15 *h*⁻CR [5]), and the wild type and various mutants of *E. coli* K 12 (a prototrophic, streptomycin sensitive derivative of HfrH, lysogenic for λ; W 1177 and CR 34, both of which are F⁻ and require threonine, leucine and vitamin B_1 although they differ in other genetic markers). The chemically defined medium employed was a modified Gray and Tatum medium[6]; the various strains were grown in this, supplemented as needed, with: L-histidine, 25 μgm./ml. (H^+ medium); DL-threonine, 200 μgm./ml. (Thr^+); L-leucine, 20 μgm./ml. (Leu^+); vitamin B_1, 0·2 μgm./ml. (B_1^+); thymine (Nut. Biochem. Corp.) 40 μgm./ml. (Thy^+); thymidine (Cal. Corp. Biochem. Res.) 20 μgm./ml. (Td^+).

For treatment the medium was also supplemented (*G*8 medium) with 12 of 14 substances the syntheses of which are thought to be inhibited by aminopterin[7] (thymidine and vitamin B_{12} were omitted, the latter for no good reason). The complete medium (*YECA*) consisted of a modified Gray and Tatum medium supplemented with 0·5 per cent Difco yeast extract, 0·5 per cent NZ-case and 0·5 per cent dextrose.

The treatment can be illustrated with the example of 15 *h*⁻CR. A single colony of this strain was inoculated into 5 ml. of *G*8 medium and incubated on a rotator at 37° C. overnight, during which time growth usually ceased at a level of 10^9 cells per ml. because of the exhaustion of dextrose (0·05 per cent). The cell suspension was diluted 10^{-1} and 0·1 ml. was added to 4·5 ml. of *G*8 medium along with 0·5 ml. of a solution of 2 mgm. aminopterin (Cal. Corp. Biochem. Res.)/ml. The mixture was incubated on a rotator at 37° C. for 24 hr., during which time the number of viable cells decreased to 10^2–10^3/ml. (*c.* 10^{-3} survival). Then 0·5 ml. of a solution of 2 mgm. thymidine (or thymine)/ml. was added and incubation continued, whereupon the cells began to grow. After 48–72 hr., full turbidity was achieved and the suspension was washed twice with saline, diluted and plated on *YECA* agar medium supplemented with 10 μgm. thymidine/ml. (*YECA*-Td^+). All *thy*⁻ mutants could not use thymine in the presence of *YECA* but would grow when thymidine was present. On chemically defined medium either compound supported growth equally well.

Colonies appearing on *YECA*-Td^+ agar medium were replicated on to H^+ and H^+Td^+ agar. Between 10 and 50 per cent were *thy*⁻ mutants, all retaining their *h*⁻ and (on the basis of limited tests) CR characteristics. When 0·5 ml. of a solution of 2 mgm.

5-bromo-deoxyuridine (Cal. Corp. Biochem. Res.)/ml. was also added to the *G*8 medium at the time of thymidine addition, up to 80 per cent of the population might be *thy*⁻.

Strain K 12 behaved somewhat differently from 15. Its derivatives grew more slowly in the chemically defined medium. When after some delay (1 day for HfrH and CR 34, 2 days for W 1177 and 3 days for wild type) they did reach full turbidity, a final concentration of 200 or 500 μgm. aminopterin/ml. was employed. Afterwards when thymidine and 5-bromo-deoxyuridine were added, it took 2 days for CR 34 and 4 days for W 1177, HfrH and wild type to reach full turbidity. The percentage of *thy*⁻ mutants present varied as follows:

	CR 34	HfrH	W 1177	Wild type
200 μgm. aminopterin/ml.	—	6 1	16	—
500 μgm. aminopterin/ml.	78	44	—	0 2

A preliminary analysis of a number of questions has been made with the following results:

(1) The pre-treatment with aminopterin is unnecessary; (2) the appearance of *thy*⁻ mutants is not due to differential survival in aminopterin, because they appear without pre-treatment and die in the presence of aminopterin about as fast as *thy*⁺; (3) the *thy*⁻ mutants are the only ones produced by this treatment in detectable frequencies; the original markers of the treated bacteria are not observed to change in the *thy*⁻ produced—for example, *h*-CR bacteria remain *h*-CR; (4) the mutants produced are stable to an ordinary extent; recombination experiments with the K 12 strains indicate that the *thy*⁺ marker is transferred from the Hfr to the F⁻ parent, which result would seem to indicate that the genetic unit concerned is not extra-chromosomal; (5) the appearance of *thy*⁻ mutants seems not to be due to mutation induced by aminopterin but rather to the selective overgrowth after the thymidine has been added.

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STATISTICS

Time-Dependent Results for a Dam with Ordered Poisson Inputs

LET the content $0 \leqslant Z(t) < \infty$ of a dam at time $t \geqslant 0$, fed by an input $0 \leqslant X(t) < \infty$ in time t, and subject to a steady release at constant unit rate, be defined by the equation:

$$Z(t + \delta t) = Z(t) + \delta X(t) - (1 - \eta)\delta t \qquad (1)$$

where $\eta\delta t (0 \leqslant \eta \leqslant 1)$ is the time during t, $t + \delta t$ that the dam is empty. $X(t)$ is such that the arrival times of inputs form a Poisson process with parameter λ, the inputs themselves being of constant sizes α_1, α_2, and always arriving in this order (α_1, $\alpha_2 > 0$).

The process $Z(t)$ is Markovian when the number of inputs up to t is known. If we define:

$$F_i(z_0,z,t) = Pr\{Z(t) \leqslant z,\ X(t) = n(\alpha_1 + \alpha_2) + \delta_{i1}\alpha_1 | Z(0) = z_0\} \qquad (2)$$

for $n = 0, 1, 2, \ldots$; $i = 1, 2$; δ_{i1} being the Kronecker delta, the transition distribution function of the dam content is:

$$F(z_0,z,t) = Pr\{Z(t) \leqslant z | Z(0) = z_0\} = F_1(z_0,z,t) + F_2(z_0,z,t) \qquad (3)$$

It is readily shown the $F_i(z_0,z,t)$ satisfy differential-difference equations:

$$\frac{\partial F_i}{\partial t} - \frac{\partial F_i}{\partial z} = -\lambda\{F_i(z_0,z,t) - F_j(z_0,z - \alpha_i,t)\} \qquad (0 \leqslant z < \infty) \qquad (4)$$

where i, $j = 1, 2$ but $i \neq j$, and $F_i(z_0,z,t) = 0$ if $z < \max(0,z_0 - t)$; these are similar to Takács'[1] equation for the distribution function of the process in the case $\alpha_1 = \alpha_2$.

The Laplace–Stieltjes transforms of (4) lead to integral equations for the transforms of the $F_i(z_0,z,t)$, which also involve the probabilities of emptiness $F_i(z_0,0,t)$ ($i = 1,2$). These do not appear to yield readily to solution. Direct probabilistic considerations will, however, lead to explicit results for the $F_i(z_0,z,t)$, and hence for the distribution function $F(z_0,z,t)$.

The probabilities of first emptiness $g_1(z_0,T_n)$ of the dam after n inputs starting with an input α_1, where $T_n = z_0 + [\frac{1}{2}(n + 1)]\alpha_1 + [\frac{1}{2}n]\alpha_2 (n = 0, 1, 2, \ldots)$, are known. In some connected work, I have[2] obtained them recursively using a modified form of Kendall's[3] equation:

$$g_1(z_0,T_n) = \sum_{j=0}^{\infty} \sum_{i=0}^{1} e^{-\lambda z_0} \frac{(\lambda z_0)^{2j+i}}{(2j + i)!} g_{1+i}(j(\alpha_1 + \alpha_2) + \delta_{i1}\alpha_1, T_n - z_0) \qquad (5)$$

where $g_i(0,0) = 1$, $g_2(w,w + r\alpha_1 + s\alpha_2)$ is obtained from the formula for $g_1(w,w + s\alpha_1 + r\alpha_2)$ by interchanging α_1 and α_2 ($s - r = 0,1$), and $g_i(w,T) = 0$ if $T < w (i = 1,2)$ for any $w > 0$, or $w = 0$ for any $T > 0$. A simpler evaluation of these by the method of truncated generating functions[4] is also given.

It is found that:

$$g_1(z_0,T_n) = \begin{cases} e^{-\lambda z_0} & (n = 0) \\ e^{-\lambda T_n} \dfrac{\lambda^n}{n!} z_0 \displaystyle\sum_{i=0}^{n-1} c_{ni} z_0^i & (n \geqslant 1) \end{cases} \qquad (6)$$

where the coefficients c_{ni} can be obtained for any value of $n \geqslant 1$. In a recent paper Gani and Pyke[6] have also derived some simple inequalities for the $g_1(z_0,T_n)$ where $\alpha_1 > \alpha_2$.

Combinatorial arguments establish that:

$$F_i(z_0,0,t) = \sum_{r=0}^{\infty} g_1(t - r(\alpha_1 + \alpha_2) - \delta_{i1}\alpha_1, t) \qquad (7)$$

where $g_1(t - r(\alpha_1 + \alpha_2) - \delta_{i1}, t) = 0$ if $r(\alpha_1 + \alpha_2) > t - z_0 - \delta_{i1}\alpha_1$, and after a transformation ($u = z + t$, $t = t$), the equations (4) may be solved jointly step by step in the consecutive intervals:

$$[\tfrac{1}{2}(n + 1)]\alpha_i + [\tfrac{1}{2}n)\alpha_j \leqslant z < [\tfrac{1}{2}(n + 2)]\alpha_i + [\tfrac{1}{2}(n + 1)]\alpha_j \quad (i, j = 1\ 2;\ i \neq j)$$

It is found that, in these intervals:

$$F_i(z_0,z,t) = \sum_{r=0}^{\infty} e^{-\lambda\{[\frac{1}{2}(r+1)]\alpha_i + [\frac{1}{2}r]\alpha_j - z\}} (\lambda\{[\tfrac{1}{2}(r+1)]\alpha_i + [\tfrac{1}{2}r]\alpha_j - z\})^r/r! \times \{\delta_{\frac{r}{2},[\frac{r}{2}]} F_i(z_0,0,z+t-[\tfrac{1}{2}(r+1)]\alpha_i - [\tfrac{1}{2}r]\alpha_j) + (1-\delta_{\frac{r}{2},[\frac{r}{2}]}) F_j(z_0,0,z+t-[\tfrac{1}{2}(r+1)]\alpha_i - [\tfrac{1}{2}r]\alpha_j)\} \quad (8)$$

where $i, j = 1, 2$, but $i \neq j$. From these, the distribution function $F(z_0,z,t)$ of (3) can be obtained; in the case $\alpha_1 = \alpha_2$, this naturally reduces to the form previously given by Gani and Prabhu[6].

The method outlined is equally applicable to the case of $p > 2$ ordered inputs $\alpha_1, \ldots, \alpha_p$. There is a corresponding increase in the complexity of the equations for the associated probabilities of first emptiness starting with an input α_1, as well as for the distribution function of the process.

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Plant Population and Crop Yield

UNDER the above title, Holliday[1] has recently published an equation which describes in a number of cases the relationship between yield and density in crop plants. In its simplest form this relationship is:

$$1/w = A\rho + B \quad (1)$$

where w is the yield per plant, ρ is the number of plants per unit area and A and B are constants. This equation was used (with these symbols) by Shinozaki and Kira[2] in 1956. An equivalent relationship connecting the total yield per unit area, $y = \rho w$, with the spacing per plant, $s = 1/\rho$, namely:

$$y = \frac{1}{A + Bs} \quad (2)$$

was proposed independently be De Wit and Ennik in 1958[3]. These authors concede that the formula may not apply at high plant densities, and Holliday has directed attention to its limitations at very low plant densities, and accordingly has proposed a modification of equation (1). Appropriate modifications for both extremes are considered by Shinozaki and Kira[2]. Holliday further points out that even his modified equation cannot describe adequately total yield/plant density relationships where the form of the curve is parabolic, that is, where a certain plant population gives higher yields than either lower or higher populations. This type of curve, it is claimed, is typical of situations where yield is a function of reproductive growth, whereas curves that reach a stable maximum with increasing plant density are typical of yield of vegetative growth, and are defined by equations similar to or derived from equation (1).

There appear to be exceptions to this generalization; thus the data of Wiggins[4] for the yield of threshed beans from soybean are adequately described by equation (1), whereas our own observations (unpublished) show that the yields of onions and lettuce frequently are not.

The Japanese contribution to knowledge of this subject does not appear to be widely known, and we therefore feel that the references given below[5] may be useful. Kira and his co-workers have shown how equation (1) can be derived from the logistic equation for plant growth together with certain other plausible assumptions, and have studied how the parameters in the equation change with time.

Hozumi, Kira and Shinozaki[6] have developed the application of equation (1) to cover the effects of any growth factor in suboptimal supply using the form:

$$\frac{1}{w} = \frac{A}{f} + B$$

where f is the amount of a factor supplied. They have developed the generalization for several factors varying simultaneously, using multilinear forms in the inverses of the amounts of the factors. Thus for two factors of amounts f_1 and f_2, they put:

$$\frac{1}{w} = \frac{A_1}{f_1} + \frac{A_2}{f_2} + \frac{A_{12}}{f_1 f_2} + B$$

and show that this model successfully describes the joint effect of light intensity and nutrient concentration on the growth of *Lemna minor*[7], and the joint effect of light intensity and density on the growth of *Hibiscus moscheutos*[8]. Although Kira and his co-workers have apparently successfully used equation (1) and their generalization of it for a number of species, we find that the relation:

$$\frac{1}{w^\theta} = A\rho^\theta + B \quad (3)$$

where θ is some positive quantity usually less than unity, frequently gives a strikingly better fit to data from spacing experiments. Equation (3) can be derived by analogous arguments to those of Kira *et al.*, the logistic equation being replaced by a generalization described by Richards[8]. By allowing the power of ρ in (3) to exceed that of w, a model can be obtained in which the yield per unit area shows a maximum at a certain finite density. A detailed account of this work will be published elsewhere.

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FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, October 24

UNIVERSITY OF LONDON (at the Postgraduate Medical School of London, Ducane Road, London, W.12), at 4 p.m.—Dr. J. Valance-Owen: "Insulin Activity and Antagonism in Plasma".*

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S.W.7), at 5 p.m.—Mr. R. A. French "Geography and Geographers in the Soviet Union".

ROYAL INSTITUTION, LIBRARY CIRCLE (at 21 Albemarle Street, London, W.1), at 5.30 p.m.—Mr. H. R. Rishworth: "Herbals and Herbalists, Ancient and Modern".

SOCIETY OF CHEMICAL INDUSTRY, CORROSION GROUP (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Cathodic Protection Panel Meeting (Brains Trust).

INSTITUTION OF ELECTRICAL ENGINEERS, LONDON GRADUATE AND STUDENT SECTION, at Savoy Place, London, W.C.2), at 6.30 p.m.—Mr. A. Porter: "Southern Region, Kent Coast Electrification Scheme—Power Supply Apparatus" (Chairman's Address).

Tuesday, October 25

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C.1), at 1.15 p.m.—Dr. A. Armitage: "Some Observatories and Observers of the Seventeenth Century".*

INSTITUTION OF ELECTRICAL ENGINEERS, MEASUREMENT AND CONTROL SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. E. H. Cooke-Yarborough and Mr. R. C. M. Barnes: "Rapid Methods for Ascertaining whether the Activity of a Weak Radioactive Sample Exceeds a Predetermined Level".

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. C. H. Andrewes: "The Common Cold".* (Second of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. Stuart Hampshire: "Feeling and Expression" (Inaugural Lecture).*

SOCIETY OF CHEMICAL INDUSTRY, PLASTICS AND POLYMER GROUP (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Prof. F. S. Dainton, F.R.S.: "The Relationship Between Structure and Polymerisability of Monomers".

Wednesday, October 26

PHOTOBIOLOGY GROUP (at Queen Mary College, Mile End Road, London, E.1), at 11 a.m.—Report on work in progress in the Botany Department, Queen Mary College. Afternoon Session: Reports from the International Congress of Photobiology held in Copenhagen, July 31st–August 5th, 1960.

UNIVERSITY OF LONDON (at the Postgraduate Medical School of London, Ducane Road, London, W.12), at 2 p.m.—Dr. J. H. Wilkinson. "Biochemistry of the Thyroid".*

INSTITUTE OF NAVIGATION (at the Royal Geographical Society, 1 Kensington Gore, London, S.W.7), at 3 p.m.—Annual General Meeting. Wing-Commander E. W. Anderson, O.B.E.: "The Philosophy of Navigation Today" (Presidential Address).

INSTITUTION OF ELECTRICAL ENGINEERS, ELECTRONICS AND COMMUNICATIONS SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. T. B. D. Terroni: "Channelling—a Sketch" (Chairman's Address).

INSTITUTION OF MECHANICAL ENGINEERS (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Prof. Owen A Saunders 'The Scientist's Contribution to Mechanical Engineering" (Presidential Address).

SOCIETY FOR ANALYTICAL CHEMISTRY, MICROCHEMISTRY GROUP (at "The Feathers", Tudor Street, London, E.C.4), at 6.30 p.m.—Discussion on "Analytical Aspects of Corrosion" opened by Mr. H. C. J. Saint.

ROYAL INSTITUTE OF CHEMISTRY, LONDON SECTION (at Goldsmiths' College, Lewisham Way, London, S.E 14), at 7 p.m.—Mr. R. B. Collins: "Modern Colour Photographic Processes".*

Wednesday, October 26—Thursday, October 27

BRITISH INSTITUTION OF RADIO ENGINEERS (at the School of Pharmacy, Brunswick Square, London, W.C.1), at 10.45 a.m. on Wednesday and 10 a.m. on Thursday—Symposium on "New Components"

Thursday, October 27

UNIVERSITY OF LONDON (in the Physiology Theatre, University College, Gower Street, London, W.C.1), at 5 p.m.—Dr. V. P. Whittaker: "The Subcellular Localisation of Neurohormonal Agents".*

UNIVERSITY OF LONDON INSTITUTE OF EDUCATION (in the Great Hall, Goldsmiths' College, New Cross, London, S.E.14), at 5 p.m.—Mr. W. G. Stone: "Some Possible Developments in the Youth Service".* (Final lecture in a series on "The Future of Education".)

INSTITUTION OF ELECTRICAL ENGINEERS (at Savoy Place, London, W.C.2), at 5.30 p.m.—Dr. A. Hewish: "The Principles and Operation of Large Radio Telescopes".

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. Wilson Smith: "Virus Flocculation Reactions".* (Third of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

CEMENT AND CONCRETE ASSOCIATION (at the Institution of Structural Engineers, 11 Upper Belgrave Street, London, S.W.1), at 6 p.m.—Mr. E. V. Finn and Mr. K. F. Shadbolt: "Structural Consideration of a New Animal Feed Mill in Belfast, Northern Ireland".

ROYAL INSTITUTE OF CHEMISTRY, LONDON SECTION (joint meeting with the BOROUGH POLYTECHNIC CHEMICAL SOCIETY, at the Borough Polytechnic, Borough Road, London, S.E 1), at 7 p.m.—Prof. C. W. Davies: "Some Aspects of Ion Exchange".

Friday, October 28

INSTITUTE OF BIOLOGY, PARASITOLOGY GROUP (in the Zoology Department, Birkbeck College, Malet Street, London, W.C.1), at 10.30 a.m.—Meeting on "Recent Advances in Fields of Parasitological Research".

LINNEAN SOCIETY and the BRITISH MYCOLOGICAL SOCIETY (in the Lecture Theatre of the British Museum (Natural History), Cromwell Road, London, S.W.7), at 3 p.m.—Miss Gulielma Lister Centenary Meeting.

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 9 p.m.—Dr. Maurice Neville Hill: "Exploring the Ocean Floor".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

LECTURER (preferably with teaching and/or industrial experience) IN PHYSICS at the City College of Technology, Byrom Street, Liverpool 3, to teach to graduate level—The Director of Education, City of Liverpool Education Committee, 14 Sir Thomas Street, Liverpool 1 (October 28).

ASSISTANT IN ZOOLOGY—Secretary to the University Court, The University, Glasgow (October 31).

ASSISTANT LECTURER IN ZOOLOGY—The Registrar, The University, Leicester (November 1).

ASSISTANT LECTURER IN PHYSICS—The Registrar, The University, Sheffield (November 5).

LECTURER IN PHARMACOLOGY—Joint Clerk to the University Court, Queen's College (University of St. Andrews), Dundee (November 5).

LECTURER IN PSYCHIATRY—The Registrar, The University, Sheffield (November 5).

LECTURER (with research experience in physical oceanography or in an appropriate branch of physics or mathematics) IN PHYSICAL OCEANOGRAPHY at the Marine Biology Station—The Secretary and Registrar, University College of North Wales, Bangor, North Wales (November 7).

RESEARCH ASSISTANT (with Ph.D. or equivalent research experience) FOR WORK ON THE ORGANIC CHEMISTRY OF FREE RADICALS—The Secretary, Birkbeck College (University of London), Malet Street, London, W.C.1 (November 7).

LECTURER (with a university degree in forestry and practical experience of forestry in Great Britain) IN THE DEPARTMENT OF FORESTRY—The Secretary, The University, Edinburgh (November 8).

ASSISTANT LECTURER (with medical qualifications registrable in this country) IN ANATOMY—The Registrar, The University, Manchester 13 (November 12).

DIRECTOR for an important RESEARCH STATION with a staff of over 30 engaged on ECOLOGICAL STUDIES—The Nature Conservancy (E), 19 Belgrave Square, London, S.W.1 (November 12).

VETERINARY PARASITOLOGIST (graduate in science or agricultural science or science with zoology as a major subject, or equivalent qualifications) AT THE MCMASTER LABORATORY, Division of Animal Health, C.S.I.R.O., Sydney, Australia, to undertake general duties in parasitology, including studies of the ecology of nematode larvæ recovered from pastures and ruminal contents of sheep and the testing of new anthelmintics against nematode infection of sheep—Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2, quoting Appointment No. 202/179 (November 12).

BOTANIST (Plant Physiologist), Division A (with a good honours degree in botany or equivalent qualification, and at least two years research experience in the field of plant physiology) in the Botanical Division, Rubber Research Institute of Malaya, Kuala Lumpur, to investigate the occurrence and function of natural auxins and other growth factors in the rubber tree, *Hevea brasiliensis*—The Secretary, London Advisory Committee for Rubber Research (Ceylon and Malaya), Commonwealth Institute, Imperial Institute Road, London, S.W.7 (November 15).

CHAIR OF PHYSIOLOGY IN THE FACULTY OF MEDICINE, University of Khartoum—The Registrar, University of Khartoum, c/o Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (November 15).

SENIOR LECTURER or LECTURER IN VETERINARY PHYSIOLOGY AND BIOCHEMISTRY at the University of Khartoum—The Registrar, University of Khartoum, c/o Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (November 15).

LECTURER IN APPLIED MECHANICS; a LECTURER IN THERMODYNAMICS; and a LECTURER IN STRUCTURES—The Registrar, The University, Leicester (November 16).

LECTURER or ASSISTANT LECTURER (preferably with research interest in marine biology or comparative physiology) IN ZOOLOGY at

the University College of the West Indies—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C 1 (November 19).

OFFICIAL FELLOW IN MATHEMATICS—The Principal, Hertford College, Oxford (November 26).

RESEARCH FELLOW (Pharmacologist, Biochemist or Organic Chemist with biological experience, and of Ph.D. standard) FOR WORK IN THE FIELD OF CHEMOTHERAPY—The Secretary, Medical Research Council of Ireland, 50 Merrion Square, Dublin (November 26).

ASSISTANT LECTURER IN PHYSICAL CHEMISTRY—The Registrar, Massey Agricultural College (University of New Zealand), Palmerston North, New Zealand (November 30).

CHAIR OF PURE MATHEMATICS—The Registrar, University College, Singleton Park, Swansea (November 30).

LECTURER or ASSISTANT LECTURER IN GEOGRAPHY at the University of Malaya, Singapore—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C 1 (November 30).

PROFESSOR OF AGRICULTURE AND DIRECTOR OF THE COLLEGE FARM—The Secretary and Registrar, University College of North Wales, Bangor, North Wales (December 1).

ASSOCIATE PROFESSOR OF MEDICINE at the University of New South Wales, Australia—The Agent-General for New South Wales, 56–57 Strand, London, W.C.2 (Australia and London, December 12).

CHAIR OF PHILOSOPHY at Victoria University of Wellington, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand and London, December 31).

ASSISTANT EXPERIMENTAL OFFICER (familiar with elementary chemical techniques and possessing H.N.C. or equivalent, or, if under 22, qualifications leading to the above) IN THE CHEMICAL MICROBIOLOGY DEPARTMENT for work on cheese flavour—The Secretary, National Institute for Research in Dairying (University of Reading), Shinfield, Reading, quoting Ref. 60/15.

ASSISTANT LECTURER (graduate in chemistry, and preferably with experience in the food industry) for duties which will include the TEACHING OF CHEMISTRY AND FOOD QUALITY CONTROL—The Principal, National College of Food Technology, St. George's Avenue, Weybridge, Surrey.

BIOCHEMICAL TECHNICIAN (preferably with experience of microbiological techniques)—Head of the Department of Physiology and Pharmacology, Chelsea College of Science and Technology, Manresa Road, London, S.W.3.

BIOCHEMIST (whole-time, non-resident) for hospital biochemical work in the Mansfield Area Pathology Service—The Hospital Secretary, King's Mill Hospital, Sutton-in-Ashfield, Notts.

BROADCASTING AND FILM LIAISON OFFICER (with a good general scientific background, familiarity with 16 mm. film production methods and equipment, and some knowledge of broadcasting techniques) at the Headquarters of the Department of Scientific and Industrial Research, London, S.W.1, for duties which will be concerned mainly with liaison between research organizations and film companies. The work also includes projection and care of equipment, selection and editing of film for T.V. use and promotion of films—Manager (P.E. 3158), Ministry of Labour, Professional and Executive Register, Atlantic House, Farringdon Street, London, E.C.4.

CHEMIST or BIOCHEMIST (with a good honours degree in science or equivalent qualification) to undertake research on the quality of protein in animal feeding stuffs—The Secretary, Rowett Research Institute, Bucksburn, Aberdeen.

GENETICIST, Principal Scientific Officer or Senior Scientific Officer grade (with Ph.D. or a good honours degree with at least two years postgraduate research experience in microbiology) TO TAKE OVER THE GENETICS SECTION—The Secretary, Research Institute (Animal Virus Diseases), Pirbright, Surrey.

LABORATORY TECHNICIANS and INSTRUMENT MAKERS for established posts in RESEARCH AND TEACHING LABORATORIES concerned with electronics, vacuum physics, ultrasonics, X-rays, solid state physics, etc.—Head of the Physics Department, Northampton College of Advanced Technology, St. John Street, London, E.C.1.

MICROBIOLOGIST (with research experience) FOR WORK ON RADIATION-INDUCED MUTATIONS IN MICROBIAL POPULATIONS—The Administrator, Radiobiological Research Unit, Medical Research Council, Harwell.

ORGANIC CHEMIST (with an honours degree in chemistry or biochemistry) to assist with research into the chemistry of micro-organisms—Prof. J. H. Birkinshaw, Department of Biochemistry, London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1.

PHYSICAL METALLURGIST or PHYSICIST (graduate, with research experience) in the Physical Metallurgy Division, Department of Mines and Technical Surveys, Canada, to work with a group carrying out fundamental investigations in metal physics—Dept. D.M.T.S., National Employment Service of Canada, 61 Green Street, London, W.1.

READER IN ANALYTICAL CHEMISTRY—The Academic Registrar, Loughborough College of Technology, Loughborough, quoting 14/2/AF.

RESEARCH FELLOW (with a higher degree or research experience), or an ASSISTANT (with a degree in chemistry or physics) IN POLYMER CHEMISTRY for work of a physicochemical nature—The Registrar, Bradford Institute of Technology, Bradford, 7.

RESEARCH FELLOWS and RESEARCH ASSISTANTS (with a good honours degree in pharmacy or other allied subjects) IN THE DEPARTMENT OF PHARMACY—The Registrar, Bradford Institute of Technology, Bradford 7.

RESEARCH FELLOWS (with a first- or second-class honours degree, evidence of high standard of ability in research, and at least two years postgraduate research experience, three years for senior fellows) AT GOVERNMENT SCIENTIFIC ESTABLISHMENTS, in a very wide range of topics, especially in the physical sciences and in various branches of biology—The Civil Service Commission, 17 North Audley Street, London, W.1, quoting S/5060/60.

TECHNICIAN (preferably with experience in microbiology) IN THE SCIENCE DEPARTMENT, to be responsible for the preparation of class materials and maintenance of stock cultures, and general duties—The Principal, Ewell County Technical College, Reigate Road, Ewell, Epsom, Surrey.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

British Rubber Producers' Research Association. Twenty-second Annual Report. Pp. 53. (London: British Rubber Producers' Research Association, 1960.) [28

Bwrdd Gwarchodaeth Natur Cymru. The Nature Conservancy. Pp. 12. (Bangor: The Nature Conservancy, Penrhos Road, 1960.) [28

Middlesex County Council Education Committee. Evening Classes. a Guide to Facilities in Middlesex, 1960–61. Pp. 50+4 plates. (London: Middlesex County Council Education Committee, 1960.) [28

Department of Scientific and Industrial Research. Forest Products Research 1959: Report of the Forest Products Research Steering Committee, with the Report of the Director of Forest Products Research. Pp. vi+62+12 plates. (London: H.M. Stationery Office, 1960.) 5s. 6d. net. [28

Electing the American President. By Keith Kyle. Pp. 25+iii. (London. The Commonwealth-American, Current Affairs Unit of the English Speaking Union, 1960.) [28

Ministry of Agriculture, Fisheries and Food. Farm Buildings Pocketbook: Some Useful Advice giving Standards, Dimensions and Data for those interested in the Design of Farm Buildings. Pp. iv+43. (London: H.M. Stationery Office, 1960.) 2s. net. [28

Other Countries

Instituto Antartico Argentino, Buenos Aires. Contribucions. No. 28: La Campana Antartica Invernal del Rompehielos "General San Martin" en 1957. Por Jorge A. Boffi. Pp. 15. No. 40: Observaciones Ionosfericas Argentinas en el Antartico. Por Jose A. Rodriguez. Pp. 11. No. 42: La Campana Antartica 1941–42. Por Alberto J. Oddera. Pp. 15. No. 43: La Campana Antartica 1942–43. Por Silvano Harriague. Pp. 12. No. 44: La Campana Antartica 1958–59. Por Adolfo A. R. Schulze. Pp. 13. (Buenos Aires: Instituto Antartico Argentino, 1959.) [267

United States Department of Health, Education and Welfare: Public Health Service. Publication No. 761: Activities of the National Institute of Health in the Field of Gerontology—Research Grant and Training Projects Active on January 31, 1960, and Intramural Research Projects Carried on during calendar year 1959. Pp. v+41. (Washington, D.C.: Government Printing Office, 1960!) 30 cents. [267

United States Department of Commerce: Coast and Geodetic Survey. Publication 65–1, Part 35: Plane Coordinate Intersection Tables (2½ minute), Oregon. Pp. iii+166. (Washington, D.C.: Government Printing Office, 1960.) 1 dollar. [267

Department of Fisheries, Ceylon. Fisheries Research Station Bulletin No. 9: Lobster Fishing in Ceylon. By G. H. P. De Bruin. Pp. 18. (Colombo: Fisheries Research Station, 1960.) [267

Engineering Experiment Station of the University of Illinois, Urbana. Engineering Departmental Reports and Theses 1958–1959: Abstracts of Engineering Departmental Reports and Titles of Theses of the University of Illinois College of Engineering. Edited by James C. Ballowe and Paul Bryant. Pp. 47. Bulletin No. 456: Titania Opacified Porcelain Enamels. By R. D. Shannon and A. L. Friedberg. Pp. 49. Circular No. 68: A Comparison of the Performance of Various Room Heating Units used in the I-B-R Research Home. By Warren S. Harris and Loren N. Montgomery. Pp. 27. A Summary of Engineering Research, 1959. Compiled and Edited by W. David Penniman, James C. Ballowe, R. Alan Kingery and Paul T. Bryant. Pp. 146. (Urbana, Ill.: University of Illinois, 1960.) [267

Hokkaido University, Sapporo, Japan. Monograph Series of the Research Institute of Applied Electricity, No. 8: Some Developments in Network Theory. By Prof. Y. Asami. Pp. iii+146. (Sapporo: Research Institute of Applied Electricity, 1960.) [28

Tokyo Astronomical Observatory. Tokyo Astronomical Bulletin. Second Series. No. 121 (November 20, 1959): Precise Measurement of Travel Times of Radio Signals between Europe and Tokyo. (Potsdam versus Tokyo) 1. By S. Ijima, K. Futsukaichi and Goro Shibutani. Pp. 1409–1495. No. 124 (February 10, 1960): Discussion of Occultations Observed in Japan with the Photoelectric Equipments from 1954 to 1958. By S. Aoki and Y. Endo. Pp. 1515–1524. No. 126 (March 5, 1960): Polar Tube Observations during 1959. By N. Sekiguchi and J. Matsumoto. Pp. 1537–1538. No. 127 (March 15, 1960): Approximate Positions of Artificial Satellites Obtained with the Baker-Nunn Schmidt Camera (2). Pp. 1539–1553. No. 130 (June 15, 1960): Approximate Positions of Artificial Satellites Obtained with the Baker-Nunn Schmidt Camera (3). Pp. 1621–1643. (Tokyo: Tokyo Astronomical Observatory, 1959 and 1960.) [28

United States Naval Observatory. Circular No. 89: Solar Eclipses, 1968–1970. By Simone Daro Gossner. Pp. 8. (Washington, D.C.: United States Naval Observatory, 1960.) [28

National Academy of Sciences: National Research Council. NAS-NS 3010: The Radiochemistry of Barium, Calcium, and Strontium. By D. N. Sunderman and C. W. Townley. Pp. vi+118. (Washington, D.C.: Office of Technical Services, Department of Commerce, 1960.) 1.25 dollars. [28

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THE LEARNED SOCIETY, THE ARTS AND THE SCIENCES

"IT is the duty of the Royal Society", said Sir Cyril Hinshelwood, in concluding his tercentenary address, "to maintain within the larger community the smaller one in which creative activity can flourish. Its members owe a multiplicity of loyalties, none of which can be fulfilled without the others: to mankind in general, to their native land, and to the Royal Society itself". "That is not all", he added, "for there are communities in time as well as in space, and the most original minds, in some sense isolated in all contemporary groupings, find their true affinities in continuing the sequence of their predecessors, and their fulfilment only in their successors".

In this concluding part of his address, Sir Cyril had been discussing the role of the scientific society in the world of to-day, and more especially its bearing on the relation of the individual to the community. The great movements of thought, he pointed out, and even the lesser ones of whim and fashion, spread from leaders, and only minorities in general exercise an independent taste and judgment or produce original thought. The propagation of an idea demands the right conjunction of unknown human factors, but even when these are propitious nothing will initiate the change save the operation of a minority small enough to defy statistical calculations.

While the majority and the minority are thus generally mutually dependent, in scientific investigations the lavish material ways and means needed, particularly the further knowledge advances, make the individual in isolation, except under rare conditions, correspondingly impotent. The community as a social and political whole cannot be expected, however, to possess the detailed understanding to support him, and with the tremendous issues at stake to-day, it is necessary to create, to mediate between the individual and the major group, a specialized minor community, large enough to command prestige and confidence, but with membership limited to those who put the claims of knowledge first. This is the part that the scientific society and academy, rather than some government institution or the universities, have to play, and Sir Cyril sees them as providing several vital things that neither government nor industry can provide so well. Sir Cyril instances non-commercial periodicals for the publication of discoveries, a measure of financial support for ideas still too embryonic to be of immediately obvious practical application, the mutual stimulus of association and discussion and the immaterial reward of honour for intellectual achievements.

If an academy maintains high standards of unquestioned impartiality, it sets the tone throughout the scientific community and exerts its influence far beyond the confines of the learned world. When the closest connexions with government organizations or industry are maintained, the professional men of science hear of the needs of the State and of industry, and these in their turn are irrigated by the currents of scientific thought. The process of communication of ideas, Sir Cyril rightly stressed, is not something purely mechanical but rather a sensitive nervous mechanism endowing the community which possesses it with capacities and potentialities realizable in no other way. The subtle co-ordinating action of an academy, he pointed out, can no more be replaced by a bureaucratic organization or a system of economic incentives and deterrents than the intrically evolved biological controls of a living organism can be replaced by widely devised mechanical appliances.

Sir Cyril Hinshelwood's remarks deserve to be deeply pondered by scientists and technologists both in relation to the scientific society and to the professional association. It is clear that both have a part to play in establishing the most effective conditions of communication and for the functioning of creative thought and work, and perhaps more especially in respect to the professional association. It is almost a generation since A. M. Carr-Saunders and P. A. Wilson published their study of the professions, and apart from the many changes in the organization of the professions, the time is ripe for a further critical examination of the functions of the professional, as well as of the scientific and learned, society in the world of to-day, and Sir Cyril's address challenges the creative thinking that is required. His comments indicate very clearly that the failure of some professional organizations to take clear decisions about individual and corporate membership may well prejudice the effectiveness with which they can serve the community as a whole.

The mutual stimulus of association and discussion is not, however, limited to the scientific society or academy as such. It can equally be carried out by a body in which the scientist and the non-scientist are brought together, as in the Manchester Literary and Philosophical Society, and in respect of promoting public understanding and creating the awareness of what is needed to support scientific activity, it may sometimes function more effectively than the purely scientific society. That Society has moved to its new buildings on the site of the premises which were destroyed by bombing in December 1940, in the hope that it may be a meeting place for people in Manchester who are interested in different aspects of the arts, science, commerce and industry. Quite apart from the fact that its own membership offers possibilities of wider contacts than the University itself could hope to provide even if not departmentalized, other societies in the city are already

arranging to use the new premises for their meetings, and there is some reason to hope the Society and its buildings may once again become the centre of Manchester's intellectual life.

Whether in the specialized scientific society or academy or in the more general society as exemplified by the Manchester Literary and Philosophical Society, this question of communication is all-important. What is needed above all is ease of communication across not merely the departments or disciplines of particular branches of science both within a university or academy and between the sciences generally and other fields of human endeavour. In addressing the Manchester Society, when he formally opened its new premises in September, Sir Cyril did not return to his earlier theme of the specific role of the learned society in the world of to-day, but he boldly challenged as artificial some of the distinctions between the arts and the sciences. He did not entirely accept as valid Sir Charles Snow's picture of the two cultures, and much that he said was not simply an eloquent plea to abolish some of the conventional distinctions between the arts and the sciences and to concentrate rather on what they had in common, but was a major contribution to the debate on general education and the education of the scientist in particular which had been a feature of the recent meeting of the British Association at Cardiff.

Prof. A. H. Cottrell, however, in a talk "Scientists: Solo or Concerted ?" broadcast in the Third Programme and printed in *The Listener* of September 15, dealt more specifically with this theme of the individual or the creative minority and the relation of individual or minority to the majority of the community in which they live, from which Sir Cyril Hinshelwood had originally approached the question of the scientific academy. Emphasizing how misleading can be the popular image of the solitary scientist withdrawn from the world, Prof. Cottrell pointed out that the scientist, however remote he may seem, is always bound closely to the scientific life around him. He cannot work in a vacuum, but has to take the ideas and problems as they exist among his fellows, transmute them in his own personal way and then bring them back as offerings to the community.

Prof. Cottrell's analysis of the way science advances is worth considering from this point of view of the function of the scientific or learned society. All scientists and technologists, he points out, are users of what has gone before them. At any instance there is a narrow frontier dividing what has gone before from the problems still to be solved, and while this frontier is occasionally stationary where it runs up against one of the big problems of science, for the most part it is steadily moving forward; and keeping in touch with its position from day to day, even on a narrow sector, has become surprisingly difficult. In Prof. Cottrell's view, it is the main problem that the modern scientist has to face in his own work, and finding it exactly is half the battle in modern research. If the scientist does not find it, he is in danger either of being too timid and wasting his talents on a stale problem or of being too bold and futilely attempting the impossible. If, however, he can pin-point its position really well, deciding the next step forward and how to make it is often surprisingly easy.

Prof. Cottrell's own deduction from the effect of this principle on the pattern of scientific research itself, and the consequent emphasis on meeting as many people working in your own field as possible and meeting them as often as possible, is that where this cannot be done every day in a great laboratory, the need should be met in a scientific conference. His emphasis, moreover, is on the informal contacts and discussions at such conferences, when proceedings in any event are often very belatedly imperfectly reported, and his address lends no support to any proposal for elaborate mechanical means of indexing or recording their proceedings. He recognizes, in fact, that the real value of such conferences is derived from personal participation, and nothing can replace this.

Here, like Sir Cyril Hinshelwood, Prof. Cottrell is emphasizing the dependence of creative work on human qualities—boldness, conservatism, originality—that run through the fabric of all human endeavours, and to his mind the big projects and great laboratories are gradually leading to a new kind of creativity in science. By pooling their individual talents and efforts in a common purpose the members of such organizations are able to attempt new ventures with a boldness and on a scale far beyond the scope of the individual, and he compares the work of many modern laboratories in science with the collective creativity involved in the production of an opera or ballet. In some parts of science it has, of course, not yet become necessary to work in these large groups, but even so, the large laboratory offers advantages in keeping in touch with the frontier and in the stimulating company of one's colleagues. In nuclear physics, however, in radio astronomy, nuclear energy and aeronautical research, the equipment is so large and costly that there is no alternative.

Here again, Prof. Cottrell's thought seems to run with that of Sir Cyril's, and he suggests, indeed, that the arts have something to teach science in the organization of large-scale scientific research and how best to encourage the delicate but all-important balance between individual creative research and collective team-work. There are questions here of education on which Prof. Cottrell just touches, but it should be clear from his remarks how important a part the scientific society or academy has to play in the advancement of modern science. It will not indeed eliminate the need for the scientific conference, particularly at the international level, and it can play a useful part in promoting the organization of such conferences where required. Its real work, however, lies in the fostering of regular and easy and informal contacts and discussions, not simply between specialists, but across the different disciplines. Moreover, Sir Cyril Hinshelwood and Prof. Cottrell agree in recognizing the value of such contacts and discussions not merely within the

sciences but also across the boundaries of science and the arts. Societies like the Manchester Literary and Philosophical Society which seek to bring the scientist into closer and regular touch with those who work in different fields of art may well have a large contribution to make in stimulating creative thought and the new studies which are required to solve some of the major problems of the organization and administration of science itself, quite apart from the value of such contacts stimulating a fresh approach to some problems of science itself. Moreover, such societies assuredly have their part to play in the task of public education, of promoting the general understanding of the nature of science and the way it works and advances, that become more and more essential as the demands of science on the public purse extend.

For all such reasons it is to be hoped that the Literary and Philosophical Society in Manchester and kindred societies throughout Britain and elsewhere, no less than learned, scientific and professional societies generally, will respond to Sir Cyril's challenge to the Manchester Society and grasp their opportunities with boldness, with vision and with imagination.

EDMUND HUSSERL: 1859-1959

Edmund Husserl 1859–1959
Recueil Commémoratif publié a l'Occasion du Centenaire de la Naissance du Philosophe. (Phænomenologia, Vol. 4.) Pp. xi+306. (La Haye: Martinus Nijhoff, 1959.) 20 guilders.

THE year 1859 in which Edmund Husserl was born was indeed a landmark in the progress of European learning. It claimed also John Dewey, Samuel Alexander and Henry Bergson. As if that were not enough, in that same year Darwin's "Origin of Species" and Marx's "Critique" made their appearance. The passage of time was in fact to show that Husserl and Alexander both died in 1938. The present volume, beautifully printed and set out, was issued as a centenary collection in honour of the master of phenomenology. The twenty-five contributors, as one would expect, are leaders and critics in that branch of philosophy, and they write, for the most part, in their own languages, namely, English, French, German and Italian. Yet these pages are a typically 'overseas' assemblage; not one of the distinguished authors comes from Great Britain. In his lifetime particularly, Husserl's force was a Continental radiation having as it were secondary foci in the United States which have sharpened with the years and yielded him praise. But, nearer home, anyone who has visited the Archives at Louvain will read Prof. van Breda's paper in this book with particular pleasure. It is outstanding for its scholarship, sympathy and charity. Possibly not too well known is the fact that the savants there assumed the responsibility not only of safe custody, but also the task of transcribing (from Husserl's shorthand) and editing the mass of material which the late Frau Husserl had been able to deliver into their hands, and thus to save from the ravages of Hitler's *Reich*. As Prof. van Breda modestly remarks, Germany has gained a little intellectual territory in the process, a scholar's embassy on Belgian soil.

But this is only the result of something that was afoot some sixty-odd years ago. Husserl's mental strife was intense: he was able (and this was the operative part of the performance) to share it with his students, and literally to compel them to labour too. Stiff and formal—not unlike Max Planck—in his university lecturing, he was creative to a high degree in his seminars. All this was to one purpose, to obtain the greatest possible rigour (in theory, a pre-suppositionless philosophy), and to ask the right questions. Husserl was an artist in the shades of meaning, and his small audiences instinctively sensed his deft use of word and phrase. Of course, such a professor–pupil relationship, almost medieval in its fervour, would be unthinkable to-day with our crowded class-rooms and tight schedules. This book is worth reading on that score alone, to catch a glimpse of the kind of detachment necessary to become an epistemologist of stature. Husserl was a great enough man to reveal to his hearers much of his own early confusions, and how he escaped from them to do battle with psychologism, that is, the subtle intrusion of psychological elements into purely logical processes. Moreover, it should not be forgotten that he came to mental manhood as a pupil of the great Weierstrass, with a dissertation on the calculus of variations (1882), which apparently was never printed. In the publication now under review the reader is presented with a full bibliography, and a worthy reproduction of the drawing of the master by Rudolf Stumpf.

Husserl's attempt to use phenomenological methods in the sphere of social science was scarcely a success, if judged in relation to any form of transcendental theory of knowledge. But he achieved an advance; if one admits the value of philosophical anthropology as at least a worth-while development of the problems of the living world. Even though much of his work in this direction was contained within the restricted field of 'reduction' or 'bracketing'—corresponding to a suspension of judgment—yet he established a vital principle in his emphasis on the place of the natural attitude. The empirical type of sociology has much to learn from this, more particularly when one recollects how hard Husserl strove to practise what he preached. Those who enjoyed the intimacy of his friendship, and accompanied him on his 'philosophical walks' at Freiburg, must have become convinced that the peripatetic schools of the Golden Age at Athens must surely have come to life again. But Husserl could be very lengthy: it was not uncommon for him to think aloud, without notes of any kind, for a couple of hours on end, an ordeal which his listeners not only survived but even enjoyed. They were there *d'assister* at the birth of ideas, and they had their reward.

An element of paradox seems inseparable from much German thought. It is displayed here in Husserl's scientific philosophy as a free gift to those who would divest any theory of knowledge of its scientific content. He fought against naturalism only to help it on to its feet. In broad outline, Husserl shares with Sören Kierkegaard, Karl Barth, and Rudolf Otto the tendency to stress the 'wholly other'. In England we do not do this: our urge to find a middle way carries us in the opposite direction. Yet there is to-day a movement towards subjectivity, not in the mathematical sciences, but in biological

studies, which may well herald the advent of biophysics as the leading discipline in future experimental philosophy.

The chapters of this admirable book, each one by an acknowledged authority on his own ground, are written to survey a wide field: reminiscent, biographical, epistemological, psychological, and experiential. The late Dr. Alfred Schutz, one of the contributors, met Edmund Husserl many times during the nineteen-thirties in Freiburg, Vienna, or Prague, and sums up the impression that was universal, when the name of the master of phenomenology was mentioned, in just two words, "*Ecce philosophus*".

F. I. G. RAWLINS

PRODUCTION AND PROCESSING OF URANIUM

Uranium Production Technology

Edited by C. D. Harrington and A. E. Ruehle. Pp. xii+579. (Princeton, N.J., and London: D. Van Nostrand Company, Inc., 1959.) 131*s*. 6*d*. net.

THIS book is the first comprehensive compilation of the technology of uranium production. The material for the book was prepared by the technical personnel of the Uranium Division of Mallinckrodt Chemical Works, under the direction and guidance of the United States Atomic Energy Commission's Division of Information Services. The Commission recently declassified virtually all the significant features of the technology, thus making possible the publication of the book.

For the benefit of the industrial chemist, the production of pure uranium from the ore concentrate is described in considerable detail both in regard to the plant and to the chemistry of the processes involved. Plant for both batch and continuous processes is described, and the accounts of advanced methods, such as ion exchange and fluidized bed techniques for the manufacture of both uranium tetrafluoride and hexafluoride, are of special interest. It is apparent that very little information has been withheld, and cost figures for many of the processes are included.

For the metallurgist and the engineer there are excellent chapters dealing with the vacuum casting and subsequent forming of the uranium metal, and again considerable detail of the plant is given.

Chapter 10 is worthy of special mention and deals with the physical metallurgy of uranium related directly to the problems of metal production and fabrication. The structure in terms of the allotropic forms of uranium, the response to heat treatment and the degree to which the grain size may be controlled are all discussed. Lists of the usual mechanical properties, showing the effect of temperature, are given, and the final section reviews mechanisms of alloy formation and shows the effects of additions on the physical properties, structure and mechanical properties. The photomicrographs showing the structure of uranium and of typical inclusions are particularly useful.

British experience of fabricating uranium metal by methods other than casting and machining is relatively limited. The next three chapters, dealing with forging, extrusion and rolling, might therefore have been expected to be of especial interest. In fact they are just a little disappointing—particularly that on extrusion—and it is difficult to believe that we are being given an adequate account of the fairly extensive body of American knowledge on these aspects. An additional chapter on fabricating high-uranium alloys gives some useful basic data; this chapter also has a very good bibliography.

The final chapter is devoted to health hazard control and gives an extensive review of this particularly important aspect of uranium processing. Shielding against beta and gamma radiation is described, and useful guidance on the methods available for dust control is given.

Few criticisms can be made of the book, and these are mainly minor ones. Its pages include a wealth of information on uranium production and processing. Extensive use is made of diagrams and photographs, and there are 750 references. The book will be invaluable to all those interested in the manufacturing processes of uranium and its compounds.

D. E. R. HUGHES

GENERAL ASTROPHYSICS

Astrophysique Générale

Par J. C. Pecker et Prof. E. Schatzman. Pp. x+756. (Paris: Masson et Cie., 1959.) Broché, 12,000 francs; cartonné toile, 13,000 francs.

ASTROPHYSICS is not a big subject in relation to some other sciences, but in my view the day has passed when any complete and satisfactory account of it can be compressed into one text-book, unless at a quite elementary level. Here two well-known French astrophysicists have attempted heroically to do the well-nigh impossible, and even if the result falls short of perfection it deserves a warm welcome, for good general text-books in this field are very scarce. We have on one hand a fair number of specialist monographs, some of them invaluable, and on the other more than enough glossy semi-popular and popular books, most of which should be avoided as the plague by any serious student. Between these extremes there is remarkably little.

The first 100 pages of "Astrophysique Générale" are given over to a summary of "what every young astrophysicist should know"—everything from hydrodynamics to Hamiltonians, statistics to spectroscopy. It illustrates the wide range of technical knowledge a theoretical astrophysicist ideally should command, but is much too compressed to be anything but a refresher course for a recent honours graduate in mathematics or physics. A whole book written along these lines would be very useful, but I question the wisdom of attempting the task in less than, say, 1,000 pages. Part 2, dealing with astronomical instruments and methods of observation, is at a very different level of sophistication. It shows signs of having been written by theorists, for there are a number of over-simplified or over-optimistic statements (for example, "Pour les étoiles jaunes et rouges, la mesure des magnitudes radiométrique permet d'obtenu aisément les magnitudes bolométriques"), as well as a few small errors. In Part 3, the longest in the book, the authors are, however, more on their own ground, discussing what we know of stars, their spectra, masses, intrinsic luminosities, radii, and the theories of their atmospheres and their interiors.

Part 4 deals with systems of stars, the structure of the Milky Way and of external galaxies. It also has chapters on stellar dynamics, interstellar matter and stellar evolution. Part 5 summarizes our knowledge of the Sun, which is regarded as a typical *G2V* star, and of the planets and other bodies in the solar system.

This is not a book for a beginner. The reader needs a solid background of mathematical physics and at least some prior acquaintance with elementary astronomy. There is a real need for astrophysical text-books at this level; but this one, it seems to me, attempts to do too much in too little space and one result is that in places it tends to be scrappy. I suspect that quite competent students, especially perhaps the more conscientious and thoughtful, might sometimes find its pace slightly bewildering.

The production is on the whole good. Too small a type for comfort has sometimes been used in subscripts, etc. The illustrations are in general good, but a few are misleading. A certain number of misprints need correction. R. O. REDMAN

PROGRESS IN THE FLORA OF CANADA

Flora of Alberta

A Manual of Flowering Plants, Conifers, Ferns and Fern Allies found growing without Cultivation in the Province of Alberta, Canada. By Prof. E. H. Moss. Pp. v+546. (Toronto: University of Toronto Press; London: Oxford University Press, 1959.) 80*s*. net.

DESPITE some 250 institutional herbaria, and some 25 journals which regularly publish taxonomic papers, in temperate North America, our broad knowledge of the flora of that continent is surprisingly fragmentary. There are large areas of the continent and large numbers of taxa which, by modern standards, have not been critically, or even adequately, examined. This should not be taken to imply that large numbers of 'new' species remain to be found in North America—for the country has generally been well explored, even if not yet thoroughly collected. Rather, it indicates the large amount of work that is yet to be done before we have even a bare catalogue which will show the extent of the North American flora.

Until very recently, the flora of Canada has been particularly poorly understood. The most south-easterly part of Canada has been treated in the two standard Floras of the north-eastern United States. Southern parts of the prairie provinces were included in the now somewhat outdated Floras of the prairies and plains, and of the Rocky Mountains of the United States. Southern British Columbia has a Flora published as long ago as 1915 (with a Supplement published in 1947). In the past twenty years, however, the botanists of the National Museum of Canada have made a concerted attack on the flora, with the view, eventually, of a proper "Flora of Canada".

The regional Floras of the National Museum of Canada, combined with Hulten's monumental "Flora of Alaska and the Yukon" (1941–50), Polunin's "Circum Polar Arctic Flora" (1959), and the various more generalized publications of the Canadian Department of Agriculture are now beginning to give us a rather good idea of the outlines of the Canadian flora. The most serious gap in our knowledge, of recent years, has been the lack of a Flora for the western prairies and the Rocky Mountains. The publication, by the University of Toronto Press, of the "Flora of Alberta", written by the distinguished Canadian botanist, Prof. E. H. Moss, is, then, an event of some considerable interest and importance.

The Province of Alberta is one of the twelve administrative divisions of the Dominion of Canada. It extends (with irregularities in the south-western corner) from the 110th degree of west longitude to the 120th degree, and from the United States boundary at 49 degrees of north latitude northwards to 60 degrees. It has an area of about 255,285 square miles. The flora, as herein enumerated, consists of some 1,605 species of vascular plants. These are the bare facts of the matter.

After some 200 years of experiment and practice, it is fairly clear to botanists what the essential qualities of a good Flora are. A Flora (as distinguished from *the* flora) is, first and foremost, a tool for the identification of any plant included within its circumscription of areal and systematic range. Basically, the most important part of the treatment is the delimitation and description of the individual taxa. These circumscriptions should be clear, precise, and as brief as possible. Supplemental data, such as descriptions of habitat, flower colour, and season of flowering are frequently of considerable practical usefulness.

For the general user, however, the most important parts of a Flora are the 'keys'—analytical tables of pairs of contrasting characters, set out in a conventionalized form, by which one should be able to be led, through the sets of alternatives, to the name and description for the taxon of which the user has a representative in hand. Indeed, many very useful Floras consist, essentially, of keys alone. To be useful, a key must be infallible. Infallible is a strong word—but if the taxonomy of the text is an accurate reflexion of the facts (plants) found in Nature, infallibility is practically possible. The large number of practically infallible keys in Floras and monographs which are in general use is sufficient proof of this statement. Keys which do not work very frequently indicate taxa which are not adequately understood.

The "Flora of Alberta" is an extremely valuable tool, which should have considerable usefulness both in the herbarium and in the field. It is obviously based on the author's first-hand knowledge of the Province. The descriptions are generally clear and concise. The keys to the families and to the genera seem to be rather good examples of their kind. The keys to the species are occasionally a little less happy, especially when qualitative, rather than quantitative, characters are relied on too heavily (*Salix* and *Senecio* afford examples of this).

The "Flora of Alberta" is, as the author comments in his preface, "a pioneer effort". As a pioneer effort we are grateful that the work has been done. It is no adverse reflexion on the work of the author if we suggest ways that future editions might be improved. I think that we would like to see a few pages devoted to a discussion of the vegetation, the geography, and the geology of the Province. A map of the area would be helpful. Illustrations of some of the more interesting taxa would be useful. A short discussion of the history of botanical exploration in the Province would also be of interest, and would add a welcome perspec-

tive. Notes of flower colour and season of flowering would enhance the usefulness of the Flora to the layman.

It is very easy for those of us who have been brought up in regions that are well known botanically to pick flaws in a pioneer work covering an area that is little known. We should remember, when we are tempted to criticize, the very great debt we owe to men like Prof. Moss (need we mention Ridley, Asa Gray, or J. D. Hooker), who, in their retirement, have not been content to rest, but have, instead, given us basic works to build on. Their errors may or may not be glaring. They, not we, have done the work.

GORDON P. DEWOLF, JUN.

THE CHEMISTRY OF AIR POLLUTION

The Chemical Analysis of Air Pollutants

By Dr. Morris B. Jacobs. (Chemical Analysis: a Series of Monographs on Analytical Chemistry and Its Applications, Vol. 10.) Pp. xviii+430. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1960.) 102*s*.

ONE need not be a chemist to appreciate the ever-growing menace of air pollution in urban communities. Too often the discomforts and dangers of the winter 'smog' descend on a choking populace, apparently powerless to alleviate the distress caused by its own machinations. This is pollution at its obvious worst, but there are many other forms of pollution which though less conspicuous are no less hazardous and indeed, in the case of radioactive contamination, can have such far-reaching effects that the entire populace of an affected area must be evacuated.

In order to control air pollution, it is first necessary to measure it, and this involves the determination of the nature and amount of the contaminating materials. In this book, Dr. Jacobs, who is a well-known consultant in this field, sets out his systematic approach to the many chemical and physical problems involved in analysis of gaseous and particulate contaminants in air.

Chapter 1 contains a general account of sampling and the available means of taking samples for analysis. Chapter 2 is devoted to the measurement of volume, quantity, and velocity of gases. Chapter 3 considers sootfall and dustfall, and the analysis of soots and dusts by a number of standard methods. Chapter 4 deals with the evaluation of atmospheric dust, particularly the particle sizes involved. Chapter 5, on suspended particulate matter, gives procedures for the chemical analysis of organic and inorganic constituents. Chapters 6 and 7 deal respectively with smoke density and smoke shade, and the sampling and analysis of industrial stack-smoke. Chapters 8 and 9 cover the chemical analysis of sulphur and halogen-containing air pollutants, Chapter 10, that of nitrogenous compounds and ozone, Chapter 11, oxides of carbon, cyanide, and phosgene, and Chapter 12, general organic compounds. In Chapter 12 these materials are arranged according to their functional groupings. Chapter 13 covers the determination of radioactivity and the detection and determination of hazardous isotopes such as strontium-90. The analysis of incinerator-flue gases and motor-vehicle exhaust gases is dealt with in Chapters 14 and 15. Chapter 16 deals with the interesting subject of 'odour' analysis, which involves the determination of the amount of a (generally) malodorous material in the atmosphere. The final chapter (18) describes instruments used to monitor particular types of air contaminants. An appendix contains a number of useful tables and data pertinent to the information given in the text.

The wealth of information given in this book and the concise and systematic way in which it is presented must make it an obvious choice for all who are interested in the control of air pollution. Its use is not restricted in any way by its contents which are directed primarily to the analyst, but are of interest to a much wider section of the community, such as engineers, factory inspectors, public health and sanitation officers. Much of the analytical chemistry can be adapted for courses in colleges and universities, and the inclusion of many simple and inexpensive methods is of great value not only to teaching institutes, but also to the many communities and industrial organizations which do not have the funds necessary to set up the more elaborate methods and instrumental techniques.

For the analytical chemist, this book provides an admirable addition to the literature on applied analysis. It maintains the high standard of its predecessors in the Interscience series of Monographs on Analytical Chemistry and its Applications, and it must undoubtedly become a standard work on the subject of air pollution.

W. I. STEPHEN

VEGETABLE PATHOLOGY

Vegetable Diseases and Their Control

By Prof. Charles Chupp and Prof. Arden F. Sherf. Pp. v+693. (New York: The Ronald Press Company, 1960.) 12 dollars.

ALTHOUGH directed primarily at the American reader this publication should prove of interest to those in Great Britain and elsewhere.

After preliminary sections on seedling diseases and those affecting a range of host plants, there are sixteen chapters each dealing with the diseases of a group of vegetables. Potatoes are not included. The book concludes with chapters on minor element deficiencies, nematodes and soil sterilization. A valuable feature is the mention of varieties that show resistance to the various diseases.

As indicated in the preface to the volume, an attempt has been made to write in as nearly a non-technical manner as possible so that the book may be of use to the amateur as well as to the commercial grower. Considerable success has been achieved in this respect and the narrative style is very readable, a feature which is assisted by the excellent clear type. The sections abound in practical recommendations for control and obviously contain the fruits of many years experience in this field.

The book is also intended to serve as a text for students, research specialists and advisers, but its value in this respect is less apparent. There are few sub-headings within the sections on each disease; with a few minor exceptions there are no drawings or photographs of the causal organisms, and little or no mention is made in the text of the references quoted at the end of each section. These therefore

lose much of their value and they may also be criticized on the grounds of incompleteness. The work and monograph of Colhoun on clubroot of crucifers, for example, receive no mention, and the chapter on soil sterilization is accorded five very meagre references (this has since been found to be due to the printers omitting in some copies a page of references).

Some of the control measures now seem rather old-fashioned (for example, soaking seeds in copper sulphate solution to control certain damping-off diseases). Errors also occur in several places. The photograph of the effect of *Verticillium* wilt on tomato leaves is not of the normal symptoms associated with the disease; Bordeaux mixture is not used (as stated) against *Didymella* stem-rot of tomatoes; the section on big vein of lettuce does not give an accurate representation of the latest information or experiments on the disease.

The publication gives the impression that in attempting to cover a very wide range of subjects and of readers the authors have only partially succeeded. Even so, the book does provide a useful compendium which may with advantage be used both as a guide to some of the other sources of information on the subject and as a supplement to them.

W. G. KEYWORTH

KNOWING OURSELVES

Understanding Human Society

By Prof. Walter Goldschmidt. (International Library of Sociology and Social Reconstruction.) Pp. 253. (London: Routledge and Kegan Paul, Ltd., 1959.) 21*s*. net.

THE distinguished editor of the *American Anthropologist*, Walter Goldschmidt, has essayed a most difficult task—to provide a guide to the development of man in society. Such a book has long been needed. The great majority of anthropologists have for too long been too preoccupied with the immediate problems of their subject. There can be little doubt that studies of kinship have dominated the anthropological horizon for a considerable time. It is refreshing, therefore, to come upon a book which attempts to deal with the broader implications of the subject.

One of the most valuable sections of this book is entitled "The Dimensions of Anthropological Theory". It begins, "The ultimate task of the anthropological enterprise is to explain the uniformities and diversities in the natural condition of mankind . . .", and proceeds to a discussion of the various approaches which have been made to the study of man. Curiously enough, the history of anthropology, with the exception of Haddon and Penniman, is extraordinarily sparse. For the student this chapter fills a long-felt want. The teacher is apt to presume a knowledge on the part of the student which does not always exist. Frequently he is too concerned with his own bias to worry about the theories of others. The individual who sat at the feet of the late Father Schmidt in Vienna would scarcely have obtained an unbiased account of, say, Malinowskian functionalism. Prof. Goldschmidt, on the other hand, is remarkably fair in his treatment of the theories of others.

In developing his theory of social evolution, which forms the core of the book, the author is at pains to point out that we must exclude any idea of moral values which so bedevilled the old evolutionary hypotheses. The theory presented is eminently respectable, and few would quarrel with it. Its fault lies in the fact that it does not take us very much further on the way. "It does not in and of itself explain these social systems, in the sense that it offers a full account of what makes them as they are." Perhaps no theory could; but we are back where we started being forced to consider each society as a unique whole.

The value of this book is perhaps not in the field of original theory but rather in the clarity and succinctness with which the author deals with the ideas of others about the nature of human society. In the jargon-ridden jungle of the social sciences, Prof. Goldschmidt has created a little oasis of simplicity for which we must be grateful. It must be admitted that Americans are not usually exemplars in this matter.

The publishers have not been too well served by the printers who, by using a different type for the concluding words or sentences of chapters, have managed to convey an arcane sense which is totally misleading.

F. HENRIQUES

SOCIOLOGY OF CASTE IN CENTRAL INDIA

Caste and Kinship in Central India

A Village and its Region. By Adrian C. Mayer. (International Library of Sociology and Social Reconstruction.) Pp. xvi+295+16 plates. (London: Routledge and Kegan Paul, Ltd., 1960.) 35*s*. net.

THIS is a sociological study of caste as it operates in Central India in the E. M. Forster country, and it provides a valuable addition to the literature on caste in India. Much has been written on this subject, but mainly on a broad and generalizing and on an India-wide scale, or in a theoretical, evolutionary or historic form. What are lacking are the detailed studies of caste as it actually functions in specific Indian communities, against which these generalizations and hypotheses can be tested. Dr. Mayer's book is one of the best studies of this sort that has yet been made and the only one that deals with the caste system as it operates in a multicaste village and its surrounding neighbourhood. It brings out very clearly the interconnexion between kinship, sub-caste and caste. Village boundaries are shown to be something more than territorial and to mark the difference between two kinds of relationship, that of common caste and of agnatic kinship (in the village) and that of common sub-caste and of bilateral and affinal kinship (in the region).

The book is divided into three parts: the first sketches the historic and economic background, the second examines intercaste relations as they affect ritual, economic and political status and the third analyses the constitution of the caste, its internal structure, the part played by unilinear descent, and the pattern of marriage and of social control within the sub-caste.

Social anthropologists interested in kinship, whether or not they are also concerned with the study of caste, will find much of value in this study, while those more immediately concerned with rural Indian political and economic development would do well to read the chapters on caste and village leadership and on the economic aspects of caste.

G. I. JONES

Advances in Applied Mechanics

Vol. 6. Edited by H. L. Dryden, Th. von Kármán, and G. Kuerti. Pp. x+294. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1960.) 9 dollars.

THIS latest volume of the series is concerned entirely with fluid mechanics. There are two chapters on boundary layers: one on unsteady layers, by K. Stewartson; the other on layers in a dissociated and ionized gas, by G. Ludwig and M. Heil. The two following chapters are on high-speed flow: the first on shock propagation along varying ducts, by W. Chester; the second, a particularly valuable account of similarity and equivalence, by K. Oswatitsch. The last chapter, a short one by R. Wille, is on Kármán vortex streets.

Reading through this latest collection of essays on topics in applied mechanics, one is made to realize once again what a remarkably sound idea the publication of this series of volumes has been. To the expert who has already formed his own balanced view of a subject, an individual essay may not always seem worth while; partly because, no doubt, he disagrees with the view taken by the author, and partly because there is not usually much original material to compensate for other shortcomings. But to the newcomer, whether he be a complete novice or a more experienced person broadening his interests, the publication of a detailed and up-to-date account of a subject, representing the personal view of someone who has usually taken an active part in developing it, is a valuable service—much more valuable than the publication of the few summarizing paragraphs, followed by several hundred references, that sometimes pass for a review. The editors, no less than the latest additions to the list of authors, are to be congratulated for maintaining this service.

IAN PROUDMAN

Viscoelasticity

Phenomenological Aspects. Edited by J. T. Bergen. (Symposium sponsored by the Armstrong Cork Co., held at its Research and Development Center, Lancaster, Pennsylvania.) Pp. x+150. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1960.) 6 dollars.

SOME explanation is required concerning the definition of terms in the title of this book. "Phenomenological aspects" are clearly defined as those concerned with the material "as a continuum which is characterized by specific, fundamental parameters"; as opposed to aspects "dealing with molecular structural or molecular model considerations". Viscoelasticity is taken to include behaviour involving flow, more often currently described as elastico-viscous. Both linear and non-linear relations are discussed but there is some confusion over the definition of "linear". One contributor gives alternative definitions implied to be synonymous (p. 28), although it is quite possible to find materials (for example, those obeying Bach's equation) the behaviour of which would be linear according to one version of the definition but non-linear following the other.

With some exceptions, the equations developed in these essays are applied by the authors to large masses of data from work published elsewhere, usually on materials which can be tested over wide ranges of stress and many decades of time. Only a few types of test are feasible under such conditions and it is remarkable that sufficient superposability exists to make possible so good a measure of agreement as has been found.

The book is important in correcting a tendency, prevalent in certain quarters, to believe that the only meaningful approach to rheology is through molecular considerations. It is a pity that one or two of the essays are written in such bad English, as judged by either British or American criteria, as to be irritating to the reader.

G. W. SCOTT BLAIR

Organic Chemistry

By Dr. I. L. Finar. Vol. 2: Stereochemistry and the Chemistry of Natural Products. Second edition. Pp. xi+834. (London: Longmans, Green and Co., Ltd., 1959.) 45*s*. net.

THE second edition of Vol. 2 of Finar's "Organic Chemistry" matches the high class of the third edition of Vol. 1. These new editions were both published in 1959. They are designed to provide a foundation for the organic syllabus of a special honours degree course in chemistry; this objective has been achieved. Present authors of text-books suitable for this level have to concern themselves with deciding what can be left out, and Finar's selection has obviously been made carefully. He has included practically all those topics of fundamental importance, but some quite recent developments are also introduced in such a way that the interest of the reader is excited. A valuable feature is the comprehensive list of reviews and monographs given with each chapter.

The discussion of stereochemistry occupies 210 pages. It is clear and covers optical and geometrical isomerism, the stereochemistry of the diphenyls and the stereochemistry of elements other than carbon. This is balanced by an introduction to more recent developments such as the stereoelectronic features of chemical change and conformational analysis.

The major part of the book is devoted to the determination of the structure and the synthesis of the more important classes of natural products. These have been carefully selected and include carbohydrates, steroids, amino-acids, proteins, alkaloids, anthocyanins, nucleic acids, porphyrins, vitamins and antibiotics. This is the best treatment of these topics which is easily available to undergraduates. There are certain gaps in the coverage provided by Vols. 1 and 2 of this work, but this is inevitable. The books are easily read, and this is a pleasant change from those which are just catalogues of structures and reactions. The second edition of Vol. 2 is a better book than the first edition and can be warmly recommended.

W. D. OLLIS

Scientific Manpower

By Joyce Alexander. Pp. viii+135. (London: Hilger and Watts, Ltd., 1959.) 15*s*. net.

WHAT factors determine whether a young person does or does not become a scientist? This is the question which Mrs. Alexander examines in this carefully documented essay. She points to the shortage of scientific man-power; she examines the educational system which has failed to overcome the shortage; and she discusses the proposals which have been made to overhaul the educational system and to equip it to serve contemporary needs. There is a very sensible chapter on scientific woman-power. This is a neat and useful little book. It does not break fresh ground, but it equips the reader to do some thinking for himself.

RECENT RE-ENTRY RESEARCH AND THE COSMIC ORIGIN OF TEKTITES

By DEAN R. CHAPMAN

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OPPOSING views have been expressed in recent years as to whether tektites are terrestrial or cosmic in origin[1–5]. The purpose of this article is to outline some new results obtained by bringing to bear on the problem recent advances from the discipline of re-entry aerodynamics. It is concluded that the australite tektites show sufficiently clear and diverse indications of atmospheric entry to enable their approximate initial velocity and flight path angle to be determined. A surprisingly narrow band of entry velocity is delineated which is in the cosmic-origin range, and, more intriguing, in that particular range uniquely compatible with origin from the Moon.

Although the present work is restricted to australite tektites, this does not limit the generality of the end result. The various tektite groups unmistakably are related by a family-like chemical composition and internal structure; hence, the determination of cosmic versus terrestrial origin for one group also applies to the other tektite groups within the family.

Australite Entry Aerodynamics

It has long been known that australites have been twice melted, and that the second melting occurred superficially on the front surface only. From this and other evidence, Baker[1] has concluded that the australites entered the atmosphere as cold, independent bodies, most of which neither tumbled nor rotated during ablation. Recent re-entry research provides three additional lines of evidence crystallizing this conclusion. During an experimental study in 1959, D. R. Chapman and H. K. Larson (at the Ames Research Center) found that the ablation of glass bodies commonly proceeds through the formation of ring waves being propagated radially away from the stagnation point; strikingly similar waves of 'flow ridges' are exhibited on many australites[1] and on a few javites[5]. A second line of evidence concerns the displacement of a glass particle within an ablation layer. Within the thin, receding, melted layer, the particle displacement near a stagnation point varies essentially exponentially with depth below the surface, and essentially linearly with radial distance from the stagnation point[6]; these same two types of mathematical variation were found in photographic enlargements of the australite thin section B in plate X of Baker's monograph[1]. The third line of evidence arises from a study of australite shapes. At least 98 per cent represent stable aerodynamic configurations in hypersonic flight when orientated in the unique manner that is compatible with the orientation demanded by the directions along which the secondary melt has flowed on their surfaces. Without going into the aerodynamic details, it is noted that such general aerodynamic stability is to be expected only in descent through the atmosphere, and not in ascent[7]. The overall evidence leaves no doubt that aerodynamic heating during entry into the atmosphere has been responsible for the second period of australite melting.

Even an absolute proof that an object has entered the atmosphere and suffered ablation at hypersonic velocity does not prove that it is cosmic in origin. The particular numerical value of the hypersonic velocity is of crucial importance. All that has been said about australite entry aerodynamics would apply, for example, equally well for 6 km./sec. entry velocity as for 12 km./sec. Yet, entry at 6 km./sec. could only be from a terrestrial source, whereas 12 km./sec. could only be from a cosmic source (since the Earth escape velocity of 11·2 km./sec. lies in between). Consequently, the aerodynamic evidence for tektite origin hinges on the magnitude of the velocity.

Only through relatively recent developments in re-entry research has it been possible to determine the entry velocity of the australites. Knowledge was required of the rate of aerodynamic heating as developed recently through both theory[8] and experiment[9], and of the rate of ablation of silica-rich glass as given by a refined version of the Bethe-Adams theory[6] recently confirmed in the laboratory[10]. In computing trajectories extensive use was made of Z-function solutions[11] for shallow supercircular entry. Through the use of high-speed digital computing machines the required Z-functions were compiled[12].

The analysis also required knowledge of certain physical characteristics of tektite glass, the most important of which is the viscosity-temperature relationship as determined from experiment[13]. Detailed data on the mass, dimensions, and radii of curvature of complete, well-preserved specimens were obtained from Baker's research[1], from additional correspondence with him, and through personal measurement of australites in the British Museum.

Entry Conditions and Geographical Distribution

The limited geographical distribution of a fall provides useful restrictions on the entry velocity. Let us consider first the hypothesis of terrestrial origin, wherein tektites are assumed to result from some violent natural phenomenon which has fused Earth material and thrown the melt far above the atmosphere (far enough to have had time to solidify before re-entering and experiencing the second melting). The exit velocity from the atmosphere would equal the entry velocity; it could not exceed some maximum value and still confine the fall to a limited geographical area. Velocities as high as the orbital velocity of 7·9 km./sec., for example, would spread the fused earth around the globe, and hence are too high to be compatible with a terrestrial origin hypothesis. If the fused earth were hurled in the manner that ejectamenta from hypervelocity impact in stone are hurled[14], then the maximum entry

velocity consistent with a terrestrial origin and confined distribution would be about 6 km./sec. According to the hypothesis of cosmic origin, however, the entry velocity would have to be equal to or greater than 11 km./sec. for direct entry (indirect entry after multiple-pass atmosphere braking[13] is not considered, as it would have resulted in global distribution of a cluster). For cosmic origin, all individual specimens in a tektite cluster would have the same entry velocity.

Results of Analysis

The approximate entry velocity has been determined from: (1) the thickness of the ablation layer near the stagnation point, as given by the displacement of internal glass striæ; (2) the amount of ablation at the stagnation point, as given by the shapes of complete, well-preserved specimens. For each entry angle γ_i (measured relative to local horizontal) the particular entry velocity V_i was calculated which would be compatible with the observed characteristics of a given australite. Entry angles were considered within the range from 90° (vertical entry) down to the overshoot boundary (nearly horizontal entry in which barely enough drag is encountered to land the tektite). In this way a V_i (γ_i) curve is obtained, some point along which the true V_i and γ_i would be located. By computing several independent curves a limited domain of entry conditions is delineated.

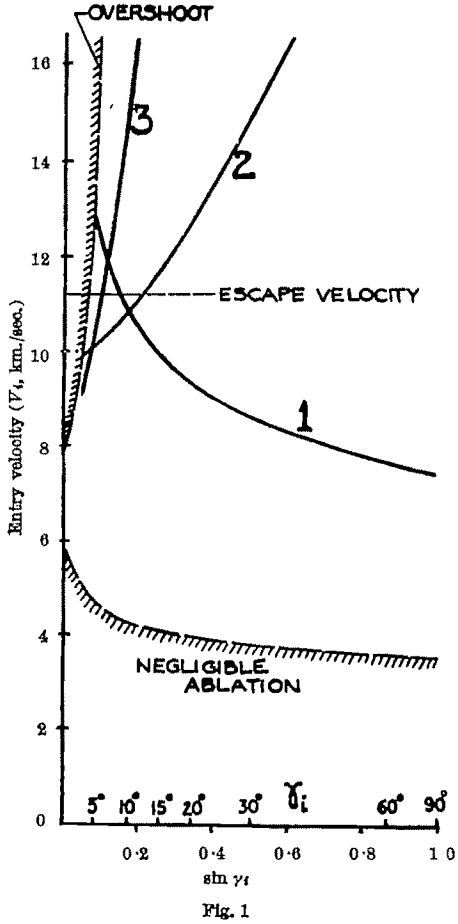

Fig. 1

The essential results are illustrated by curves in Fig. 1. Curve 1 corresponds to the entry velocity computed from the displacement of glass striæ in thin section B of plate X of Baker's monograph. Curve 2 corresponds to the velocity computed from the amount of ablation of "perfect button 1212" in Baker's collection. This particular button possesses a complete flange large enough to account for nearly all of the mass melted during entry. It is representative of those buttons which have lost the least amount of mass during entry. Curve 3 corresponds to the same type of calculation as curve 2 only for a large core (Reg. No. 1926–349 in British Museum). This curve is representative of an average large core. Some cores show less ablation and would fall between curves 2 and 3—where most buttons also would fall—while other cores show more ablation and would fall a short distance to the left and above curve 3. All three curves represent specimens found locally in a relatively small area of Victoria. In order for these australites to have entered with essentially a common velocity, this velocity would have to be in the range between about 10 and 13 km./sec.

By invoking certain dynamical limitations, the range of australite entry velocity is narrowed to considerably less than the 10–13 km./sec. band. At the lower end, entry in the 10–11·2 km./sec. range would correspond to terrestrial origin; at the entry angles indicated such velocities would have resulted in world-wide tektite distribution, and hence are rejected. At the upper end, velocities much above 11·2 km./sec. also are rejected, although for entirely different reasons. At 12 km./sec., for example, the required difference in entry angle of between 6° and 17° would correspond—for two specimens falling on the same spot—to impact about an hour apart. Since the approach velocity far from the Earth is 4·4 km./sec. for V_i = 12 km./sec., a time-interval of 1 hr. between impacts in Victoria would correspond to a distance interval when far from the Earth of greater than the Earth diameter. It is unreasonable to expect a cluster of such dimensions to land on a confined area of Australia. At entry velocities only slightly greater than the escape velocity (say, V_i of about 11·3 km./sec.) the approach velocity far from the Earth is small, so that the cluster dimensions implied by the indicated differences in entry angle also are small, and thus compatible with the limited area of the australite strewnfield. After imposing such limitations, the only entry velocity range we are left with is the narrow interval a fraction of a km./sec. above the escape velocity. This velocity band is compatible with a lunar origin of the australites In fact, the Moon is the only known celestial body for which the entry velocity would be expected to be in this particular narrow range.

A note is in order here about the accuracy of the calculations. All equations employed are based on analytical methods that have been verified in the laboratory. However, several physical approximations were employed for simplicity in the computations. For example, in making trajectory calculations the variable mass was approximated by the average before and after entry (specimens were selected which have lost only a small or moderate amount of mass during entry in order to minimize this uncertainty). The estimated accuracy is less than about 2 km./sec. in velocity. Shifts in the various curves of an amount corresponding to the estimated accuracy would not affect the end-result that the

observed features of australites are compatible with a cosmic entry velocity of essentially the Earth escape velocity, and incompatible with the hypothesis of a terrestrial origin.

Among approximately thirty serious hypotheses known to me which have been advanced during the past century in an effort to explain the perplexing origin of tektites, the Moon has had a fair share of supporters, just as have the stars, the Sun, Earth lightning, volcanoes, comets, lost planets, lost Earth satellites, and unknown prehistoric races remarkably advanced in glass technology. In view of this, it seems appropriate to mention the early advocates of a lunar origin. In 1897 Verbeek[15] suggested that volcanic eruptions on the Moon were a possible source of tektites. An alternative mechanism was suggested in 1940 by Nininger[16], who regarded meteorite impact on the Moon as a probable mechanism for dislodging lunar rock with sufficient velocity to escape the Moon and land on Earth.

Neither lunar volcanic activity nor meteoritic impact on the Moon can be ruled out to-day as being unrelated to tektites. For decades the Moon has been generally regarded as a dead celestial body without remnants of any volcanic activity it may have had in the past. This view has been drastically shaken recently by Kozyrev[17], who obtained spectroscopic evidence of gas escaping from Alphonsus crater in 1958, and of a 1200–1500° K. surface temperature temporarily existing in the same crater in 1959. Inasmuch as lava can bring up material which is lighter and also richer in radioactive elements than the average lunar composition, this provides a simple explanation of why the density of tektites (2·3–2·5) is significantly lower than the Moon's average (3·3), and also why tektites, just like Earth eruptive rocks, are relatively more rich in uranium and thorium than are meteorites. Thus, lunar volcanism may enter the tektite picture, at least indirectly. At the same time, the recent experiments of Charters and Summers on hypervelocity impact in stone[14] have indicated a ratio of backsplash velocity to impact velocity (about 0·3) which leaves no doubt that it is possible for meteorites coming from the asteroidal belt to eject debris beyond the Moon's gravitational field. Present knowledge is too primitive to warrant complacency as to how lunar material may have arrived on Earth.

In summary, the new results from the discipline of re-entry aerodynamics assign a cosmic origin to tektites, and point firmly at the Moon as somehow being involved in the act of hurling tektites to the Earth.

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MEASUREMENTS OF CÆSIUM-137 IN HUMAN BEINGS DURING 1958-59

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EVER since the first reports in 1956[1] that cæsium-137, a fission product from nuclear bomb explosions, was present in human beings, there has been considerable interest in estimating the contribution which this material makes to man's radiation dose. In view of this we have, since January 1958, attempted to measure the amount of cæsium-137 in all persons who have been referred to us for a measurement of their body radioactivity. By far the largest group of these people were women who had worked in the radium-luminizing industry and had ceased working at the end of the Second World War. There is no reason for suspecting therefore that any of them had been in contact with cæsium-137 other than that from nuclear bomb fall-out. They came from a wide area around London, the majority living within 50 miles of the City, although some came from so far afield as Leicester, Swansea and Folkestone. We are now reporting the results of our measurements up to the end of 1959 on 203 of these luminizers, 182 females and 21 males. Besides measuring their radium and cæsium contents we have also estimated their body potassium from a measurement of its naturally occurring isotope, potassium-40. In addition, we have estimated the mean dose of radiation received by these people as a result of the cæsium-137 in their bodies. For comparison, we are including the results of cæsium-137 measurements and calculations of dose for the same period on 16 members of the staff of the Radiological Protection Service.

The amounts of all three materials were estimated by measuring their gamma-ray activities. This was

done in a low-background laboratory using, as the detector, four sodium iodide (thallium activated) crystals situated above the surface of the body. The crystals were optically coupled to photomultiplier tubes, the outputs of which were amplified and fed to a 100-channel pulse-height analyser.

All persons were measured for a period of 1 hr., preceded or followed by a measurement of the background with a water-filled inert model of the human body weighing 70 kgm. in place of the subject. The amounts of the radioactive materials in the people were then determined by comparing the gamma-ray spectrum from each subject with that from calibration sources. It was assumed, in accordance with the views of the International Commission on Radiological Protection[2], that cæsium-137 and potassium would be uniformly distributed throughout the whole body and that radium would be uniformly distributed in the skeleton only. For cæsium-137 or potassium, the calibration sources were polythene models of the human body filled with solutions either of cæsium-137 chloride or of potassium chloride of known concentration. We have found that the calibration so obtained varied very little with the size of the model. Calibration for radium consisted of determining the response to a point source of radium at several positions along the central axis of the model used for the background measurements. The positions used corresponded to the anatomical regions, head, thorax, pelvis, thighs, legs and arms. In order to obtain a calibration which would approximate to that from a uniform distribution of radium in the skeleton, the contribution from the source at each position was weighted according to the mass of the skeleton in each of the six regions.

Cæsium-137 and potassium-40 emit single gamma-rays of 0·66 MeV. and 1·46 MeV. respectively, and the scintillations which they generate in the crystals following photo-electric absorption produce peaks in the counting-rate spectrum obtained from the 100-channel analyser. The body burdens of cæsium-137 and potassium-40 were determined from the counting-rate in their respective photo-peaks. However, some photons from potassium-40 lose energy due to scattering in the body and in the apparatus, and then contribute to the counting-rate in the cæsium-137 photo-peak. An appropriate allowance must be made for this when estimating cæsium-137. An additional uncertainty arises when the subject also contains radium, since this element, together with its radioactive daughters, emits a series of gamma-rays with energies ranging from 0·2 MeV. to 2·4 MeV., and so contributes to the counting-rate in both the cæsium-137 and potassium-40 photo-peaks. The radium burden of the subject may be determined unambiguously from the counting-rate corresponding to photons having energies greater than that from potassium-40; in practice, an energy-band from 1·7 MeV. to 2·6 MeV. was used. It is clear, however, that where radium poisoning is suspected, even if the radium burden appears to be zero, an additional uncertainty is introduced into the measurement of cæsium-137 and potassium-40 by the error of the radium measurement. For this reason, the standard error of estimating potassium due to counting errors alone increases from 8 gm. where radium can be ignored to 13 gm. for a luminizer, and that of cæsium-137 from 1 mμc. to 2 mμc. These additional errors vary only slightly with the radium content. As the radium burden increases, however, the identification of the cæsium-137 and potassium-40 photo-peaks becomes increasingly difficult, and it was necessary to limit the cases selected to those having small radium burdens. The 203 luminizers selected all contained less than 0·02 μc. radium-B in equilibrium with radium-C, the principal gamma-emitting daughters of radium; these were about 85 per cent of the luminizers referred to us.

The principal interest in these measurements is in estimating the radiation dose from cæsium-137, and this depends on its concentration in different parts of the body. It has been suggested by Langham and Anderson[3] that since cæsium is chemically similar to potassium they might also behave the same metabolically. These authors and others[4] have therefore expressed the concentration of cæsium-137 in the body in terms of a cæsium-137/potassium ratio. From a mean value of this ratio for a group of individuals, they have calculated the mean radiation dose to the group, assuming that the average man contains about 140 gm. potassium and that the cæsium-137 is uniformly distributed throughout his body of weight 70 kgm. However, if the isotope is distributed uniformly throughout all body tissues, it is important to know the way in which cæsium-137 varies with the weight of the individual. We have therefore analysed the way in which cæsium-137 varies with body-weight and potassium in the largest group of our series of measurements, namely, the 182 female luminizers. Their average age was 41·6 yr. with a standard deviation of 8·5 yr. The youngest member of the group was 27 and the oldest 75.

In order to test any possible trend of the body-burden of cæsium-137 with time, the results for eight quarters during the period January 1958–December 1959 were analysed separately. For each quarter it was possible to fit a multiple linear regression of cæsium-137 on potassium and body-weight. This fit was compared with the linear regression of cæsium-137 on either weight alone (ignoring potassium) or on potassium alone (ignoring weight). It was found that there was a small increase of cæsium with both body-weight and body potassium. However, the correlation of cæsium-137 with potassium could be entirely accounted for by the fact that both potassium and cæsium-137 tend to increase with increasing body-weight. (The increase of potassium with increasing body-weight is well known[1]. In our group of females, the least squares fit to all 182 measured values was $K = 71 + 0{\cdot}51\ W \pm \Delta$, where K is the potassium content in gm., W is the body-weight in kgm., Δ is a random variable with zero mean and standard deviation of 15 gm. The standard error of the estimate of the slope was 0·12. Anderson[5] also finds a non-proportional increase of potassium with body-weight that is about the same as ours, but for the same body-weight the average potassium values found by him are about 15 gm. less than ours.)

In other words, an equally good fit to the data was obtained by the linear regression of cæsium-137 on weight alone. The slope of the line was actually calculated for each quarter and its variation appeared to be random. Since we would not expect it to change with time, a mean value was taken for all eight quarters. The fitted parallel lines for the separate quarters are given by:

$$Z = A + Bx \pm \varepsilon$$

where Z is the cæsium-137 content of any individual in the group in mμc.; A is the average cæsium-137

Table 1. AVERAGE CÆSIUM-137 CONTENT OF AN INDIVIDUAL OF WEIGHT 60 KGM.

		No. of people measured	A. (in mμc.)
1958	1st quarter	11	5 83
	2nd ,,	22	6 15
	3rd ,,	25	5 53
	4th ,,	36	5 80
1959	1st quarter	31	5 67
	2nd ,,	22	3 59
	3rd ,,	10	5 45
	4th ,,	25	6·46

content of an individual of weight 60 kgm. and is given in Table 1 for each quarter; B is $0 \cdot 051 \pm 0 \cdot 017$ mμc./kgm.; x is (body-weight $- 60$) in kgm. ε is a random variable with zero mean and standard; deviation of 2·24 mμc. (a large fraction of this may be attributed to the standard deviation of the counting (2 mμc.), so that the standard deviation attributable to individual variations about the mean is about 1 mμc. cæsium-137 [$\sqrt{(2 \cdot 24^2 - 2^2)}$]).

Table 1 shows that there is no obvious trend of A with time. The result for the second quarter of 1959 appears to be low. This result was not due to any change in the sensitivity of the apparatus, nor does it appear that the ages of the persons examined in this period or the localities in which they live present any unusual features. In the absence, therefore, of any explanation for the low value, a mean value of A was calculated for all eight quarters. This was found to be 5·5, so the average cæsium-137 content of an individual in the series during 1958 and 1959 is given by:

$$Z = 5 \cdot 5 + 0 \cdot 051\, x \text{ m}\mu\text{c.} \qquad (2)$$

or

$$Z = 2 \cdot 44 + 0 \cdot 051\, W \text{ m}\mu\text{c.} \qquad (3)$$

where W is the body-weight in kgm.

Although this represents only a small increase with body-weight, it is much too large to be attributed to chance. Obviously, the cæsium-137 content in different people is not proportional to their body-weight, nor to their potassium.

As yet there is no information available to indicate whether cæsium-137 is better correlated with any body parameter other than total body-weight, and we have therefore assumed that it is uniformly distributed throughout the body. Following the calculations outlined in the Recommendations of the International Commission on Radiological Protection[2], the average dose-rate to the whole body, D, for an individual of weight W kgm. and cæsium-137 content Z mμc. is given by:

$$D = 11 \frac{Z}{W} \text{ m.rems/year} \qquad (4)$$

The value of D for a female luminizer during the period in question may then be derived from equation (3):

$$D = \frac{27}{W} + 0 \cdot 56 \text{ m.rems/year}$$

The lowest weight in the 182 cases was 33 kgm. and the highest 95 kgm. The corresponding dose-rates are about 1·4 m.rems/yr. and 0·8 m.rem/yr. respectively. About half this range of body-weights would include nearly two-thirds of the 182 cases. If the radioisotope is not uniformly distributed throughout the body, some body-organs will, of course, receive a greater dose.

The number of persons measured in the other three groups, the male luminizers and the male and female staff at the Radiological Protection Service, were too small to justify an analysis of the type described above. We have, however, compared their measured cæsium-137 content with those which would be predicted by equation (3) and the mean values for each group are given in Table 2. The measured cæsium-137 content of the male luminizers during 1958 and 1959, and of the female staff at the Radiological Protection Service during 1958, were not significantly different from those predicted. However, the measured values were higher than the predicted values for the male staff at the Radiological Protection Service during 1958 and for both male and female staff during 1959. The reason for these higher values is not obvious. It is possible for members of the staff at the Radiological Protection Service to have ingested or inhaled these small additional amounts of cæsium-137 while at work, but the people found to have most cæsium-137 were not those exposed to the greatest risk. (It might be noted that the staff at the Radiological Protection Service are much younger than the luminizers; mean ages 24 against 42 for the females and 25 against 50 for the males).

The radiation dose-rate for each individual was calculated from the measured cæsium-137 content using equation (4). The mean values for each group are given in the final column of Table 2. They are very similar to those obtained for the female luminizers, and again there was no obvious change with time. This was in marked contrast to the local gamma-ray dose-rate from fission products on the ground, which changed appreciably during the same period[6].

Table 2

Subjects	No. measured	Mean cæsium-137 content (mμc.)		Mean dose-rate (m.rems/yr.)
		Measured	Predicted	
		1958		
Male luminizers	6	6 8±1·2	5 8±0 3	1 2±0·2
Male R.P.S. staff	10	9 4±0 8	6·0±0 1	1 5±0 1
Female R.P S. staff	5	5 6±0 4	5·5±0 2	1 0±0·1
		1959		
Male luminizers	15	5 8±0·8	6 1±0 1	0·8±0 1
Male R.P.S. staff	6	10 0±1 8	6 1±0 3	1·5±0 3
Female R.P.S. staff	4	7 2±0 4	5·3±0·1	1·4±0·1

In 1958 and 1959, therefore, the mean annual dose received by the adults measured, due to cæsium-137 in the body from nuclear test explosions, was less than 2 per cent of that from natural sources, which is about 100 m.rems/yr. (ref. 7). It was also small compared with, for example, the difference of about 20 m.rems/yr. between the doses received from the natural background by persons in Leeds[8] and Belmont[9].

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THE EPIDERMAL CELL AND THE METAMORPHOSIS OF INSECTS*

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THE visible form of the insect is defined by the outer skin or cuticle; which is the product of the single layer of epidermal cells lying beneath it. The form of the insect is thus determined by the growth changes and the secretory activity of the epidermal cell. My purpose is to approach the subject of metamorphosis through a consideration of the physiology of the epidermal cell.

The epidermal cell is interesting because it combines within itself so many functions, actual and potential—social functions as a member of the community of cells of which it forms a part, and individual functions where it is concerned primarily with its own affairs. The cell that is used to illustrate this theme is the ordinary epidermal cell of the abdominal wall in the blood-sucking bug *Rhodnius prolixus*. In its resting state this cell is flattened and attenuated. But if a wound is made in the integument, the dormant epidermal cells are stimulated to activity. The injured cells die, and their autolytic products diffuse out and 'activate' the surrounding cells; their cytoplasm increases and so does its ribonucleic acid content; mitochondria become swollen and more numerous. These activated cells migrate by amœboid movement to the wound, leaving a peripheral zone of sparse cells among which active mitosis follows and restores the normal cell density.

The response of the epidermal cells to lack of oxygen is quite different. They normally are furnished with oxygen by a rich supply of tracheoles. If the trachea to an area of the epidermis is cut, the epidermal cells restore the supply by sending out elongated filaments which attach themselves to the air-filled tracheoles of a neighbouring area and pull these towards them. These filaments may be 100–150μ long; they are clearly contractile structures which are re-absorbed into the cell when their task is done. By this means tracheoles may be brought in from distances up to 750μ.

The chief function of the epidermal cell is the provision for growth; that is, the secretion of a new and larger cuticle and the moulting of the old cuticle. The growth process in *Rhodnius* is initiated by the meal of blood. This distends the abdomen and sends a nervous stimulus to the brain which causes the neurosecretory cells to discharge their hormone. This activates the thoracic gland and causes it in turn to secrete the growth and moulting hormone (ecdyson).

The effects of the moulting hormone resemble those which follow injury. The cells are 'activated' within a few hours. By four days, cell division has begun, and by seven or eight days the epidermis forms a regular columnar epithelium ready to begin the deposition of the new cuticle. This is a complex process involving the secretion and subsequent expansion of the lipoprotein layer (cuticulin), and deposition of the inner layers of chitin and protein During this most active phase, the epidermal cell has an elaborate cytological structure; it contains granules of a pterin pigment, great amounts of ribonucleic acid, abundant filamentous mitochondria, innumerable double membranes of endoplasmic reticulum, glycogen and various demonstrable enzymes.

When the new cuticle is nearing completion, the epidermal cells produce and discharge the enzymes protease and chitinase, which digest the inner layers of the old cuticle and absorb the products of digestion through the substance of the new cuticle. Then they secrete a mixture of protein and phenolic substances which impregnate the cuticle and form a film over the surface. They then secrete wax which crystallizes over the surface to form a waterproof film. Finally, when the residue of the old skin is shed, they secrete the phenoloxidase which oxidizes the phenolic substances to the quinones that tan and harden the cuticle, and the tyrosinase which forms the melanin pigment of the blackened regions.

Thus the epidermal cell is a functional cell with an amazing range of chemical and physiological activities. But at the same time it is an embryonic cell which retains a large capacity for differentiation.

During each moulting stage the ordinary epidermal cell may retain its ordinary form or it may differentiate to produce (i) a pair of œnocytes, perhaps responsible for lipoprotein synthesis; (ii) a dermal gland made up of four cells which contributes a layer of 'cement' to protect the waterproofing wax; (iii) a small sense organ or sensillum made up of four cells one of which is a primary sense cell that gives rise to an axon growing inwards and ultimately finding its way to the central nervous system.

It may be that this differentiation among the epidermal cells is controlled by gradients of some chemical inductor substance; and there is evidence for the existence of some kind of 'cytoskeleton' within the epidermal cell which determines its polarity in the general integument.

Apart from this differentiation which can be observed during post-embryonic life, the epidermis has already become differentiated during embryonic development into the pattern which forms the basis of the body-form. When the epidermal cells migrate and multiply during the repair of an injury, they carry with them the potentiality to form their specific component of the body pattern—such as black pigment spots or intersegmental membrane. At the next moult, when the new cuticle is laid down, there is found to be a corresponding displacement of the pattern.

Now the pattern of the abdomen in the adult *Rhodnius* is very different from that of the larval stages; and if injuries of this kind are inflicted in the larva, there are quite different changes produced in the pattern of the adult. These results serve to emphasize that the adult pattern is already latent within the larval cells; and that when these cells divide, the capacity to form particular elements in this adult pattern is transmitted to the daughter cells. But these properties remain latent and unrealized until metamorphosis occurs.

Metamorphosis is controlled by hormones. Throughout the larval stages the corpus allatum, a

* Substance of a Royal Society Tercentenary Lecture delivered on July 23.

small gland immediately behind the brain, secretes the so-called 'juvenile hormone' or 'neotenin'. In the presence of this hormone, the epidermal cells all lay down cuticle of larval type. Their capacity for forming adult cuticle remains latent. But if growth and moulting take place in the absence of the juvenile hormone, the latent adult characters are realized, and adult cuticle is laid down. That is what happens in the last stage of *Rhodnius* when metamorphosis occurs.

As can be proved by implantation of the corpus allatum or by the application of active extracts of the juvenile hormone to the surface of the insect, the hormone acts directly on the epidermal cell, producing localized patches of larval cuticle. Under experimental conditions, the adult *Rhodnius* can be induced to moult again; and if the cells are exposed to the juvenile hormone they will lay down cuticle showing a partial return to larval characters—a partial reversal of metamorphosis.

Thus the epidermal cell has an extensive latent capacity for differentiation. It can differentiate to give rise to one or other of the various elements which make up the spatial pattern of the integument: hairs, pigment spots, intersegmental membrane and so forth; and the same cell can produce this element in cuticle of larval type or of adult type.

The different elements in the pattern may perhaps be produced by differences in the concentration gradient of one or more chemical substances. That certainly seems to be true of the differentiation between larva and adult. Intermediate forms can be produced by intermediate amounts of juvenile hormone. In insects which have a pupal stage, there is evidence that the larva is produced in the presence of a large amount of juvenile hormone; the pupal form arises when only a very small amount of juvenile hormone is present, and the adult appears in the absence of juvenile hormone.

The larva, pupa and adult are three forms in a polymorphic animal the manifestation of which is controlled by the timing and amount of juvenile hormone secretion. According to this way of looking at things, metamorphosis, polymorphism, and the differentiation of the various parts of the body are closely analogous phenomena, each of which can be described in terms of the controlled realization of genetic potentialities in the epidermal cell.

LEADERSHIP IN RURAL SOCIETIES

ON Friday, September 2, the Geographical and Anthropological Sections of the British Association for the Advancement of Science held a joint symposium at Cardiff on "Leadership in Rural Societies", under the chairmanship of Lord Rennell of Rodd. The organizers of the symposium had arranged for four opening speakers drawn from England, Scotland, Ireland and Wales, respectively, hoping in this way to obtain as complete a coverage as was possible of the general conditions in the British Isles at present. The opening speakers dealing with sample studies drawn from England and Scotland were lecturers in geography, while those who dealt with Irish and Welsh conditions were university teachers specializing in social anthropology.

Two matters were at once apparent. The four opening speakers were concerned with the rapid decline of native leadership in face of the ever-increasing centralization of authority and control in present-day society in Britain. Leadership in rural societies was becoming leadership from without, more particularly at the hands of agricultural advisers. Secondly, the geographers were obviously reading papers in social anthropology and not in geography. Although this was inevitable in view of the topic under discussion, it did, nevertheless, prevent the symposium being in any sense a joint discussion. Professional geographers in the audience felt that in the very nature of the case they had little to contribute.

The opening speaker (or, more accurately, speakers, as Mr. H. A. Moisley read a paper on "Leadership and Innovation in the Crofting Communities of the Outer Hebrides" of which he was the joint author with Mr. J. B. Caird) had a considerable advantage. The crofting communities of the Outer Hebrides represent on one hand a remote rural society on the very fringes of centralized control, yet, on the other hand, before the days of agricultural advisers, management under such a system of partly co-operative farming tended to be primitive, no one wishing to take the onus of introducing changes and few, if any, of the shareholders had sufficient knowledge to know what changes were desirable and what was feasible. So long ago as 1919 an agricultural adviser was appointed for Lewis and resident advisers were appointed for South and North Uist in 1941 and 1954. The advisers are members of the staff of the North of Scotland Agricultural College, and this alone gives them a status which they would not have if they were regarded merely as government officials. Moreover, being permanently resident, they have become accepted as members of the community. The constant presence of such a source of advice is a very real re-assurance to the crofters embarking on some new scheme. In this way the agricultural advisers have taken over the functions of leadership and innovation in agriculture which have long been defunct. It was pointed out that in the Hebrides this natural reluctance to adopt innovations applies not only to agriculture but also to industrial and commercial pursuits. This is particularly the case with the fishing industry. The Harris tweed industry, however, provides the outstanding and perhaps the best-known example of initiative and enterprise; but, nevertheless, mainland interests may yet swallow up the one native industry which has really flourished in the Hebrides. The lack of natural leadership in these islands can, therefore, be attributed to inhibitions due to inherent conservatism, the patriarchal influence and the tradition of equal shares. Until some means can be devised to diversify the size of agricultural units, the emergence of local natural leaders is unlikely.

No other opening speaker had such a remote and isolated society to describe, but Mr. Dafydd Jenkins's study of South Cardiganshire revealed several interesting features. He described the changes in leadership that had taken place within living memory. This Welsh community, like that of the Outer Hebrides, was basically a society organized for the

working of the land. It differed, however, from the Scottish example in that some sixty years ago social stratification was more pronounced than it is to-day. At this time the local gentry were definitely the leaders. It was they who set the standards for emulation and were the innovators of changes in agriculture. This would appear to confirm what Mr. Moisley had said about Hebridean society, namely, that diversification in social structure and in size of land-holding facilitates natural leadership. The contrast between the Anglicized, church-going squires and the Welsh-speaking, Nonconformist peasantry in Wales at the turn of this century was great indeed, and leadership in many matters fell to the squires. Two World Wars and the coming of the Welfare State eclipsed the squires, and Mr. Jenkins showed that those who took their place in South Cardiganshire were not necessarily the agricultural advisers but individuals who for some reason or other did not conform to the conventions of the existing society. For example, a man who was not a member of any chapel and went to the South of France for his holidays might be the first farmer to introduce a tractor or a combined harvester on his farm. Similarly, a farmer who was known to be in debt and had quarrelled with his minister and never appeared in chapel or frequented the local public house was likely to be the first to introduce electrical fencing on his farm. Other farmers later would follow suit. It was clear that in this society there was a sharp distinction between 'bobl y capel' (the chapel people) and 'bobl y byd' (the people of the world). Leadership and innovation after the eclipse of the squires came, as it were, from 'the odd man out' in the local social set-up, and he would inevitably belong to 'the people of this world' rather than to 'bobl y capel'.

The importance of the religious factor in social leadership was stressed also by Miss R. L. Harris, whose contribution to the discussion dealt with leadership in a border community in Northern Ireland. She emphasized the distinction between formal and informal leadership and stressed that the local clergyman was unquestionably the most important formal leader in this society. Members of the community were very reluctant to assume the role of overt leader. Miss Harris paid special attention to the relationships between the local people and such leaders. The local people tended to judge the overt leader on his or her ability to meet outsiders on equal terms, and it was only natural that Irish people would keep a very close watch on overt leaders from outside the community.

The fourth speaker, Mr. M. Kirk, whose study concerned villages in Yorkshire and Devonshire, made the audience feel the force of the impact of urban civilization on rural life in modern times to a much greater extent than any of the other speakers were able to do. One felt that Mr. Kirk's studies of these English rural communities had the advantage of emphasizing how important are the urbanizing and centralizing forces in modern English life. His title told the whole story—"The Suburban Community in the Countryside". He showed how a large number of English villages were no longer traditionally rural, because so many of their inhabitants included those who had chosen to live in the country, but derived their economic and social status from an urban setting. Village life, in consequence, has decayed. Very often the nominal leader (for example, the elected representative of the community on the rural district council) would be a retired city businessman who had come to live in the village. On the other hand, the native villagers complain that there are not enough men to form a football team, or enough women to run a successful dance. The village is clearly not what it was—in fact, according to Mr. Kirk it has ceased to exist, although its population is actually increasing. Under these conditions local leadership is at a low ebb, while initiative and innovation tend to pass to the central administration functioning through the national ministries.

The general discussion that followed the opening papers may be said to have been disappointing. There are several reasons for this. In the first place, the opening papers were specialized and presented by experts who had the advantage of considerable experience in the field. It is difficult to discuss factual data presented in this way. Furthermore, the four papers were so diverse in character that they did not lend themselves to the formulation of general conclusions, while, in addition, there was the point concerning the geographers already mentioned. One of the speakers in the open forum stressed the importance of university extension classes in rural areas in the training of leaders, while another underlined the fact, already apparent, that as centralized controls increase, local leaders decrease.

E. G. BOWEN

PESTS OF STANDING CROPS

SECTION D (Zoology) of the British Association, during the recent meeting at Cardiff, arranged a morning session under this title since the problems raised in the attempts to understand animal population dynamics are not only interesting in themselves, but also have important applications to studies of crop pests, and some of the basic ideas are relevant to human population studies. At the plenary session of the Association on "World Food and Population", Sir Charles Darwin expressed a point of view close to that of many zoologists, but he spoke for less than five minutes. So it was fortunate that Section D had the opportunity for its own discussion, during the following morning, under the chairmanship of Mr. H. R. Hewer.

Prof. G. C. Varley, of Oxford, sought to relate the contribution of zoologists to problems of human food supply and human population. The symposium of the previous day showed the extent to which men of science are still working as if in watertight compartments. Their work is unco-ordinated, and in human affairs its impact is in opposing directions. Advances in medicine have enormously reduced human suffering and (to our satisfaction as individuals) increased our expectation of life. The reduction of mortality from disease and the increased fertility which accompanies good health have, however, increased the rate of population growth in many parts of the world.

Agricultural experts tend to accept as inevitable

a great rise in human population, and rightly claim that if given the means they can provide the extra food required—for the next forty years at least. Is it not time now to take a long view and to consider how the world population is to be stabilized? Present work is tending to make the eventual solution more difficult. If gerontologists find an easy way to prolong human life far beyond the normal span, the resultant change in the age structure of the population and its rapid increase in size might in fact precipitate a great disaster for the human race.

Many zoologists find ideas like those of Malthus still helpful in studies of animal populations. His prediction late in the eighteenth century that "misery and vice" would result if the population of the British Isles rose much further seemed so convincing that plans for a regular census of the population were made. Now, when the population has risen more than fourfold and the standard of living has also improved, how wrong poor Malthus appears! But was not his error simply his failure to foresee the industrial revolution, with its railways, road transport and steamships to bring food to these islands?

Forty years ago, Pearl fitted sigmoid logistic curves to human populations and extrapolated these to find steady limiting values. We shall not know for another century how right he was, but similar logistic curves describe very well the growth of populations of some insects, such as flour beetles, given a regular energy supply in the form of food. The population limit is reached when the birth-rate equals the death-rate; as crowding increases, the death-rate rises and the birth-rate falls. Whether the differences in human birth-rate between urban and country districts are a similar phenomenon is debatable.

The more complex problems of animal populations of two or more species living together are by no means fully understood. Consideration of the energy-flow in such systems helps in understanding them. Solar energy (about 0·1 per cent of it) is made available as human food by crop plants. Insect pests compete for this energy, and themselves serve as an energy source to their predators and parasites, which may be eaten by other animals. The fraction of available energy lost at each stage of conversion is very high. To support the greatest human population, pests must be kept down in numbers. Sir Alexander Fleck suggested that chemists have provided the method to do this and indeed they can give great help; but it must be emphasized that the problems raised are biological problems of some complexity. Animal populations in the wild and laboratory populations under constant conditions both can show violent fluctuations in numbers, the interpretation of which is still a subject for controversy. Although as yet insufficiently tested, mathematical models are available which can explain population-cycles, and some models can explain in principle why insecticides reduce the average population-levels of some pests but increase the population-levels of certain others.

Mr. D. W. Wright, of the National Vegetable Research Station, Wellesbourne, described his work on the cabbage root fly, the maggots of which feed on the plant's root system. The cabbage then suffers from water- and mineral-deficiency and is stunted or killed. Commonly about a third of the yield is lost, but this can be prevented by the careful application of suitable insecticides to the roots. However, where insecticides like DDT are used broadcast, or applied with plant fertilizers, very severe pest damage may result. This is because a high proportion of root fly eggs, clustered around the cabbage stem, are normally eaten by predatory ground beetles of the genus *Bembidion*, and low concentrations of insecticide affect these wandering predators far more than the relatively immobile maggots. Field experiments designed either to eliminate the beetles, or to concentrate them within certain areas, have shown conclusively the important role these beetles normally take in limiting the severity of damage by the cabbage root fly.

Dr. G. H. L. Dicker and Mr. R. C. Muir, of East Malling Research Station, considered some fruit pest problems. Toxic chemicals are widely used in commercial orchards and the obstacle to success is usually lack of knowledge of the biology of the pests and their natural enemies, and of the behaviour of the chemicals in the field, rather than a shortage of suitable chemicals. Regular applications of insecticides in early spring have virtually eliminated some pests like the once troublesome apple blossom weevil. Codling moth presents much greater problems. This moth lays its eggs on the young fruits of apple over a period of eight weeks or more. Very soon after hatching, the young caterpillars enter the fruits, where they can no longer be reached by insecticides. Whereas DDT suitably applied can remain sufficiently toxic over the long period of caterpillar hatching and will kill most of the larvæ before they enter a fruit, trees so treated commonly suffer severe damage from red spider mite, the predators of which are killed by DDT. The use of a further chemical spray to kill the mites was formerly effective, but the mite has now evolved resistance to a wide variety of chemicals. Special spray schedules designed to interfere as little as possible with predators of the mites are at present under investigation both in Kent and in Nova Scotia, and the results are promising.

The basis of plant resistance to insect attack remains poorly understood, but an apple rootstock resistant to woolly aphis is now available; this project took thirty years from its inception to eventual release on a commercial scale. Even so, success may only be temporary: a raspberry variety supposedly resistant to raspberry aphid was found susceptible to attack by a previously untested strain of the aphid.

A paper by Dr. R. F. Morris and Dr. C. A. Miller, of the Forest Biology Laboratory, Fredericton, N.B., Canada, on the population dynamics of some native and introduced forest insects in the Atlantic Provinces of Canada summarized long-term population changes and went a considerable way to suggest causes for them. Many of the native pests of the extensive spruce and balsam fir forests seem to have small population peaks every five to eight years, but never become common enough to cause visible damage to the trees. In contrast, the black-headed budworm has maxima on the average every seven years, and in the late 'twenties and again in the late 'forties trees were defoliated; but the population-level diminished again without the trees being killed. A study of the changes in the numbers of the hymenopterous parasites of the budworm suggests that this is an example of Nicholsonian host-parasite population oscillations. The cycles in widely separated populations in eastern Canada seem to be in phase, which suggests that some common extrinsic factor such as weather has an

effect on the periodicity. Cycles of abundance of the fall webworm can be traced from historical records so far back as 1770. The interval between outbreaks is between nine and thirteen years. In Nova Scotia the population peaks are high enough to defoliate trees whereas in New Brunswick the maxima are never so high; this curious difference in status could provide a lead to new methods of control and it is being investigated.

The spruce budworm is the major native pest of the spruce and balsam fir forests. At intervals of some forty years it has killed the trees over hundreds of square miles. The numerous species of parasites and predators which attack the spruce budworm when its numbers are low seem unable to increase quickly when the budworm outbreaks begin, and indeed seem to shun defoliated areas of the forest. The most recent outbreak began in the middle 'forties and, at its height, to save the trees more than 200 aircraft were used to spray insecticide over some 5 million acres of forest.

The introduced European spruce sawfly caused serious damage to the trees in the 'twenties. Various parasites were then imported and liberated, and some became established. For the past twenty years, these and a virus disease which was apparently introduced accidentally have kept the species below a level at which damage is significant. Time will show whether current projects for the biological control of the introduced winter moth, larch case bearer and balsam woolly aphid will eventually be successful. Only a very few years ago, biological control was regarded as possible only on oceanic islands or perhaps as an exception in California!

These papers are representative of the sort of long-term work which is now being undertaken in agricultural and forest entomology. There is clearly a great need for more applied research, but this will be easier to plan when there is more basic knowledge of the behaviour of pests and their predators and parasites, especially in relation to changes in their food supplies and population densities. G. C. VARLEY

GULIELMA LISTER CENTENARY

MISS GULIELMA LISTER, born on October 28, 1860, at 871 High Road, Leytonstone, Essex, where she died on May 18, 1949 (ref. 1), was one of those distinguished amateur naturalists of professional competence who have done so much to advance and deepen biological knowledge. She came of an intellectual Quaker stock—her father, Arthur Lister, F.R.S. (1830–1908), was a son of J. J. Lister, F.R.S. (1786–1869), and a brother of Lord Lister (1827–1912), the surgeon—and apart from a year at Bedford College she was educated at home. The course of her long life showed her to be able and industrious, economical and generous, a painstaking and accurate observer, and artistic, while her attractive personality gained her many friends. Her interests in natural history were exceptionally wide, and her detailed field knowledge of both the fauna and the flora must frequently have embarrassed specialists. Miss Lister was for many years an active member of the Essex Field Club, towards which she maintained a special affection, the Nature Study Union, and the Linnean Society, and she was twice president of the British Mycological Society. She had many calls on her artistic ability, and made notable minor contributions to botanical art in such works as her cousin F. J. Hanbury's "Illustrated Monograph of the British Hieracia" (1889–98), with its beautiful hand-coloured plates, and in addition did more utilitarian illustrations for Dallimore and Jackson's "Handbook of the Coniferae" (1923), and other publications.

Miss Lister and her father will for long be best remembered as world authorities on the Myxomycetes or Mycetozoa, an interesting, distinctive, and compact group of organisms which, as its names imply, has been approached by botanists and zoologists with a certain ambivalence. The slime moulds, now generally accepted as a fungal group, are æsthetically attractive and are of world-wide distribution. Their classification is based mainly on their macroscopic and gross microscopic characters, and as they make excellent herbarium specimens they have been widely collected and preserved so that ample material is available for their study. It is to the Listers that much credit must be given for the reasonable chance of success that now attends the attempted identification of a myxomycete from any part of the world.

Arthur Lister, like his father, a wine merchant, had life-long interests in natural history and first turned his attention to Myxomycetes in 1887, his fifty-seventh year. After a hesitant start, he applied himself to the group with vigour, and accompanied by his daughter (as amanuensis and artist, though no mean draughtsman himself) he worked over the collections of Myxomycetes at the British Museum, the Royal Botanic Gardens, Kew, and the Paris Natural History Museum, as well as de Bary's collections at the University of Strasbourg, and as a result the first edition of his "Monograph of the Mycetozoa" appeared in 1894 under the imprint of the British Museum (Natural History). After the death of her father, Miss Lister continued to study Myxomycetes for another forty years. She was responsible for the second edition of the "Monograph" (1911) and for the enlarged third edition (1925) (now unfortunately out of print and much sought after), which were lavishly illustrated in colour due to Miss Lister's generosity.

The "Monograph" is firmly based on specimens, many of which are in the British Museum (Natural History), and its background is well documented not only by the published papers of the Listers themselves and their correspondents but also in a series of seventy-four manuscript note-books (now in the possession of the British Mycological Society[2]) extending over a continuous period of sixty years, which give a fascinating picture of the day-to-day progress of the investigation, the routine of which went on uninterrupted whether at home in Leytonstone or at the Listers' seaside house at Lyme Regis. The method of notekeeping was simple. Strongly bound, thick, school exercise books of lined paper were used, and notes were entered chronologically. Entries were made giving details of collections examined, the gist of letters received and of the replies, the notes frequently being accompanied by elaborate and often highly artistic water-colour drawings—

executed directly on the lined paper, drawing paper being reserved for illustrations intended for publication. Reprints, original letters, photographs of correspondents and other matter were also loosely inserted. Separate books were devoted to material from special collections such as the Paris Museum or from important correspondents such as T. Petch (when in Ceylon). Each book when completed was indexed, and a general index to the whole series and a letter register were maintained in a folio ledger. Thus they kept their many records under continual review and easily accessible.

It was this interest in Myxomycetes which led to the long association of the Listers with the British Museum (Natural History), which Miss Lister first visited with her father around 1890 when, as mentioned above, she was helping him prepare his "Monograph". She continued her connexion with the Museum until 1939, being virtually honorary curator in charge of the Mycetozoan collection, which she helped to make the most complete and valuable in the world. With the outbreak of war, at the age of seventy-nine, the exigencies of travel made the journey from Leytonstone to South Kensington no longer possible for her.

Those of us old enough to have worked in the Botany Department of the Museum before the Second World War remember both her and her very dear friend, Miss Annie Lorraine Smith, the great lichenologist, for their ready interest, kindness and patience in helping and teaching younger workers.

Many of the Listers' specimens were deposited in the British Museum (Natural History) during their lifetime. Miss Lister bequeathed her mycological library and her Myxomycete notebooks to the British Mycological Society and her personal collection of slides and specimens to Mr. H. J. Howard of Norwich, another amateur myxomycetologist. On his death in 1957 this material was divided between the British Museum (Natural History) and the Royal Botanic Gardens, Kew.

The Linnean Society of London and the British Mycological Society arranged a meeting, held on October 28 at the British Museum, to commemorate the centenary of Miss Lister's birth and her long association with the two Societies and the Museum.

G. C. AINSWORTH
FRANCES L. BALFOUR-BROWNE

[1] Ramsbottom, J., *Nature*, **164**, 94 (1949).
[2] Ainsworth, G. C., *Trans. Brit. Mycol. Soc.*, **35**, 188 (1952).

OBITUARIES

Sir George Stapledon, C.B.E., F.R.S.

SIR GEORGE STAPLEDON, who died on September 16, was world renowned as the first director of the Welsh Plant Breeding Station at Aberystwyth; he was indeed its inspiration and the architect of its work during its formative years from 1919 up to the late 1930's.

Reginald George Stapledon was a kindly man and one whose prime interest was the human both as an individual and as part of a community. He was born in 1882, was educated at the United Services College, Westward Ho!, in North Devon, and Emmanuel College, Cambridge, where he read biology under Prof. A. C. Seward. For a period after leaving Cambridge he joined the family shipping concern, but soon returned to Cambridge, where he gained the University diploma in agriculture. In 1910 he became professor of agricultural botany at the Royal Agricultural College, Cirencester, and in 1912 went to Aberystwyth as agricultural botanist. After the outbreak of the First World War he joined the Ministry of Agriculture's Food Production Department in London. At the end of hostilities he became the first director of the newly formed Official Seed Testing Station, Cambridge, but in the summer of 1919 accepted the invitation to establish and to direct the Welsh Plant Breeding Station which was to be set up in Aberystwyth as a result of the monies given for the purpose to the University College of Wales by Sir Laurence Philipps, Bart. (now Lord Milford). Stapledon remained at Aberystwyth until the outbreak of the Second World War, when the Minister of Agriculture invited him to establish the Grassland Improvement Station at Stratford-on-Avon and to become its director. On his retirement in 1945 he joined Dunns Farm Seeds, Ltd., as scientific adviser and was soon invited to join the board of directors, a post he held until his death.

It was as director of the Welsh Plant Breeding Station that Stapledon would wish to be remembered. To him this very rightly represented the central core of his professional work. His influence, however, went far beyond Wales—indeed, it is world-wide. His was a genial personality; he was a man who worked hard and never spared himself if there was a job to do. He had the capacity also to instil into others those same personal qualities for hard work done willingly, loyally and with affection towards the leader. Stapledon was a man of ideas and of great ideals. He will be renowned in history as one of the great, and among grasslanders, as the greatest of them all. He was a notable figure in any gathering, particularly where the conversation and discussion found his interest and were to his liking.

His personal work at Aberystwyth (he himself was the cocksfoot breeder) resulted in the creation of new varieties of herbage plants, and in all essentials the types then selected are still embodied in the 'S.' varieties which are to-day widely used in Britain and in many countries overseas. It was Stapledon's creative mind which outlined the need for the study of pasture plants and to apply existing genetical and agronomic knowledge to this end. He went further, however, and insisted that there should be built up a mass of new knowledge, much of which by now has become embodied in the new science of grassland.

Stapledon was at heart a farmer. His sympathies were with the farmer and with the land. He was at once scientist, artist and humanist, a combination which was bound to culminate in an enthusiasm for applying his science—and indeed all his other talents—and bringing them to bear upon the day-to-day problems of the grassland farmer.

Early in his professional career he recognized that in grass we have a crop, the potential contribution of which to material welfare was not appreciated by the agricultural community itself, let alone by the

nation at large. This concept fired his enthusiasm, with the result that he led the British nation to plough up their derelict pastures and replace them with high-yielding leys. This process still goes on throughout Britain, which at the present time is universally acknowledged as the leader of ley farming techniques among the countries of the world.

WILLIAM DAVIES

Dr. D. Chatterjee

DR. DEBABRATA CHATTERJEE, superintendent of the Indian Botanic Garden, Sibpur, Calcutta, was shot dead at point-blank range on September 24 by one of his subordinates, who, having committed this utterly wanton and senseless crime, turned the gun on himself and successfully brought his own life to an end. It appears that the assassin aspired to a post in the Botanical Survey of India, and although he did not possess the necessary qualifications he fancied that Dr. Chatterjee was not active enough in furthering his claims. Homicidal mania, inflamed by an insane sense of injustice and frustration, was responsible for the death of one of India's leading botanists at the early age of fifty.

Dr. Chatterjee received his early botanical training at the Presidency College, Calcutta, obtaining his M.Sc. in botany in 1937. From Calcutta he proceeded to the University of Edinburgh, where he worked for two years under the late Sir William Wright Smith. He obtained the Ph.D. degree for a thesis dealing with endemism of Indian plants. On his return to India he worked for a time in the herbarium at Sibpur and then went to Burma as a lecturer in botany at Mandalay College. He escaped to India when the Japanese invaded Burma in 1942 and lectured at the Cotton College, Gauhati, Assam, for four years. He became botanist for India at the Royal Botanic Gardens, Kew, in 1946, and in 1949 was appointed to the post of systematic botanist at the Indian Agricultural Research Institute, which he held for six years. He succeeded Dr. K. Biswas in 1955 as superintendent of the Indian Botanic Garden.

Dr. Chatterjee's botanical interest lay mainly in the taxonomy of Indian and Burmese plants, and he published papers in a number of journals including the *Kew Bulletin*, *Hooker's Icones*, *Nature* and several others. Since leaving Kew he had never really had the opportunity of developing his undoubted taxonomic ability. For part of the time he had to work without an adequate herbarium or library, while during the past few years he had been overwhelmed with the numerous details inherent in the administration of the Botanic Garden. Even so, his loss will be severely felt in India, where there is a conspicuous shortage of competent taxonomists.

At Kew he will be remembered as a congenial colleague who did valuable work for India during the period he worked there.

He is survived by his aged parents and by his only daughter, to whom our sympathy is due. His wife died some years ago.

N. L. BOR

NEWS and VIEWS

Nobel Prize for Medicine

THE Nobel Prize for Medicine, amounting to about £15,000, has been awarded jointly to Sir Macfarlane Burnet, director of the Walter and Eliza Hall Institute for Medical Research and professor of experimental medicine in the University of Melbourne, and Prof. P. B. Medawar, Jodrell professor of zoology and comparative anatomy in University College, London. Both recipients are well known for their work on acquired immunological tolerance, which has initiated a new era in experimental biology and medicine. (See p. 376 of this issue.)

A.R.C. Institute of Animal Physiology, Babraham: Dr. R. Keynes, F.R.S.

A NUMBER of new appointments to senior posts at the Agricultural Research Council's Institute of Animal Physiology at Babraham, near Cambridge, has recently been made.

Dr. Richard Keynes has been appointed head of the Physiology Department. He succeeds Dr. I. de Burgh Daly who was head of this Department as well as being director of the Institute. Dr. Keynes's scientific work has mostly been done in Cambridge, but, during the War, he worked for five years with the Navy on asdic and radar. His best-known researches are concerned with the movement of ions in nerve and muscle and the origin of the discharge in electric fish. He measured the quantities of radioactive sodium and potassium which cross the surface membrane of a single nerve fibre during the passage of an impulse. More recently he has studied the movements of these ions against concentration differences during recovery, and has become interested in the metabolism of potassium in the whole animal. He has been a member of the editorial board of the *Journal of Physiology* since 1954 and is now chairman. Dr. Catherine Hebb has become head of a Sub-Department of Chemical Physiology.

Dr. T. Gillman

DR. THEODORE GILLMAN succeeds Sir Alan Drury as head of the Experimental Pathology Department. Sir Alan went to Babraham in 1952 and established this Department as an active centre for work on cell surfaces, immunity, and blood groups in cattle and sheep, with especial reference to genetics. Dr. Gillman graduated in the University of the Witwatersrand and became lecturer in clinical pathology. He was appointed professor of physiology in Durban in 1951, but he has not been confined by the title of his department, and has worked, not only on gastric physiology, but also on iron metabolism, malnutrition, neoplasms, and liver disease. Recently he has been interested in tissue reactions in wound healing, the ageing of arteries and the transplantation of tissues. Dr. Gillman is an energetic person; while he was in Durban he built up a large and active department from nothing, replanning the architecture and organizing courses in physiology, biochemistry and pharmacology, and wrote many scientific papers.

Dr. G. D. Greville

DR. G. D. GREVILLE has become head of the Biochemistry Department in succession to Sir Rudolph Peters, who went to Babraham in 1954 and built up a distinguished staff of biochemists. Dr. Greville graduated in Cambridge and then worked during 1932–37 at the Middlesex Hospital in London. He was biochemist to Runwell Hospital for seven years, and returned to the Biochemical Department in Cambridge in 1944. He has worked in many fields, including glucose tolerance, carbohydrate chemistry, blood coagulation and mental disorder, but his main interest has been in tissue metabolism. He was responsible for an early demonstration of the uncoupling effect of nitrophenols and has studied the effects of various metabolic ions. Recently he has published an interesting series of papers on the metabolic changes associated with the swelling of mitochondria.

Dr. Marthe Vogt, F.R.S.

DR. MARTHE VOGT has become head of a new Pharmacology Unit at Babraham. Her early work was done in Berlin under her famous father, Dr. Oskar Vogt, and Profs. Neuberg and Trendelenberg. She came to Britain in 1935 and showed, with Dale and Feldberg, that acetylcholine is liberated at motor nerve endings in voluntary muscle. She worked with Verney in Cambridge during 1935–39 on renal hypertension in dogs. From there she went to the laboratories of the Pharmaceutical Society in London and started work on the adrenal cortex. She showed that the output of hormones in the blood was large compared with the amounts stored in the gland and that adrenaline increased the rate of liberation. She still works on the adrenal cortex and is one of the leading authorities on the subject, but she has also done distinguished work in other fields. In 1946, she followed Gaddum to Edinburgh and became interested in adrenaline and noradrenaline. It was her work, published in 1954, which convinced the world that these catecholamines are likely to play some part in the physiology of the brain, since they have a specific distribution and are affected by such factors as the injection of drugs. This has led to a great deal of work on the biochemical mechanisms by which drugs may cause tranquillity or arousal.

The National Institute of Sciences of India: Honorary Fellows

THE following have been elected Honorary Fellows of the National Institute of Sciences of India: Prof. D. Bovet (director of therapeutic chemistry, Istituto Superiore de Sanità); Sir John Cockcroft (Master of Churchill College, Cambridge); Dr. W. Shockley (Shockley Transistor Corporation, Mount View, California); Prof. E. C. Titchmarsh (Savilian professor of geometry, Oxford).

The NATO Summer Schools Programme

THE North Atlantic Treaty Organization was created as a defensive organization, and is usually thought of only in a military context. The changing nature of the challenge to NATO countries during recent years, however, has caused NATO to widen its outlook, and in 1957 a Science Committee was established to promote scientific co-operation between NATO countries, and among the schemes adopted is the NATO Advanced Study Institutes Programme. NATO spent 100,000 dollars in 1959 and 200,000 dollars in 1960 on these 'summer schools'. Grants to individual schools varied between 3,000 and 45,000 dollars, normally being between 10,000 and 15,000 dollars. The grants are used to cover overhead expenses, to facilitate publication of the proceedings, and a considerable part is usually available to subsidize foreign visitors. In 1959 all five schools were on subjects in physics, and in 1960 nine of the fifteen schools were also in physics. Among the other schools in 1960 was a course at the Royal College of Science and Technology, Glasgow, on food science, and another at the Max-Planck-Institut fur Tierzucht und Tierernährung at Mariensee dealt with methods of improving productivity with livestock. Both these topics range widely over a number of academic disciplines, and the lecture courses were arranged to survey the whole field. Rather different in intention were the courses on crystallography at the Manchester College of Science and Technology, and on protein analysis at the Medizinische Forschungsanstalt der Max-Planck-Gesellschaft at Gottingen, both of which were highly practical in outlook. Attendance at the schools was not restricted to people from NATO countries.

Naturally, the NATO grant does not cover all costs, but it often enables the quality of the summer schools to be considerably improved by inviting foreign scientists. It is expected that 300,000 dollars will be available in 1961 for the Advanced Study Institute Programme. Courses already arranged for 1961 include the following: theoretical physics (Dr. L. W. H. Trainor) at Montreal; theoretical chemistry (Prof. C. A. Coulson) at Oxford; use of computers in engineering problems (National Laboratory of Civil Engineering, Lisbon) at Lisbon; solid state theory (Prof. W. Dekeyser) at Ghent; medical documentation (Dr. O. Nacke) at Bielefeld. Anyone interested in organizing such a course, and requiring financial assistance from NATO, should write to the Office of the Science Adviser, NATO, Place du Maréchal de Lattre de Tassigny, Paris 16e, before December 15.

Safety in Mines Research

THE annual report of the Safety in Mines Research Establishment of the Ministry of Power for 1959 contains sections devoted to explosives and blasting devices, explosion hazard, rescue apparatus, fire hazard, engineering and metallurgical research, investigation of mining incidents and examination of equipment after mine service, dust measurement and the pneumoconiosis hazard, and testing services (Pp. 66+4 plates. 4*s*. 6*d*. net. London: H.M. Stationery Office). Among the most interesting topics of the report are those concerned with firedamp roof-layers, investigation of incidents and pneumoconiosis. During the past two years problems connected with the formation and movement of firedamp roof-layers have been intensively studied and a parameter, the layering number, has been developed which will be of importance in the work of ventilating engineers. A new section, the Incidents Section, has been established within the organization to co-ordinate the work concerned with investigation of actual incidents and to provide men specially trained in scientific aspects of mine disasters, particularly actual underground explosions and fires. Although the pneumoconiosis research has followed broad lines similar to those of previous years, much interest has

been directed towards the development of a gravimetric sampler for measurement of respirable dust, and the opinion is expressed that measuring the mass concentration of respirable dust may prove more useful and convenient than the present practice of measuring particle-number concentrations. Altogether a variety of topics is covered within the sections of the report and many of these are of scientific and technological interest to a wide range of industries in addition to the mining industry.

The International Journal of Heat and Mass Transfer

THE wide application of heat and mass transfer, including almost every form of engineering, chemistry and physics, has made it inevitable that much valuable information has hitherto appeared in specialized journals which pass unnoticed by workers in other fields, who might well find use for such data. The very large number of papers now published indeed makes it impossible to examine all the journals containing such subject-matter. The addition of a new monthly journal, published by the Pergamon Press, and entitled *The International Journal of Heat and Mass Transfer*, will be welcomed by all engaged in such work (1, No. 1; June 1960. Pp. 114. Subscription rates: (*A*) for Libraries, Government Establishments, Research Laboratories, etc., £7 (20 dollars) per vol.; (*B*) for individuals who place their orders directly with the publisher and certify that the journal is for their personal use, £5 5*s*. (15 dollars) per annum). Six distinguished editors drawn from Great Britain, the United States, U.S.S.R. and Germany, assisted by some fifty advisers representing major academic and industrial concerns from all over the world, should ensure a truly international journal with a succession of papers of high standard. The first issue contains an editorial article and ten papers, two of which are in German, one in French, the remainder in English; all papers have an abstract in English, French, German and Russian. There is also a "Bibliography of Heat Transfer", presumably of publications written in the past few years only, though this is not stated. Research workers already familiar with advanced concepts will find the contents of the most value. It is to be hoped that the editors will from time to time include fundamental but more elementary articles for the benefit of less erudite students, such as those in their first year of Ph.D. work.

Bibliography of Research at Oak Ridge National Laboratory

A LIST of articles by members of the staff of the Oak Ridge National Laboratory (operated by the Union Carbide Corporation for the United States Atomic Energy Commission) published during 1959 in technical journals has been issued by the Laboratory, and requests for reprints where available, as indicated by the prefix *R*, should be addressed to the Central Research Library at the Laboratory (Pp. v + 84. Oak Ridge, Tennessee: Oak Ridge National Laboratory, U.S. Atomic Energy Commission, 1960). The articles are arranged alphabetically by author under nine divisions: biology; chemistry; general; health physics; instrumentation; mathematics; metallurgy and materials; physics; and technology. There is an accompanying list of reports issued by the Laboratory, and these, except when indicated as "Not for sale", should be ordered through the Office of Technical Services, Department of Commerce, Washington 25, D.C. A third list, similarly arranged, records the titles of papers presented at scientific meetings, and requests for information regarding these papers should be addressed to the authors concerned. Titles of eighteen theses completed at the Laboratory during the year are given in a fourth list, alphabetical by author, and finally there is a list of sixty-eight inventions disclosed during the year.

Research Into Electricity Supply

As a postscript to an article on the supply of electricity in Great Britain, Arthur Palmer suggests unified areas where research could be carried out (*Research Applied in Industry*, 13, No. 9: September 1960). These include investigations into fundamental questions of electricity production and use: for example, ways and means of escaping the limitations of the thermodynamic cycle and methods of solving the outstanding energy storage problem; investigations into reductions of cost in all the fields of generation, transmission, distribution and utilization—this is primarily a scientific and engineering matter, but it must occasionally take account of psychology or even sociology; investigations into techniques for reducing the social nuisance of electrical processes—in an island packed with more and more human beings demanding simultaneously the often mutually contradictory ends of higher and better standards, this is no easy task; and investigations into the possibility of maintaining human interest in an industrial environment which when ideally organized and arranged will record the almost effortless glide of electrons from genesis to consummation.

Poison Sprays and Wild Life

A JOINT Committee of the Royal Society for the Protection of Birds and the British Trust for Ornithology has been formed under the chairmanship of Mr. S. Cramp to study the effect of toxic chemicals on birds. The Committee is anxious to obtain evidence of kills of birds due to agricultural chemicals used in sprays or in the form of seed dressings. The basic information needed is the date and locality of the kills, the species and number of birds affected and the chemical used. The Committee would appreciate prompt notification of birds the death of which is thought to be due to agricultural chemicals, so that if necessary corpses may be collected for chemical analysis. Information should be sent to the secretary of the Committee, Mr. P. J. Conder, Royal Society for the Protection of Birds, 25 Eccleston Square, London, S.W.1.

Insulin

A RECENT issue of the *British Medical Bulletin* deals with insulin in its varied aspects (16, No. 3; September 1960). Prof. Charles H. Best describes his pioneer work with Banting and developments which have occurred during the past forty years. This is followed by an account by Dr. F. Sanger of the chemistry of insulin based on his Nobel Prize Lecture. Other articles include one by Dr. Ieun Harris on the chemistry of pituitary polypeptide hormones; methods of insulin assay by G. A. Stewart; insulin antibodies by Dr. P. H. Wright; the action of insulin on carbohydrate metabolism by Dr. R. B.

Fisher; fatty acid metabolism by Drs. S. J. Folley and A. L. Greenbaum and the mechanism of the action of insulin by Dr. P. J. Randle and Prof. F. G. Young. Prof. F. G. Young has acted as scientific editor of this issue.

Inhibition of Development in Rust Fungi

D. J. SAMBORSKI and F. R. Forsyth have reported on the inhibition of the development of rust fungi, on detached wheat leaves, by various metabolites, antimetabolites and enzyme poisons (*Canad. J. Bot.*, 38, 467; 1960). This is part of a series of investigations in which attempts are being made to correlate changes in the reaction of the pathogen with changes in endogenous levels of substrate in the host. In the experiments, detached leaves of Little Club wheat were floated on solutions containing benzimidazole and the compound being tested. The effects of purine and pyrimidines, vitamins, amino-acids, carbohydrates and enzyme poisons were examined. A number of these compounds inhibited leaf and stem rusts at concentrations that were not injurious to the host. Of the purines and pyrimidines tested, thymine and the analogue azathymine were the only effective inhibitors. The antivitamin oxythiamine was inhibitory, the inhibition being completely reversed by thiamine. A few natural amino-acids, notably histidine, *iso*leucine, methionine and serine, inhibited rust development. The inhibition was reversed by glycine in all cases except with serine. Amino-acid analogues, particularly canavanine, ethionine and *p*-fluorophenylalanine, were very good inhibitors, the inhibitions being reversed by comparable levels of arginine, methionine and phenylalanine, respectively. The carbohydrates lyxose, xylose, sorbose, and all the sugar alcohols tested were effective inhibitors of rust development. Of the enzyme poisons tested, sodium fluoride and sodium azide differentially inhibited rust growth.

The Gairdner Foundation: Awards

AWARDS totalling 30,000 dollars for medical work in arthritis and heart disease have been made by the Gairdner Foundation to four American and two British medical scientists as follows: Prof. John H. Gibbon, jun., professor of surgery and director of surgical research, Jefferson Medical College, Philadelphia; Prof. William F. Hamilton, professor of physiology, University of Georgia School of Medicine; Dr. Karl Meyer, dean of medicine at Columbia University, New York; Prof. Arnold R. Rich, Baxley professor emeritus of pathology, Johns Hopkins University; Prof. J. McMichael, professor of medicine, University of London; Prof. J. H. Burn, recently professor of pharmacology, University of Oxford. The awards will be worth 5,000 dollars each, and are prizes for achievements rather than for the support of future research.

U.S. Society for the Study of Development and Growth

THE following were elected officers of the U.S. Society for the Study of Development and Growth for the year November 1960–November 1961: *president*, Prof. William P. Jacobs (Princeton University); *secretary*, Prof. Armin Braun (Rockefeller Institute); *treasurer*, Prof. H. Clark Dalton (New York University). The other members of the executive committee are: Prof. Clifford Grobstein (newly elected), and Profs. Arthur Galston and Dietrich Bodenstein.

The Association of Clinical Biochemists

THE Association of Clinical Biochemists has elected the following officers for the session 1960–61: *president*, Dr. C. P. Stewart; *chairman*, Dr. A. L. Latner; *honorary treasurer*, Dr. R. Gaddie; *honorary editor*, Mr. H. Varley; *honorary secretary*, Dr. J. H. Wilkinson (Westminster Medical School, Horseferry Road, London, S.W.1).

Announcements

MR. A. D. MCKNIGHT, executive commissioner of the Australian Atomic Energy Commission, has been elected chairman of the Board of Governors of the International Atomic Energy Agency for the next year.

THE eleventh session of the United Nation's Educational, Scientific and Cultural Organization is to be held at Unesco House, Place de Fontenoy, Paris, during November 14–December 13. The main subject for discussion will be International Co-operation for Oceanographic Research.

AN all-day session of the Welsh Soils Discussion Group will be held in the Department of Geography and Anthropology, University College, Aberystwyth, on November 16. The theme will be: "Glaciation in Wales as related to Soil Profile Development". Further information can be obtained from Mr. James A. Taylor, Department of Geography, University College of Wales, Alexandra Road, Aberystwyth.

A SYMPOSIUM on "Inorganic Polymers" is being sponsored by the Chemical Society, and will be held at the University of Nottingham during July 18–21, 1961. Further information can be obtained from the General Secretary, Chemical Society, Burlington House, London, W.1.

THE 1960 meeting of the American Association for the Advancement of Science will be held in New York City during December 26–31. Further information can be obtained from the director of public information for the meeting, Sidney S. Negus, Medical College of Virginia, Richmond, Virginia.

THE Plant Phenolics Group is holding a one-day meeting on "The Stereochemistry of Natural Phenolic Compounds" at the Department of Engineering, University of Bristol, on December 16. Further details can be obtained from the Honorary Secretary of the Group, Low Temperature Research Station, Downing Street, Cambridge.

THE third international conference on "Analogue Computation" will take place in Belgrade during September 4–9, 1961. The conference is being organized by the International Association for Analog Computation. Further information can be obtained from L. Radanović, Yugoslav Committee for Electronics, Telecommunications, Automation and Nuclear Engineering, Tarazije 23/VII, Belgrade.

DIAMOND PHYSICS

A CONFERENCE on diamond physics was held during September 22–23 at the J. J. Thomson Physical Laboratory, University of Reading, under the auspices of the Institute of Physics and the Physical Society. More than a hundred delegates attended, and twenty-one papers were presented, most of which originated in Great Britain, but contributions were also received from the United States and one from Stockholm. Most of the contributions were experimental; two theoretical papers on related topics were those of P. Ewald (United States) on the electron density of diamond and of H. Bolton and H. Clark (Newcastle) on the nature of the bond orbitals. It was generally agreed that the electron density is much less concentrated than the word bond might imply, but it still remains very difficult to account theoretically for the intensity of the (222) X-ray reflexion observed in some specimens.

Two papers were devoted to synthetic diamonds. That on their production by E. Lundblad (A.S.E.A., Stockholm) compared different methods of synthesis using various catalysts and conditions of temperature and pressure but no direct transition of graphite to diamond has yet been achieved. The results therefore confirm these of the General Electric Co. (United States).

G. Kennedy (United States) and others, however, pointed out that they were convinced that the pressures at present quoted on the Bridgman scale were about 30 per cent above the true value at pressures greater than 25,000 atm. Consequently diamond formation occurred considerably below the region indicated by the Simon graphite-diamond equilibrium curve, which therefore needed revision.

The diamonds produced synthetically may have either type I or type II characteristics according to the method of production.

The other paper, by S. Tolansky (University of London), on optical and interferometric studies on the surface characteristics of diamonds compared the synthetic products from several different sources. A wide variation in crystal perfection was observed, some batches of specimens consisting of 'hopper-type' crystals whereas other batches were relatively perfect. Growth spirals were detected on specimens from one batch.

There were several contributions on semi-conducting diamonds. H. Farnsworth and J. Marsh (United States), using normal incidence on the (100) face, showed that the electron diffraction pattern below 350 eV. contained no half-integral order surface grating beams, thus indicating that the positions of the atoms in the surface monolayer are not displaced from their 'normal' positions as for silicon and germanium. Changes in the intensity of the diffraction pattern on heating treatment are interpreted in terms of variations in adsorbed oxygen, but there was some disagreement on details of the interpretation.

F. C. Champion and J. Male (London) compared the luminescence excitation spectrum of a semi-conducting specimen with its absorption spectrum and showed that the former method sometimes gave information absent from absorption data. For example, it showed quite clearly a level agreeing with an acceptor-level at 0·35 eV. from the valence band. Measurements of the anisotropy of the magnetoresistance in three oriented crystals of p-type semi-conducting diamond by P. J. Kemmey and E. W. J Mitchell (Reading) were compared with calculations based on the approximate model of two warped and one spherical energy band surface, degenerate at $K = 0$.

Contributions to the study of graphitization were made by M. Seal (United States) and by T. Evans and C. Phaal, and Evans and H. Sauter (Reading), the two latter emphasizing the aspect of etch-rate determination and etch-pit orientation on diamond surfaces. It was shown that trigons oriented such that the apices of the triangles on the octahedral face were pointed towards the sides of the face, as in naturally occurring trigons, could be produced by etching with an oxygen and water vapour mixture above about 800° C. Below that temperature the trigons had the usual etch orientation with sides of the trigons parallel to the sides of the crystal face. High-temperature and high-vacuum graphitization experiments on diamond were also described by V. Howes (Reading).

Experiments on irradiation damage to diamonds by electrons of energies up to 2 MeV. were described. Changes in the optical absorption of a type IIa diamond near 2 eV. were compared with the theoretically expected rate of defect production and agreement below 1 MeV., obtained if the displacement energy is $E_d = 80$ eV. Corresponding measurements on the change of resistivity of a IIb diamond with radiation dosage were in agreement with the absorption data up to 1 MeV., but above this energy C. Clark, P. J. Kemmey and E. W. J. Mitchell (Reading) found poor agreement, the explanation of which is uncertain. D. Palmer and C. D. Clark (Reading) showed from corresponding absorption changes with temperature that complex annealing processes occurred indicating a wide range of activation energies. Tentative models of the various annealing stages over the range 150°–800° C. were proposed. It was suggested during discussion that the interpretation of these experiments would be far more definite if in the first instance the energy of the bombarding electrons was confined to a value just above threshold (say, 0·5 MeV.), so that only one predominant type of defect was produced, namely, close vacancy-interstitial pairs. The number of possible activation-energies required to interpret the annealing data would then be a minimum and the significance of the present results, obtained at bombarding energy up to 2 MeV., could be more fully appreciated.

A two-phonon process was suggested by J. R. Hardy and S. Smith (Reading) to account for specimen-independent absorption between 3·75 and 7·5μ. It confirmed that long-range forces are far less important in diamond than in silicon or germanium. Phonons and also excitons were invoked by F. C. Champion and J. Male (London) to explain specimen-independent broad bands in the luminescent excitation spectrum of all types of diamond except type IIb at energies greater than 5·45 eV., but bands at 5·25, 5 36 and 5·39 were attributed to some defect other than nitrogen.

J. Male and J. R. Prior (London) also reported the first examples of fluorescent emission in the ultra-violet from diamond at energies near 5·1 and 5·3 eV.

The growing interest in silicon carbide was shown by four papers on practical aspects involving various mechanical properties such as friction and wear of diamond and silicon carbide, by C. Brookes, by D. R. Miller, by L. M. Fitzgerald and by F. Field and N. L. Hancox, all from Cambridge. The steady improvement in the purity control of silicon carbide was described by W. F. Knippenberg (Holland). Using as starting material cubic silicon carbide prepared by decomposition of chlorosilanes, the total content of foreign atoms, which were mostly chlorine, could be reduced to less than 10^{16} cm.$^{-3}$. Using such pure material, H. Daal, W. Knippenberg and J. D. Wassher measured the Hall constant and the resistance of silicon carbide from 80° to 1,400° K. Much lattice imperfection is indicated since the number of acceptors and donors exceeds the number of chemical impurities by an order of magnitude. Occupying as it does a key intermediate position between silicon and diamond, all the properties of silicon carbide are of great interest and importance. However, because of the different possible atomic arrangements such as cubic and such polytypes as 4H and 6H in the hexagonal form, the interpretation of the optical and electrical properties of silicon carbide is complex. D. Hamilton, W. J. Choyke and L. Patrick (United States) have examined the optical absorption and photoluminescence of 4H silicon carbide, extending earlier work on the 6H polytype. A characteristic edge luminescence was observed in the pure 4H crystals and parts of the spectrum were found to have photon energies greater than the energy gap of polytype 6H. Corresponding absorption experiments showed that the 4H energy gap exceeds the 6H energy gap by 0·25 eV. The transitions are indirect and exciton absorption is observed.

The impression gained from the Conference was that although diamond physics is still in its infancy, sufficient experiments have now been performed over a wide range of properties and techniques to indicate that a relatively few well-chosen experiments, such as the investigation of radiation damage close to the threshold energy, should throw real light on fundamental problems in solid state physics. As Prof. R. W. Ditchburn pointed out at the beginning of the Conference, the unique property of diamond is its stability and the simplicity of its composition. These striking advantages compared, for example, with the alkali halides, as set out in a conference on crystal luminescence held two weeks earlier in Turin, seem to me far to outweigh the relative intractability of diamond as a material in that it prevents the overwhelming flood of experimental data which would undoubtedly ensue if simple methods of 'doping' diamond were available. Diamond physics is on an orderly march which should lead to a real advance in our understanding of solid state physics.

Advantage was taken of the opportunity provided by the Conference to present the Duddell Medal to Prof. R. V. Jones, who then spoke on some developments of the optical lever. In an excellent lecture, enjoyed by all, Prof. Jones described in particular the development of the optical lever in the past ten years up to the present stage when the performance approaches the limit set by the statistical fluctuations of photons in the light beam. Applications covered the evaluation of the thermal fluctuation limit for galvanometers, the detection of the change of linear momentum in a beam of light after refraction, and the development of a sensitive infra-red detector based on linear thermal expansion. The method failed to detect any deviation of a beam of light in an inhomogeneous transverse magnetic field of mean value 8,000 oersteds, although a change in the velocity of light of about 70 μsec.$^{-1}$ should have given a deviation equal to the r.m.s. error.

F. C. Champion

THERMAL MOTION IN CRYSTALS AND MOLECULES

THE fifth international congress of the International Union of Crystallography which was held recently in Cambridge was followed by two symposia, one of which was devoted to papers on Thermal Motion in Crystals and Molecules. This symposium lasted for two days, August 22–23, apart from an introductory lecture which was given during the main congress in the previous week. It consisted of five invited papers and thirty other contributions, abstracts of which had been published in advance of the meeting by the International Union of Crystallography.

In the early days of crystallographic studies by X-ray diffraction techniques, thermal motion was a disturbing factor for which rather empirical correction had to be made, by means of the familiar Debye–Waller theory, before the crystallographer could make a crucial comparison of his experimental intensity results with deductions from any postulated structural model. Since then the increasing accuracy of measurements and ease of interpretation have permitted the process to be largely reversed and experiment now allows a detailed assessment of atomic motions to be made and analysed into various types of vibration. Investigators are no longer restricted to the use of X-rays for electrons, and neutrons are now being widely used in support. Moreover, further theoretical work on the various scattering processes and improvements in experimental techniques have played their parts in increasing the interest in this field of work. During the past few years it is particularly noteworthy that rather empirical descriptions of atomic motions are being superseded by much more comprehensive descriptions of co-operative motions of molecules and crystals as a whole. To a considerable extent, interest has been fostered by the increasing availability of computing machines and programmes able to analyse the experimental results in terms of the many parameters needed for a full description of thermal motion.

Although receptive of any aspect of thermal motion in crystals and molecules, the symposium was aimed at providing discussion of three particular topics: first, the study of the elastic and inelastic scattering of X-rays and neutrons by solids, as a

source of information on the amplitudes and frequencies of motion in crystals and their dependence on temperature; secondly, the use of electron diffraction measurements to study molecular motion in gases; and thirdly, data on residual motion in crystals at low temperatures. The introductory lecture by Prof. J. C. Slater served as a general lecture to the whole congress and was entitled "The Interaction of Mechanical and Electromagnetic Waves in Crystals". While summarizing the more conventional aspects of the scattering of radiation by phonons in crystals, this lecture surveyed the interactions over a very wide range of frequency, and included an account of recent work on the explanation of ferroelectric transitions from the point of view of lattice dynamics. The treatment of Cochran, whereby a ferroelectric transition is emphasized as being a limit of stability against a particular mode of vibration, was shown as a development of the much earlier work of Huang and others on anomalous dispersion in the infra-red region, where a transverse electromagnetic wave interacts with transverse mechanical oscillations in a crystal.

The main symposium began with an invited paper by Dr. D. W. J. Cruickshank, who discussed, chiefly from a theoretical point of view, the determination of atomic vibration amplitudes from X-ray diffraction data, particularly in molecular crystals where the motions are anisotropic. For each atom a vibration tensor with six components can be deduced and these tensors can then be combined to give a picture of both rigid-body vibrations of the molecule as a whole and of internal vibrations within the molecule. At room temperature the latter are relatively small, but they become of greater importance as the temperature is reduced. It was emphasized that X-ray diffraction data alone are not sufficient to give an unambiguous solution, and it is necessary to employ spectroscopic evidence as well in order to distinguish, for example, between internal twisting vibrations and angular oscillations as a rigid body. Investigations concerning the perchlorate ion in perchloric acid monohydrate ($H_2O.\ ClO_4$) and of ethane were described as examples of the essential part played by spectroscopic data in the analysis of the various motions. The following, complementary, paper by Dame Kathleen Lonsdale surveyed the problems from a more practical point of view in the light of much experimental information accumulated by the author and her colleagues at University College, London. In practice, before true thermal vibrations can be studied, allowance has to be made for zero-point energy, structural disorder and bonding anisotropy. Measurements at reduced temperature and parallel studies with X-rays and neutrons may be necessary in order to secure unequivocal results. The partition of the total thermal motion among internal and rigid-body vibrations was discussed, taking urea, hexamine, naphthalene and anthracene as examples. In the latter case where the directions of the principal axes of atomic vibration are not fixed by crystal symmetry, wide discrepancies in their specification from different, seemingly accurate, sets of results were found. It would seem to be well established that there is still a considerable need for data with improved accuracy, more free from both random and systematic errors, if the detailed conclusions which are drawn from structural analyses of this type are to be justified.

These two general review papers were followed by several descriptions of structural analyses which depended on the principles previously enunciated, illustrating in the main the relation between atomic motion and the environment of an atom, both within its own molecule and among its neighbours, and with some attention being directed to developments of experimental technique. Increasing attention is certainly being given to measurements at low temperature, but there are still only a few substances for which a detailed analysis has been made at more than one temperature. The value of supporting evidence from other physical methods of analysis, such as specific heats, nuclear magnetic resonance and spectroscopy, is very great.

Both Dr. Cruickshank and Dame Kathleen Lonsdale referred to the information on molecular motion which could be obtained from work on the diffuse inelastic scattering, as distinct from the elastic Bragg peaks, and this theme was taken up in more detail by later contributors. Papers by Dr. W. Cochran and Prof. W. Hoppe described the theoretical calculation of the diffuse scattering from molecular crystals, pointing out the relative significances of the displacements due to translation and rotational motion, and distinguishing between the enhancement of diffuse scattering in the neighbourhood of reciprocal lattice points and that over extended areas. Several succeeding contributions described the experimental verification of these ideas and their value in structure determination. A paper by Dr. M. L. Canut illustrated how experimental measurements of the shape and location of the extended regions of diffuse scattering were in good agreement with calculations made from the shape and orientation of the molecules for substances such as hexamine, pentaerythritol and naphthalene. A related contribution from Drs. E. Sandor and W. A. Wooster emphasized that the detailed interpretation of the diffuse scattering might be carried out accurately enough to be of value in structure analysis. Particularly for planar molecules, the orientation in the structure of a molecule of known shape could be predicted and a molecular Patterson function could be calculated.

In a group of papers on electron diffraction work on gases, it was evident that the greatly increased experimental accuracy which can now be attained has stimulated interest in more detailed work on the diffraction process and the force fields in molecules. Prof. Y. Morino discussed the exact relation of the experimentally determined quantities—the mean atomic distance and the mean square vibration amplitudes—to the actual equilibrium distance and the detailed molecular field. Prof. O. Bastiansen and his colleagues showed that certain linear molecules may appear to be bent on account of vibrations perpendicular to the bond, because the longer interatomic distances within the molecule appear to be shorter than expected from a summation of observed bond distances. Carbon suboxide was shown to be a case where it is difficult to distinguish between a linear molecule with large out-of-line vibrations and a bent equilibrium configuration. One was impressed by recent improvements in experimental techniques; for example, K. Hedberg described how it was now possible to measure the increase with temperature of the vibration amplitudes in phosphorus trichloride, in fair agreement with predictions from spectroscopic data. In discussions of these electron diffraction papers, attention was directed to the importance of using complex scattering factors, reliable values of which are now becoming known and listed.

The influence of atomic vibrations on measured values of lengths of bonds is not, of course, limited to electron diffraction work, and a paper by H. Levy discussed this problem in relation to precise structure refinements by X-ray and neutron diffraction methods. It was shown how the apparent interatomic distance for a pair of atoms depended on whether or not their individual thermal motions were linked or independent. Any attempt to deduce the equilibrium distance of separation, as distinct from the centroid separation, depends on reaching a precise knowledge of the atomic vibrations after making measurements at various temperatures, followed by an extrapolation and allowance for zero point motion. In discussion it was made clear that whenever corrected distances are given it is very essential to specify on what assumptions the corrections have been made. The effects are of particular importance when the motions of hydrogen atoms are being considered and are of especial interest in work on neutron diffraction. This paper, in fact, formed part of a session which was devoted to the contribution of neutron methods to our knowledge of thermal motion, which Dr. W. Cochran opened with a discussion of the great value of measurements of energy distributions of scattered neutrons in a review of recent work on lattice dynamics by neutron spectroscopy at Chalk River. Of particular interest were an extensive series of precise measurements of the dispersion relation, between frequency and wave-number, for the acoustic vibrations in single crystals of lead. In order to interpret the results it is necessary to assume that long-range forces are important in the solid and it is shown that their range becomes less as the temperature is increased. From the widths of the peaks in the neutron-energy spectrum it is possible to deduce the life-time of the phonon vibrations. In a further comprehensive set of measurements the lattice dynamics of the alkali halides and of lithium hydride were investigated. As an example of the contribution of neutron methods to disentangling the effects of thermal vibration and bond anisotropy, a paper given by Dr. R. S. Calder described concurrent neutron and X-ray work on lithium hydride.

In the final session of the symposium, Prof. I. Waller described some recent theoretical work on the frequency distribution and dispersion relations for alkali halides at low temperatures, with particular reference to the approximations which have been made in calculating the form of the zero-point energy vibration amplitudes. The conclusions are in good agreement with results of diffraction experiments. In an interesting survey of a wide range of experimental data, F. H. Herbstein examined the values of Debye temperature determined for cubic crystals by methods such as specific heat and elastic constant measurement, as well as by diffraction studies at one or several temperatures. At room temperature there is reasonable agreement between different methods, but at low temperatures such meagre X-ray data as exist suggest that the apparent θ values may be lower than those found by other methods. It would seem that some accurate and comprehensive X-ray work in this field would be rewarding.

Two papers were given on the contribution of nuclear magnetic resonance to studying thermal motion. In a review of this application, Prof. E. R. Andrew emphasized that whereas previous speakers had been concerned solely with 'vibrations', there were other forms of motion, such as hindered rotation and self-diffusion, which only occurred infrequently—though involving much greater movements—and which could not be examined by diffraction techniques. Examples were given of how these topics can be investigated quantitatively by nuclear magnetic resonance techniques and how the postulated effects on the spectrum can also be demonstrated by absorption measurements with rotating crystals. Dr. J. A. S. Smith described an application of nuclear magnetic resonance methods to the examination of single crystals of urea and thiourea which demonstrated the onset of hindered rotation about the C=O and C=S bonds in the two cases. As a result the molecules flip between two possible equilibrium configurations, giving rise to large apparent temperature factors for some of the atoms as judged by X-ray diffraction work.

In conclusion, it may be worth recording two personal impressions which remain from the papers and discussions. First, although the precision of experimental measurements in these investigations is very high, there still remain some significant gaps in interpretation which leave room for systematic errors and may make some of the apparent accuracy illusory. Secondly, in spite of the increasing identity of equipment used over the world, one can still be struck by the individuality of thought and methods of approach which characterizes the different schools of investigators.

The symposium was attended by about 400 persons, mainly accommodated in the large lecture theatre of the Arts School at Cambridge, but with an over-flow in the adjoining Cavendish Laboratory served by a closed-circuit television set. It was perhaps significant that even for the less-crowded sessions there were many who preferred the quieter, airy contemplation of the television screen to the hurly-burly of the lecture room.

G. E. BACON

THE INTERNATIONAL SCIENTIFIC FILM ASSOCIATION

THE fourteenth annual congress of the International Scientific Film Association was held in Prague during September 16–24. It was attended by 120 delegates and observers from twenty-four countries. The British delegation of twenty people was led by Mr. Edgar Anstey, president of the Scientific Film Association. Associated with the congress was the Third Festival of Films presenting Science.

The International Scientific Film Association is a non-profit-making and non-governmental organization, officially recognized for consultative status with Unesco. Membership is open to any organization representative of the science film movement in the country of that organization.

The congress were welcomed officially by the Czechoslovak Minister of Education and Culture, Dr. Frantisek Kahuda, and by the managing director of Czechoslovak Film, Mr. Alois Poledrnak.

The Czech Organizing Committee—led by Dr. Vladimir Vaclavek—provided a delightful centre in

the form of the Film Club, at which members of the congress could meet and also dine and drink until the early hours of the morning. They also provided facilities for many visits in their beautiful city of Prague, and opportunities for meeting film makers and scientists in their studios and laboratories. The social life was full and active.

The first International Library for Scientific Film is to be set up in Brussels. It is the result of an agreement between the International Scientific Film Association and the Belgian Institut National du Cinéma Scientifique. There has been much discussion over this film library, and the stage has now been reached where the final documents are likely to be signed sometime in 1961. Van den Borre, director-general of the Belgian Ministry of Education, expressed to the general assembly his Government's keen determination to see the project through, and gave some details of financial support. The main tasks of the Library will be to gather together and keep copies of the best scientific films, to classify them, to publish general and specialized catalogues, to organize congresses, and to arrange special showings of films.

Because cinema and television are rapidly becoming closely linked, resulting in many new problems and possibilities for scientific film makers and users, it was agreed to set up a commission to study television in relation to the aims of the scientific film.

Unesco has suggested a study be made on the provision of films in the natural sciences for use in high-schools in newly developing countries. The International Scientific Film Association has been asked to undertake the research, and a commission was set up for this.

Closer co-operation between the Association and specialized international bodies and associations having film sections, for example, the World Veterinary Association, is to be secured by making provision for observers from these bodies to attend Association's congresses.

Greece and Israel were admitted to full membership of the Association, bringing the number of member countries to twenty-eight. It is expected that next year the American Science Film Association is likely to become a member.

The annual congress provides the main discussion opportunity for international science film makers. To meet their needs, there are three sections, each having its own programme of work. They engage in a vast range of activities.

In the Research Section, 11 lectures and 35 reports were delivered, and 68 specialized films were shown. In the Education Section, 4 lectures and 24 reports were made and 62 films were shown. In the Popular Science Section, there was a major discussion on definition of popular science films, two reports were made, and 72 films were shown. In addition, the Popular Science Section organized for the first time three special meetings of television workers from different countries at which ten TV films were shown.

Two B.B.C. producers—Aubrey Singer and James McCloy—presented a clear picture of what was being done in B.B.C. television, and the B.B.C. won much praise for its co-operation in making available a large amount of TV recording.

The question of definition has very much bogged down discussion in the past, and for the first time this year it was felt that the beginning of a successful solution to this problem had been made. In the Popular Science Section, a paper entitled "Types and Genres of Popular Science Films" was read by Mr. Igor Vassilkov (U.S.S.R.). He divided popular science films into two groups—the didactic and the imaginative—and then used the terminology of literature, because the film has as yet developed no comparable language, to describe the different kinds of films to be found within each category. It was agreed that the nature of such a film is determined by what the writer and director have set out to do. There was long discussion on this paper, in which the writer of this report found general acceptance for his view that the didactic film was now being taken over by TV and specially-made educational films, and that the future for the popular science film lay with the imaginative type of film. It was no longer necessary to popularize science among young people, but to stir their imagination with an understanding of the social implications of scientific development. It was mainly an older generation who had not been taught science at school, who still required the didactic type of popular science film.

The Popular Science Section has agreed to ask member countries to provide details of all the films already made or which will have been finished before January 1, 1961, concerned with the history of science and technology, or of the lives of eminent personalities in science and technology whose discoveries and inventions are of international significance. It will form the basis for a comprehensive catalogue to be published by the Russian branch of the Association.

Among problems that concerned the Education Section was the role of the film in speeding up the rate of learning, that is, to increase the amount learned without increasing the time spent in school. Mr. Vitali Jemtchujni (U.S.S.R.) gave details of a series of new teaching films in physics which were being prepared for production in his country and which were part of an overall attempt to find a solution to this urgent problem.

The Research Section considered films in medicine, biology and botany. Two Russian papers that aroused particular interest were on new Soviet equipment for high-speed still photography and cinematography, and the use of high-speed and ultra-speed filming of technological processes pertaining to agricultural machinery. The latter work has risen from problems caused by the mechanization of cotton harvesting. Film was used to obtain a picture of what happens in separating cotton lobes from the boles when cotton is picked with pneumatic harvesters. It was claimed that economies in picking and an increase of production resulted from the application of these studies.

The general assembly agreed to award diplomas to the following films shown during the Festival: "The Mountain Canal" (China); "Passsport to Space" (Czechoslovakia); "Sea Dancers" (France); "The Magic Tape" (German Federal Republic); "Living Traps" (Hungary); "Morning Sun" (Japan); "Sources of Energy in the Blood Circulatory System" (Poland); "The Revealing Eye" (Great Britain); and "Atomic Ice-Breaker" (U.S.S.R.).

In addition, "Symphony in Steel" (Japan) was given a special commendation for its use of cinemascope, as was "Timber" (Bulgaria) for its witty treatment of a static subject.

Mr. Alexandre Zgouridi (U.S.S.R.) was re-elected president of Association, and the vice-presidents are Mr. Edgar Anstey (Great Britain) and Mr. J. Varossieau (The Netherlands); the honorary secretary remains Mr. John Maddison, one of the founders of the Association, who this year wished to resign, but

was persuaded to stay on for another term. Mr. Mohamed Afifi (Morocco) was appointed assistant to the honorary secretary. The honorary treasurer is Dr. Vladimir Vaclavek (Czechoslovakia). The honorary life members remain M. Jean Painlevé (France) and Mr. Jan Korngold (Poland). The editor-in-chief of *Scientific Film*, the journal of the Association, is Mr. Maurice Goldsmith (Great Britain).

The liaison officer of the Association with the International Science Film Library is Mr. Luc Haesaerts (Belgium); the chairman of the Television Study Commission is Mr. John Maddison, and of the Unesco–International Scientific Film Association Science Films Commission, Mr. Bernard Chibnall (Great Britain). The chairmen of the Standing Committees are: Research, Dr. R. Robineaux (France); Popular Science, Mr. V. Tosi (Italy); and Education, Prof. J. Jacoby (Poland). Next year's Congress is likely to be held in Rabat, Morocco.

MAURICE GOLDSMITH

A BRITISH SOURCE OF NATURAL GAS

THAT in Britain there should be in daily use a supply of natural gas may well surprise many well-informed people. Indeed, it was in 1938 that two discoveries of natural gas in Britain were made, one at Cousland, south-east of Edinburgh, and the other west of Whitby at Eskdale. At that time no commercial outlet existed for these potential supplies and the wells were sealed off for eventual future use. The Cousland discovery has been harnessed by the Scottish Gas Board for the use of Musselburgh, where after being suitably treated it forms part of the gas supply.

Now there comes the news of interest more particularly to the inhabitants of the Whitby district of the actual utilization of the gas from the Eskdale area. The wells are situated in moorland of much natural beauty; but there is no fear that the amenities of that fair land will be impaired by the small surface equipment that marks the source of a sufficient supply of gas to serve a new but sole production unit in the Whitby Gas Works.

Two wells, of some eleven that have been drilled, have proved to be gas producers. These wells have a closed pressure approximating to 2,000 lb. per sq. in., and draw their gas from limestone layers, respectively 4,196 and 4,807 ft. below ground-level. It was only in April this year that these wells were re-opened and now the laying of a 3-in. pipe-line has been completed. Further, in order to produce from the natural gas, which contains 93–94 per cent of methane and has a calorific value of 1,000 B.T.U. per cu. ft., a final gas for public distribution of 500 B.T.U. per cu. ft., a conversion plant has also been installed.

The conversion process of the gas is known as a reforming process. It consists essentially of the reaction of the natural gas with steam to produce hydrogen and carbon monoxide. It is carried out in special heat-resisting steel tubes which are heated to about 1,100° C. and contain a nickel catalyst. It is then enriched with some cold natural gas, and flue gas from the tube-furnace, fired by natural gas. This is necessary to adjust it to the correct calorific value and density for public distribution.

It is also interesting to note that the gas is of such a freedom from sulphur impurity that in order to ensure that gas supplied to the town should have a distinct odour, equipment for the purpose has been installed, employing tetrahydrothiophen as odorant.

The two wells available have a combined flow-rate up to 4 5 m. cu. ft. per day. Three reformer units have been provided, each having a daily capacity of 625,000 cu. ft.

The plant has been put to work in recent weeks, and the venture is so new that the performance tests have yet to be carried out.

R. J. SARJANT

THE LIBRARY IN SCIENCE AND TECHNOLOGY

OF the papers of scientific interest presented at the annual conference of the Library Association at Scarborough, September 12–16, that of Dr. D. J. Urquhart describing the planning of the National Lending Library for Science and Technology and the ideas and motives behind it is undoubtedly the most important, but some of the other papers should not be overlooked by the scientist and technologist. In his presidential address on September 13, Mr. B. S. Page, librarian of the Brotherton Library, University of Leeds, discussed librarianship as he saw it practised in English universities of the twentieth century, and more particularly the research side of such work. Research, he suggested, in fact determined the extent, and very largely the character, of the collections and greatly influenced every aspect of the work of a university librarian, and Mr. Page emphasized, first, that the librarian and his readers were members of the same university community, with all it implied, and secondly, that the reader regarded the library less as an amenity than as a necessity; his use of it was regular and professional; normally his work could not proceed without it, and how it operated made an immense difference to the reader's peace of mind and perhaps his hopes for the future. From this Mr. Page argued that because selection had to make the most of very limited resources, buying must be largely related to specific interests which have to be known and understood by the library staff, while at the same time important works had to be acquired for future needs and a close watch kept over special collections and special emphases in general collections. The librarian must be thoroughly equipped to make the most of the potential co-operation of the experts in the teaching departments surrounding him and, pointing out that a university

library is being assembled for generations of scholars, Mr. Page claimed that the quality of library development could do much to make or mar the future welfare and importance of the university.

Mr. Page again emphasized the importance of the personal qualities of the librarian in referring to problems of cataloguing and classification, urging that the schemes to be adopted should not be such as to cause irritation or hindrance to the reader, and, besides putting in a word for the value of browsing among the open shelves as a source of inspiration and insight, he pleaded for imagination as well as knowledge on the part of the librarian and his staff. Techniques, he insisted, were means to an end and the librarian must be prepared to meet his readers on their own ground and to speak their language. Moreover, besides professional techniques, he needed specialized knowledge, experience of research, and the enthusiasm which came of such specialization. The ideals of personal acquaintance with books, personal help to readers, and unselfish devotion to the advancement of knowledge were as valid as when Henry Bradshaw formulated them in 1882.

Mr. M. C. Pottinger's account of libraries in the Soviet Union was of general rather than scientific interest. He commented on the generous provision of reading or study rooms as a common feature of Russian Libraries, and on the claim of the Bibliographical Reference Department, with a staff of about 100, at the Lenin State Library, Moscow, to supply bibliographies on any topic. In a subsequent paper to the conference, Mr. R. G. Surridge referred to the lack of attention to bibliography in libraries in Britain and suggested that a new well-designed Chaucer House, in co-operation with the National Central Library, should provide a comprehensive Bibliographical Department.

Miss L. V. Paulin's paper on "Technical Library Services" described some of the co-operative schemes that had been set up in Manchester, Sheffield, Liverpool and elsewhere in a field where any general co-ordinated policy was completely lacking. Most of the schemes, however, were for large cities where many highly developed libraries were already available and the greatest need was in the counties. The rapid development of adequate libraries in technical colleges provided an opportunity for remedying this position, and Miss Paulin quoted from the Ministry of Education's report on Technical Education of 1956 to indicate the opportunity that existed to build up a really integrated technical library service between the public library and the technical college. The most rural county to tackle the problem so far was Herefordshire, where a County Technical Library service, based on the Herefordshire Technical College, would begin in January 1961, but Northumberland and Durham were already co-operating with a Newcastle scheme, and Middlesex with a West London scheme. The Northamptonshire County Technical Library Service, started in July 1957 and based at Corby Technical College, was already experiencing a large potential demand, while in Hertfordshire a technical library and information service was based on technical colleges and completely integrated with the County Library. This pilot scheme was described in some detail by Miss Paulin, who stressed that such services in the country as a whole must be based on co-operation. The main requirements were receptiveness of mind among members of industrial and commercial firms and an awareness of the value of up-to-date information; a comprehensive, easily accessible collection of books, pamphlets and periodicals in the care of knowledgeable librarians, with the occasional assistance of technologists in dealing with inquiries; and equipment for documentary reproduction.

A following paper, by Dr. H. Coblans, on "International and Local Information", attempted to assess the present structure and likely trends of scientific and technical information services from a survey of a few characteristic countries, such as Switzerland, West Germany, France and Poland. On the international plane there were now signs of a more generous policy towards co-operation, and the International Atomic Energy Agency has created a Division of Scientific and Technical Information which publishes a number of bibliographical tools to implement the Agency's statutory responsibility to further the exchange of information among its member States. Urging caution as to the value of some of the new technical possibilities for transmission of information, such as 'Telex', which admittedly if imaginatively used could transform the effectiveness of information services, Dr. Coblans said that each country should endow and maintain a National Science Library adequately staffed to provide the rapid service that new techniques permit, while international governmental organizations must place their great resources of information fully at the disposal of the national centres. The technical advances, however, involved the obligation to re-think and re-shape some of the British principles of publication, bibliography, abstracting, copying and copyright and inter-library loan. Ultimately this should be done by international discussion and agreement, but national associations, such as the Library Association and the Association of Special Libraries and Information Bureaux, must take the first step.

Dr. Urquhart said that the site of 60 acres at Boston Spa, where it was hoped the first buildings of the new National Lending Library for Science and Technology would be ready at the end of this year, allowed for considerable elasticity in planning, and the present aim was to provide the practitioner in science or technology with all the current literature of the world he might need. They were only trying to obtain the older literature where they had evidence of demand, or where it did not exist in a readily accessible collection, but they were prepared to accept and make available scientific and technological literature of any age. The Library should become fully operational in September 1962, and only then could the extent to which it would be able to meet the demand on its services be measured; at present, however, its collection could provide about 90 per cent of the Russian literature and translation which are requested. Staff was being selected so that collectively it could understand not only the language of science but also the increasing number of national languages in which science was written. It was hoped to transfer the 1,000 tons of literature from London to Yorkshire without closing any service, and although it was expected that some requests would go to the Science Museum Library which should have been sent to Boston Spa, the handling of such requests would be simplified by use of the same type of forms.

Dr. Urquhart said it was not intended to start any large technical information service, but rather to

assist existing services where possible by directing attention to any literature in their fields of which they might otherwise be unaware, though it would be part of the new Library's responsibility to see that attention was given to any gaps in the technical information services which might develop: one such gap had emerged with regard to Russian translations, on which the Library was now spending more than £100,000. Dealing more particularly with the relations of the new Library to the rest of the library system, Dr. Urquhart said that in the near future some of the larger libraries and the special libraries would be invited to notify the Library systematically about new serials or conference proceedings which they decided not to acquire, but for which they might have some future need. On the collecting side they would invite all libraries to let them know of publications in the National Library's field for which they received an embarrassing volume of requests for inter-library loans. By collecting such material the new Library would help the inter-library loan arrangements to work more smoothly, but at present the potential loan demand on the new Library seemed to be increasing, and Dr. Urquhart thought the tendency was likely to continue, particularly because the new Library's loan service would be faster than the existing services. Accordingly, they were very interested in efforts to tune up the inter-library loan system. He thought there was no fundamental reason to prevent evolution of a national inter-library loan form using the prepaid flat-rate system for postage.

Irrespective of its effect on inter-library loan procedure, the existence of the National Lending Library for Science and Technology might well have more profound effects, such as producing a demand for a national lending library for the humanities, possibly based on the National Central Library. Dr. Urquhart, however, left this for future consideration and referred them to the relations of the new Library with local libraries, emphasizing that the potentialities of the comprehensive collection of scientific literature at Boston Spa could not be fully utilized unless the potential users in each locality could discover what they wanted to read, that is, unless guides to the literature of science were available locally. We needed a form of co-operation in which local libraries would assist potential users to find out what they wanted to read, and the National Lending Library would, if necessary, supply this literature. It was intended that such co-operation would be based on the idea that each partner in the scheme would pay his own expenses, and they had recently written about this idea to every local authority and technical college in the United Kingdom. At present, however, standards of technical library service available to the public in many areas were not high: a standard which technologists might criticize as inadequate was attained by only eighteen public libraries and seventeen technical college libraries, and in consequence the National Library was building up some sets of bibliographical tools to lend to libraries which are considering developing their bibliographical collections. They had also been thinking about relations with the public libraries and about the training of librarians, and in conclusion Dr. Urquhart urged that future policy must be based on the scientific analysis of the facts.

CHEMICAL DOCUMENTATION

CHEMISTS nowadays are increasingly eager to receive new chemical matter "hot from the press" but many find it impossible to cope quickly with the mass of information contained in the many traditional journals appearing almost hourly. A few years ago the Chemical Society made a great effort to save the chemist's time by introducing a monthly publication, *Current Chemical Papers*, in which some hundreds of selected titles of papers taken from more than four hundred chemical journals of note were set down under their appropriate sections. The undoubted success of *Current Chemical Papers* has led the American Chemical Society to copy the essentials of the scheme with the publication on an experimental basis of *Chemical Titles**.

The major difference is that *Chemical Titles* is produced by machines and thus may claim a potential wider coverage and give greater detail.

The titles of some five hundred journals, translated where necessary, are punched on to I.B.M. cards together with the authors' names and journal references and are then fed to computers. Within two hours the new journal appears containing three parts. The first part consists of a permuted title index in which key-words from each title have been arranged alphabetically down the centre line of the column. The second part consists of an alphabetical list of first listed authors together with the titles of their current papers published in the selected journals. The third part (in No. 2 only) gives an index of authors other than the first listed for each paper along with the code reference for the paper.

In addition to the key-word, each horizontal line contains as much of the remainder of the title as the machine's programme permits and thus assists in selection of significant titles.

The system is used by scanning vertically the alphabetical key-word list and then, when interest is seized, by reading the horizontal text. When more information is required the reference code on the right-hand side of the entry is noted and located in the alphabetical author index.

The whole system of making the reference code, etc., and for using the system are described fully in the introduction. It is a very clever and easily understood system which appears to work.

The contents of some 550 journals have been dealt with, and it is planned to make a semi-monthly issue of 2,000–3,000 titles.

A good many improvements have been made in No. 2, especially in editing, and more will be made as experiments proceed and as suggestions and criticisms are received. The printing will need to be much better and larger if possible.

The publication fully justifies the claim that it increases "current awareness". It will probably be of

* *Chemical Titles* No. 1, April 1960, 101 pp.; No. 2, May 1960, 89 pp. Chem. Abs. Service. American Chemical Society

particular value to the industrial chemist anxious to keep "right up to date on the literature".

The course of such an experimental system will be watched with great interest. Its eventual success may well depend on the cost of its production and it remains to be seen whether American machines directed by Malcolm Dyson can do a cheaper and more useful job for chemical documentation than is being done at present by the carefully selective man- and woman-power behind *Current Chemical Papers*. M. STACEY

MEASUREMENT AND CONTROL OF MOIRÉ FRINGES

THE illustrated booklet "Moiré Fringes for Measurement and Control", prepared by the National Physical Laboratory and the National Engineering Laboratory for members of the machine-tool and engineering industries, gives a brief account of the essential features of moiré-fringe methods and some of their engineering applications (Pp. 11. London: Department of Scientific and Industrial Research, 1960).

Moiré fringes are the pattern of relatively broad equidistant bands produced when two gratings with equal-line spacings are placed face to face, but with the sets of lines not quite parallel to each other. When one of the gratings is moved in the direction at right angles to the lines on it, the fringes move through exactly one fringe spacing as the fringe moves through one grating-line spacing. The variation in brightness as the fringe moves can be detected by a photoelectric cell and the linear movement can therefore be converted into a corresponding electrical signal. Gratings can be produced with radial lines also and thus angular movement can be measured or recorded electrically. Methods for the production of gratings at a reasonable price in the quantities and sizes for industrial use have recently been developed, and copies of master gratings produced at the National Physical Laboratory and National Engineering Laboratory are now available commercially. For most engineering applications gratings with about 1,000 lines per inch are required, but gratings up to 10 in. long with up to 10,000 lines per inch or even glass gratings up to 3 ft. long for special purposes can be produced.

Since moiré fringes are produced by very many accurately spaced grating lines and the effect of any errors of spacing of individual lines is reduced by the averaging process which occurs in the production of fringes, great accuracy in measurement is obtainable by using the fringes. Both analogue and digital systems can be used to handle the photoelectric signals, and various applications related to the automatic positioning of machine tools are described in the booklet. It is emphasized that the successful use of moiré-fringe systems requires specialized optical and electronic techniques and that to obtain maximum advantage from the use of moiré fringes in the machine tool field, close co-operation is required between the mechanical engineer and optical and electronic experts. Future developments of the application of the moiré-fringe technique may revolutionize the design of machine tools and the accuracy of their products.

The secondment of members of the staffs of industrial firms to the National Physical Laboratory and National Engineering Laboratory would be a particularly valuable way of speeding up progress, and the laboratories extend, in the booklet, an invitation to firms with electronic, optical or engineering interests to work with them on projects of mutual interest.

GRAFT VERSUS HOST REACTIONS ON THE CHORIOALLANTOIC MEMBRANE OF THE CHICK EMBRYO

By SIR MACFARLANE BURNET, O.M., F.R.S., and DEBORAH BURNET

Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia

THE clonal selection theory of immunity[1] in its present form postulates that in the normal animal a large proportion (perhaps all) of the mesenchymal cells could be divided into clones, each of which is pre-adapted to react with one or other of two antigenic determinant patterns. (The alternatives of being able to react with one, three or four such determinants have not yet been excluded.) The initial distribution of these reactivities is essentially at random, and in the present context there is no call to discuss how the patterns have arisen or how this random distribution to the ancestors of the marked clones could be accomplished. By hypothesis, in the adult there are no clones which can react with normal accessible components of the individual concerned, but there are present clones representing all types of antigenic determinant not present in the body.

Antibody production is presumed to occur in two phases corresponding (1) to the inductive phase and (2) to the productive phase of orthodox immunological theory. In the inductive phase two processes occur: there is proliferation of the clone to produce many more members and the newly produced cells have an increased reactivity with the corresponding antigenic determinant. In the second phase, renewed contact with the antigenic determinant results in proliferation, conversion to the plasma cell form and production of antibody.

According to orthodox immunological theory (for example, ref. 2), the interpretation of the secondary productive phase is not significantly different

from one based on clonal selection. For quantitative experiments on antibody production, it is almost obligatory to use the secondary phase simply in order to have an adequate concentration of antibody. No possibility, therefore, exists of differentiating directly between the two theories by any experiments in which serum antibody is measured.

For the inductive phase, we have two very different conceptions. On the 'instructive' Landsteiner–Pauling theory the period is occupied by the entry of antigen into macrophages, its conversion into a template form and its transfer to plasma cells in one form or another. On the clonal selection theory the inductive period represents the time needed for stimulated cells of pre-existent clones to multiply to a detectable level and in the process increase their reactivity so as to respond by antibody production to a new stimulus.

To differentiate between the two theories we need to find a technique by which it can be shown that a given population of normal lymphoid cells is either: (*a*) uniform or nearly so in its immunological potentialities, or (*b*) contains a minute proportion of cells differentiable from the rest by their ability to react with a definable antigen.

One could establish an 'instructive' theory by showing that, no matter how small the number of lymphoid cells taken, antibody could be produced or some other definable immunological competence demonstrated against a range of antigens.

To establish a selective theory, we need the equivalent of a plating method. If we are looking for a mutant (or a contaminant) present in a bacterial culture in a proportion of 10^{-4}, the only way to detect it is to plate the culture on some medium so chosen that the normal form gives no evidence of its existence while the mutant or contaminant discloses its presence by forming a colony. Colony counts on a series of normal and differential media will allow a quantitative analysis of the different clones in any bacterial culture.

In the method we have devised for studying the Simonsen phenomenon[3] on the chorioallantoic membrane[4,5], we have something closely resembling a plating method. Briefly, blood or separated leucocytes from a normal fowl is inoculated in 0·1 ml. amount corresponding to about 5×10^5 leucocytes on to the dropped chorioallantoic membranes of 12-day chick embryos. When examined four days later, discrete focal lesions, in number usually between 10 and 100, and with a general resemblance to viral lesions such as those produced by herpes simplex, are observed.

Our own experience is in line with Terasaki's[6] finding that the cells responsible for the Simonsen phenomenon judged by splenic enlargement after intravenous inoculation are lymphocytes. His estimate that the minimum effective dose is of the order of 10^4 lymphocytes also agrees with our estimate of 2×10^4 leucocytes per chorioallantoic focus.

To be effective leucocytes must be from an immunologically mature bird; embryonic blood or spleen is inert. Further, when the donor of leucocytes and test embryos are from the same pure line, a high proportion of membranes show no foci. By analogy with a wide variety of similar quantitative methods, it can be assumed that each focus is induced by a single cell and that basically it is initiated by an immunologically competent cell which either possesses or can acquire specific reactivity against a foreign antigenic determinant in the chick embryo.

Table 1. TITRATION RESULTS USED FOR FIGS. 1 AND 2

Donor	Foci on substrain (1) membranes	Adjustment
4318 1*	0 0 0 0 0	—
2*	3 2 1 1 1 0 0 0 0 0 0	× 2
3763 1	*57 33* 5 4 4 1 1 1 0	× 1 1
2	120 100 *90 86 85 82 78 75 75* 57 52 40 34 20 15 10 3 1 1 1 1 0 0	× 0·62
3	*34 34 33 31 30* 20 15 8 7 7 1 0 0 0 0 0	× 1 5

* Counts on random membranes inoculated in parallel included 4318 (1) 40 35 30 19 (2) 36 35 26 22

Through the co-operation of Dr. J. M. Rendell and Dr. J. A. Morris, we have had an opportunity of using two relatively pure-line stocks of White Leghorns maintained at the Werribee Poultry Research Section of the Commonwealth Scientific and Industrial Research Organization. Most of the experimental work in 1959–60 was done with substrains (1) and (2) of their *B*1 line. As many workers have found, pure-line eggs tend to show a low proportion of fully viable embryos, and we have had to deal with smaller groups than we would like; but the trend of results has been quite consistent.

From a preliminary survey of results when cells from the present fowls were tested on embryos of the same group, it was clear that a large proportion of membranes showed zero or very low counts from inocula producing normal numbers of foci on unrelated embryos. Two birds of group (1), the cock 4318 used for fertilization (by artificial insemination) of the whole group and one of the hens 3763, were chosen for more detailed examination. The results are shown in Table 1. It is clear that the pattern of counts differs, 4318 producing few or no foci on all membranes, while 3763 in each experiment gave a conspicuous group of high counts as well as a large number of zero or very low counts. In order to allow consolidation of the whole series in one figure, the three experiments with 3763 were brought into conformity by taking the level of the 'high sequence' as 45, 80 and 33 respectively, and adjusting this to 50 by multiplying each observed count by the appropriate factor (1·1, 0·62, 1·5).

In the graphs, each adjusted value is shown as a dot and the distribution indicated by the use of a moving aggregate covering five digits on either side of each unit on the abscissae. Ordinates therefore represent the number of embryos showing counts over the range ± of the value indicated.

In order to provide a model against which the observed distributions can be compared, we have made the preliminary assumption that in our 'pure line' stock (1) we are dealing with two unlinked loci each with three possible alleles ABC and DEF and that antigens ABCDEF are directly related to the corresponding genes. There are probably many other genetic models which could replace this one but it is preferred merely as being simple to handle. By the clonal selection theory each bird will have lymphocytes of those patterns among a, b, c, d, e, f, which correspond to the antigens not present in its cells. If we have a bird of genetic constitution AA/DD, its relevant clones will be of patterns *b*, *c*, *e* and *f*, while AB/DE will have only *c* and *f*. We assume that our flock has come to approach the degree of homozygosity indicated by AA/DD so that although all genes are present the combinations AA and DD are four times and AB and DE twice as frequent as any of the others. If a sire AB/DE covers a flock of such composition one can deduce the distribution of

genotypes among the embryos from eggs he has fertilized. We can also assume that in any given blood sample the proportion of cells in the allowable clones will have some characteristic value not necessarily the same for each clone. By a process of trial and error to find conditions that will fit the observations, we have arbitrarily assigned to our two 'pure-line' donors cock 4318 and hen 3763, the constitutions shown in Table 2. The sort of counts of foci that would be obtained by this hypothesis on embryos sired by 4318 from a flock of the type postulated can be seen from Table 3. On a random set of embryos produced under the conditions mentioned earlier, one can readily calculate the distribution to be expected with these two sets of leucocytes.

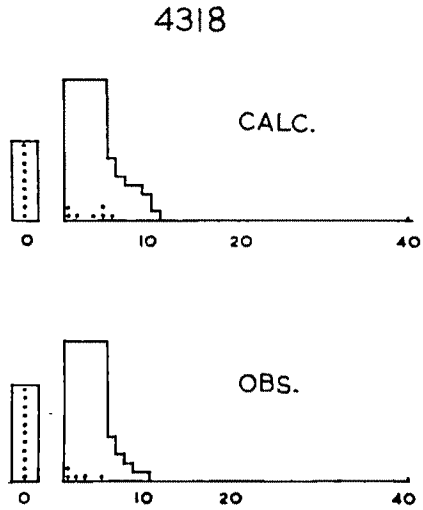

Fig. 1

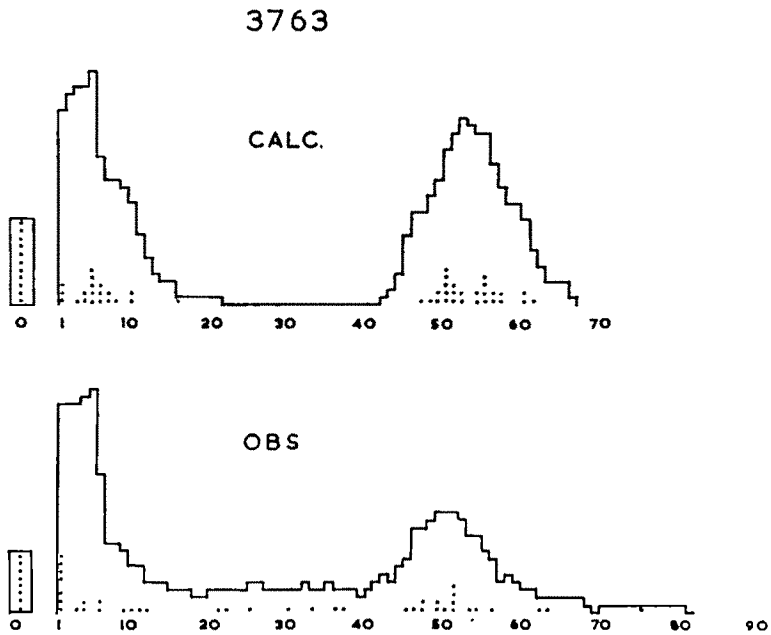

Fig. 2

Figs. 1 and 2. Distribution of focal counts when leucocytes from birds shown—4318 (*m*) and 3763 (*f*)—were tested on chorioallantoic membranes of the same pure line. Each dot represents one count of the value shown by the abscissæ and the line is a moving aggregate to include the number of counts within the range ± 5 of each value. Calc.: the results expected from the assumptions described in the text

Table 2. Hypothetical Constitution of Donors of Leucocytes

Bird	Genotype	Antigens	Clones and number of cells per 0·1 ml.
4318	AB/DE	ABDE	*c*(5) *f*(1)
3763	AA/DD	AD	*b*(50) *c*(5) *e*(5) *f*(1)

Table 3. Calculated Counts of Foci on Different Embryo Genotypes

Embryo genotype	Counts from standard inocula from	
	3763 AA/DD	4318 AB/DE
AA/DD	0	0
AA/DE	5	0
AB/DE	55	0
AB/EF	56	1
BC/EF	61	6

These calculated distributions are compared directly with those observed experimentally in Figs. 1 and 2, which show that by appropriate assumptions it is possible to obtain an excellent agreement between observed and calculated results. The agreement itself is unimportant but the general character of the experimental distribution is unmistakable and significant.

With completion of the laying period of the fowls used in the 1959–60 studies, the birds were divided into pairs and reciprocal skin grafts made. These tests made in collaboration with Dr. J. K. Dineen involved 20 double tests. The overall results were: 6 (15 per cent) rapid rejection, 25 (62·5 per cent) slow rejection and 9 (22·5 per cent) prolonged survival beyond 30 days. This is in accord with the degree of heterozygosis to be expected from the results of the chorioallantoic membrane tests.

The findings so far discussed were made in season 1959–60. With the availability of new-season birds of the next generation, we have now been able to obtain similar patterns of segregation, in groups descended from both substrains (1) and (2) of 1959–60. In one set of tests an unusually large set of eggs of group (2) allowed the use of several embryos of identical parentage. The embryos were all sired by cock 106 on seven of his full sisters, and were tested with leucocytes of the sire and of one of the hens 4442. The results are shown in Table 4. Other tests have shown that patterns similar to those obtained with substrain (1) (3763 and 4318) can be obtained with birds and embryos of the same substrain of the 1960–61 stock. Again as in the previous year when substrain (2) leucocytes are tested on substrain (1) embryos, there is no significant reduction in focal count below that obtained on random embryos. In expressing the results in provisional genetic form, different symbols must therefore be used for the two substrains.

For substrain (2), the symbols PQR may be used for the genes and antigens concerned. If we neglect all low counts, the results in Table 4 can be expressed in terms of 2

Table 4. RESULTS OF TESTS ON INBRED LINE (2), 1960–61 SEASON

Leucocyte donor	Tested on embryos	Focal counts	Random control. median count
106 (M)	683 × 106	1, 1, 1, 0, 0	52
,,	4385 × 106	4, 2, 1	
,,	4525 × 106	150, 123, 0, 0	
4326 (F)	276 × 106	65	70
,,	4326 × 106	5, 5, 2, 1, 0	
,,	4525 × 106	0	

alleles only—birds 106, 683, 4326 and 4385 can be classed as PP with leucocytes of reactivity *q*, 4525 being PQ and 276 PQ or QQ. Obviously minor interactions also take place, but these need not be elaborated on here.

These finding are in accord with what would be predicted on three assumptions: (*a*) that preadapted immunologically competent cells, presumably lymphocytes, are present in normal fowl blood and that the immunological patterns they carry correspond to antigenic determinants not present in the donor; (*b*) that the focal lesions are initiated by an immunological reaction; (*c*) that tissue antigens in chickens are genetically controlled. Since no immunologist is likely to dispute (*b*) and (*c*), the results can be claimed as providing at least *prima facie* support for the clonal selection theory.

If one seeks to interpret the present findings on any other general hypothesis of immunity or antibody formation, the following points seem to be relevant: (1) The histological development of foci suggests strongly that the effective cell initiates the focus, presumably by starting to multiply, within a few hours of lodgment on the chorioallantois. 'Recognition' that the cell is in contact with a foreign antigen is therefore a rapid process. (2) Washed cells are effective so that Jerne's selection theory[7] cannot be invoked. (3) If the clonal selection theory is not accepted, each effective cell must carry all the necessary information to recognize the foreignness of its surroundings and then develop an immunological reactivity directed against the foreign element.

By appropriate *ad hoc* qualifications it would undoubtedly be possible to describe our findings in terms of an instructive hypothesis of the Landsteiner–Pauling type or of a selection theory by which each mesenchymal cell carried all potentialities of immunological reactivity. The advantage of the clonal selection hypothesis lies simply in the natural fashion with which it covers the results.

The most important points against the clonal view that we have been able to recognize in the present results are: (*a*) Allowing for a 'plating efficiency', which is probably below unity, the number of foci obtained when by hypothesis only one foreign antigenic determinant is present is sometimes higher than it seems reasonable to expect. (*b*) Just as many, or more, foci are produced when there can be only one foreign antigen as are obtained on random embryos where there should be several foreign antigenic determinants.

Both findings suggest that the number of cells capable of initiating lesions in response to the antigenic determinants involved is not determined wholly by random processes. We can reasonably hope that with progressive clarification of the immunogenetics of our system, it will become possible to examine in some detail the processes which determine focal counts and by implication the proportion of immunologically competent cells. Irrespective of theories of immunity, the special virtues of the chorioallantoic membrane system can scarcely fail to provide important opportunities to improve understanding of cellular immunology.

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DEVELOPMENT OF A SUB-LINE OF MOUSE SARCOMA-180 CAPABLE OF GROWING IN PYRIDOXINE-DEFICIENT ANIMALS

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THE occurrence of various adaptive processes in populations of neoplastic or bacterial cells is indicated by the tendency of such cells to increase their capacity for growth under adverse conditions. Changes in the growth capacity of neoplastic cells have been associated with the development *in vitro* and *in vivo* of tumour sub-lines resistant to treatment with antimetabolites. Several observations indicate that available antimetabolites of pyridoxine and folic acid do not always duplicate the effects of the nutritional deficiency of these vitamins[1–3]. In experiments described here, a nutritional depletion of an essential factor *in vivo* has been used, to our knowledge, for the first time as a selective pressure to alter the growth capacity of mammalian cells.

During work on the influence of vitamin deficiencies on experimental tumours in rodents, a high incidence of complete regression of mouse sarcoma 180 (*S*-180) following impairment of tumour growth was observed in Swiss mice which were fed a pyridoxine-deficient diet[4]. These observations provided a basis for attempting the selection of a sub-line of *S*-180 capable of growing in the deficient animals. The development of such a tumour was achieved following repeated transplantations in vitamin B_6-depleted mice.

Mammalian cells cultured in a semi-synthetic medium have a definite requirement for pyridoxine[5]. A similar requirement for the optimal growth of tumours may be indicated by the impaired growth of some induced and transplantable tumours in animals depleted of this vitamin[4,6–9]. Inhibition of growth and occasional regressions also occurred when, in addition to receiving the deficient diet, the tumour-bearing animals were treated with the pyridoxine

antagonist, 4-deoxypyridoxine[10–15]. Experiments were carried out in this laboratory on several transplantable tumours using dietary depletion alone to avoid any non-specific effect which may be associated with treatment with such antagonists. Marked retardation of neoplastic growth was observed in most cases; this effect, however, was transient. In some instances the sensitivity of different hosts to the vitamin deficiency did not permit a selective anti-tumour effect[16]. The impairment of *S*-180 in pyridoxine-deficient *HaICR* Swiss mice was striking, however, not only because the growth of the tumour was selectively inhibited, but also because 30–80 per cent of the implanted neoplasms regressed completely after initial growth[4]. Of several thousand compounds tested for activity against *S*-180, a limited number of these depressed the rate of growth of this tumour. Complete resorption of *S*-180 has been observed, however, only after treatment with 6-mercaptopurine and related purine analogues[17]. Thus, the regression of this tumour in pyridoxine-deficient animals is of particular interest.

The sub-line of *S*-180, designated *S*-180/B_6, was developed over a period of eight months by a gradual increase of the severity of vitamin depletion of the host mice. The standard procedures followed for the implantation of the tumours, the evaluation of tumour growth, and the preparation of the purified diets have been described previously[4]. Tumours were implanted into groups of 3–5 mice. In initial experiments *S*-180 was implanted in mice which were fed the pyridoxine-deficient diet beginning two weeks prior to implantation; this period of dietary depletion has been, in our experience, the minimum one which caused significant effects on the tumour[4]. These neoplasms, however, were invariably lost on two to three repeated transplantations into similarly depleted mice. Further attempts were successful when the period of depletion of the animals in which *S*-180 was to be implanted was prolonged gradually.

The growth of the tumour at different stages during the process of selection is indicated in Fig. 1 by the size of the tumours on the 8th day after implantation. In Fig. 2, progressive rate of growth of successive implants is shown. The sub-line was developed as follows. An 8-day-old *S*-180 tumour (8·3 mm.) grown in mice which were fed a complete diet was transferred

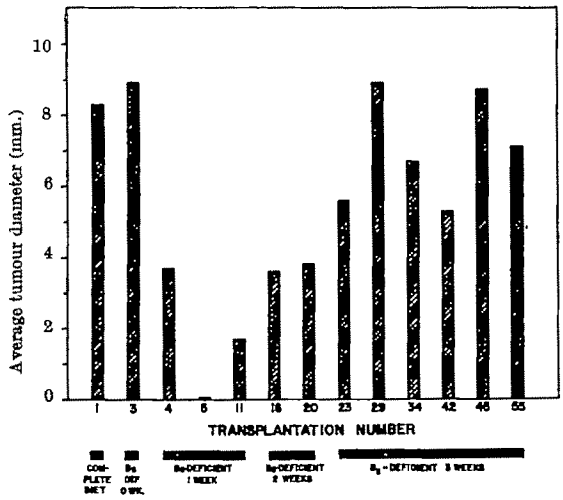

Fig 1 Selection of a sub-line of *S*-180 capable of growing in pyridoxine-deficient mice

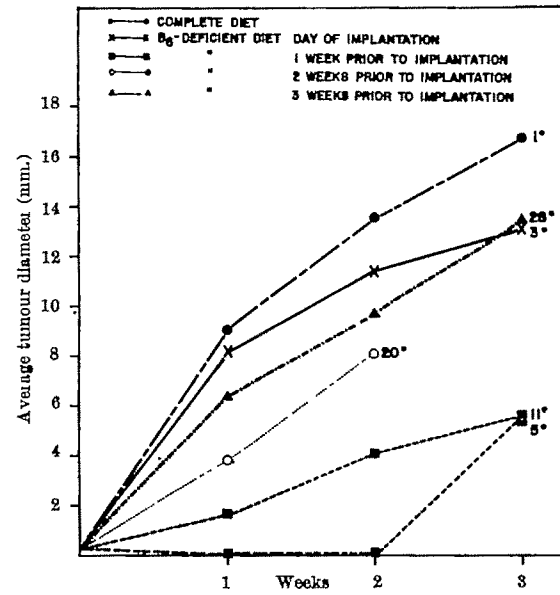

Fig. 2. Growth of *S*-180 during the course of successive implantations in pyridoxine-deficient mice

* Serial numbers of transplantation from the beginning of the experiment

to mice fed the deficient diet from the day of implantation. On the 8th day of growth these tumours (7·8 mm.) were implanted in mice which were then fed the deficient diet (transplant No. 3). Eight days later the tumours (8·9 mm.) were implanted in mice fed the deficient diet starting one week prior to implantation. When these tumours were 8-days old (3·7 mm.) they were implanted again in similarly depleted mice (transplant No. 5). The tumour did not grow for 2 weeks (see Fig. 2); during the 3rd week 1 tumour out of 3 grew to a size of 5·4 mm., and this tumour was transferred to mice depleted of pyridoxine for 1 week before implantation. Following the next 5 successive transfers in similarly depleted mice, the tumour reached a size larger than 4·0 mm. in 2 weeks and was transplanted at the end of this period. Growth following transplant No. 11 is shown in Figs. 1 and 2. At this point the rate of growth of the tumour seemed well stabilized, and transplantations into mice fed the deficient diet for 2 weeks prior to implantation were begun. The rate of growth of the tumour increased gradually during the 9 subsequent passages (the size of the tumour was 4·2 mm. 2 weeks after transplant No. 12 and 8·1 mm. 2 weeks after transplant No. 20). From transplantation No. 21 on, the tumour was repeatedly implanted in mice which were fed the deficient diet for 3 weeks prior to implantation. At transplantation No. 23 and thereafter, the tumour reached a size larger than 5·0 mm. in 1 week and was always transplanted at the end of this period (growth following transplantation No. 28 is shown in Fig. 2). Growth was variable in subsequent transplantations (see Fig. 1), but in every instance the tumour, now called *S*-180/B_6, maintained its capacity to grow in the deficient mice. This tumour is currently carried in our laboratory in mice fed the pyridoxine-deficient diet beginning 3 weeks prior to implantation and is now in its 125th passage.

Simultaneous transplantations of *S*-180/B_6 into the right axilla and of *S*-180 into the left axilla of the same deficient or normal animals were performed at

Table 1. GROWTH OF S-180/B_6 AND S-180 IMPLANTED BILATERALLY IN THE SAME MICE FED A COMPLETE OR A PYRIDOXINE-DEFICIENT DIET*

Diet	8th day after implantation Av. tumour diam ± S.D		15th day after implantation Av. tumour diam. ± S D.		Week preceding death† Av. tumour diam. ± S.D		No. of regressions	
	S-180/B_6 mm.	S-180 mm	S-180/B_6 mm	S-180 mm.	S-180/B_6 mm.	S-180 mm	S-180/B_6	S-180
Complete	8 3 ± 0 8	10 4 ± 1 4	11 5 ± 1·1	10 0 ± 2·0	9 7 ± 1 9	9 7 ± 1 1	0	0
Pyridoxine-deficient	7·7 ± 0 6	2 0 ± 0 6	11 8 ± 2·0	1 4 ± 2 1	15 4 ± 5 0	2 4 ± 3 1	0	5

* The purified diets were fed starting 3 weeks prior to implantation Ten animals were used in each group. Transplant No. 28 of S-180/B_6 was used in this experiment

† The figures shown were derived from the last measurements of the palpable tumours which were taken prior to the death of the animals. The mice fed the complete diet died as a consequence of tumour growth during the 2nd and 3rd week after implantation; those fed the deficient diet died during the 2nd to the 5th week after implantation

the 28th passage of S-180/B_6 (Table 1). S-180 and S-180/B_6, implanted bilaterally in animals fed the complete diet, grew at a comparable rate. In contrast, when the two tumours were implanted simultaneously in the same pyridoxine-deficient mice, S-180/B_6 grew progressively whereas S-180 was greatly impaired and regressed in half of the animals. A similar test using 10–30 mice per group was performed at the 23rd, 41st, 57th, 72nd, 81st and 104th passage of S-180/B_6 with comparable results. Similar differences of growth were observed when the two tumours were implanted in separate mice fed complete or pyridoxine-deficient diets. This observation excluded the possibility of any interference of one tumour on the growth of the other when both of them were implanted bilaterally in the same mice.

The results reported above clearly indicate that S-180/B_6 is capable of growing progressively in deficient mice in which S-180 is greatly impaired. If this adaptation concerns an alteration in metabolism involving pyridoxine, the pertinent biochemical changes would be of particular interest. If, on the other hand, the selection *in vivo* involves the outgrowth of cells less influenced by host defence mechanisms, an opportunity is provided for the study of factors modifying the tumour–host relationship.

Following partial hepatectomy of pyridoxine-deficient rats, the content of vitamin B_6 in the regenerated liver was similar to that of the surgically excised portion of the same organ, suggesting that the vitamin might be transferred to the liver from other tissues[18]. Similarly, the adapted tumour might have greater capacity than the parent tumour to bind pyridoxine derivatives. Therefore, the vitamin B_6 content of the two tumours was measured. Both S-180 and S-180/B_6 tumours, grown in deficient hosts, had a similar low content of total vitamin B_6 (Table 2). The striking difference in rate of growth of the two tumours in the same deficient host, despite the similar vitamin content of the two tissues, infers that differences in the efficiency of enzymatic reactions related to growth might occur. Since such differences could be associated with the function of specific forms of the vitamin, experiments are in progress in collaboration with Dr. James A. Bain of Emory University to measure the content of pyridoxine, pyridoxal, pyridoxamine and their phosphorylated derivatives in S-180 and S-180/B_6.

Table 2. PYRIDOXINE CONTENT OF S-180/B_6 and S-180 FROM ANIMALS FED COMPLETE AND PYRIDOXINE-DEFICIENT DIETS

Tumour	No. of assays*	Average content of pyridoxine ± S.D. Complete diet†	Pyridoxine-deficient diet†
		μgm. per gm. wet weight	
S-180	12	0 66 ± 0·16	0 17 ± 0 07
S-180/B_6	8	0 78 ± 0 24	0 14 ± 0 04
S-180‡	1	0 50	0 14
S-180/B_6‡	1	0 50	0 12

* For each assay, 5 to 20 tumours of each experimental group were pooled on the 8th day after implantation The microbial assay (*Saccharomyces carlsbergensis*, ATCC No. 9080) measures the total content of the different forms of vitamin B_6 following acid hydrolysis of the samples. All values are related to pyridoxine as the free base.

† Diets were fed starting 3 weeks prior to implantation.

‡ Tumours were implanted bilaterally in the same animals.

Although the Swiss mouse is not genetically homogeneous and S-180 is not, therefore, truly compatible with this host, this tumour does not normally regress in these animals. Indeed, regressions were not observed even after treatment with compounds capable of depressing markedly the rate of growth of S-180[19,20]. As mentioned previously, regressions of this tumour in Swiss mice following chemotherapy were observed only in animals treated with certain purine analogues[17]. The observation that cortisone prevented the regressions of different tumours induced by 6-mercaptopurine suggested that this effect was partially dependent upon host factors[21]. The regression of S-180 in Swiss mice depleted of pyridoxine seems also partially dependent on host mechanisms directed against this tumour. Indeed, treatment of the depleted mice with cortisone[4], and total-body irradiation of the depleted animals prior to tumour implantation[22] markedly reduced the incidence of regression of S-180. That the Swiss mouse possesses potential defence mechanisms against S-180, which can become evident in certain experimental conditions, was suggested, also, by the regression of this tumour in mice treated with 'Zymosan'[23] or infected with BCG (Bacillus Calmette-Guérin) as long as two months prior to tumour implantation[24]. Although the nature of these defence mechanisms has not yet been clarified, the possibility exists that the regression of S-180 in Swiss mice depleted of pyridoxine may be, in part, the result of a change in the immunogenetic balance between this tumour and this host. This change might occur either by a change of 'antigenicity' of the tumour, or by some alteration of the host responses to the tumour. Indeed, in either case, the development of S-180/B_6 may be somewhat similar to the changes in immunogenetic specificity and growth capacity of a tumour which have been observed during growth under various selective pressures[25].

The delayed emergence and gradual development of a tumour capable of growing in pyridoxine-depleted hosts is reminiscent of the pattern of growth observed during the development of drug resistance by a transplantable leukæmia[26]. This analogy suggests the possibility that a similar selection from a mixed population of cells has conditioned the development of S-180/B_6.

The development of this sub-line of S-180 provides experimental material for further study of the contribution of metabolic or immunogenetic factors to the altered growth capacity of a mammalian tissue.

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BIOCHEMISTRY OF BOVINE KETOSIS: THE THERAPEUTIC USE OF FUMARATE AND CYSTEAMINE

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THE principal biochemical symptoms of bovine ketosis are a high level of ketone bodies in the body fluids and a hypoglycæmia of variable severity; a considerably lowered hepatic glycogen-level has also been observed[1]. There are reasons for believing that the enforced milk production in the post-parturient animal imposes a severe strain on its carbohydrate and fat metabolism, and that ketosis constitutes an aggravation of this metabolic imbalance.

Suboptimal Reaction-rates in the Citric Acid Cycle. We have shown (ref. 2) that the citrate-level in the serum of ketotic animals is only approximately 20 per cent of the normal. As a working hypothesis, it was suggested that this finding could signify a diminished rate of condensation of acetyl coenzyme *A* with oxalacetate to form citrate (Fig. 1). In support of this, it will be seen from Fig. 2 that when the citric acid cycle was stimulated by injections of sodium fumarate into ketotic animals, the citrate concentration increased to attain a normal level. One of the principal reasons for such a diminished utilization of acetyl coenzyme *A* in the cycle was thought to be its competitive use for fat synthesis in the post-parturient animal. In this, at the peak of milk production, the utilization of acetyl coenzyme *A* for the formation of fat may take preference over that for citrate synthesis (Fig. 1). An over-production of acetyl coenzyme *A* through activation of large quantities of ruminal fatty acids by coenzyme *A* would, according to accepted views[3,4], lead to excess formation of ketone bodies; another contributing factor may be a diminished supply of reduced pyridine nucleotides (see below). Some evidence for the preferential direction of acetyl coenzyme *A* towards fat metabolism is provided by the accumulation of coenzyme *A* in the lactating gland[5]. Attempts were made to shift the equilibrium between the two competitive reactions of acetyl coenzyme *A* towards the citric acid cycle in the ketotic animal by administering fumarate, which would stimulate the cycle and, in particular, would provide an extra supply of oxalacetate for the condensation with acetyl coenzyme *A*. From Fig. 3 it will be seen that this treatment had the expected effect, namely, that the level of the ketone bodies in the serum was considerably reduced.

Although the diversion of the metabolism of acetyl coenzyme *A* from its oxidative path towards fat synthesis is considered to be one of the general causes of the apparent suboptimal reaction-rate in the cycle, there is also some evidence for an interference with two specific reactions in the cycle, namely, with the oxidation of pyruvate and with that of oxoglutarate (Fig. 1); for we have shown[2] that in bovine ketosis the levels of both these oxo-acids were several hundred per cent greater than normal and that that of succinate was considerably depressed. The idea of a retarded oxidation of these oxo-acids suggested itself. Both reactions proceed by a common unique mechanism and require the same

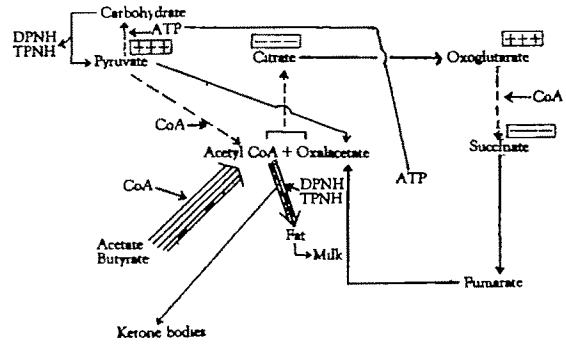

Fig. 1 Metabolic pathways relevant to bovine ketosis. Reactions represented by broken lines are believed to occur at suboptimal rates. + + +, in rectangle, elevated serum levels; — — —, in rectangle, depressed serum-levels

co-factors, among them coenzyme *A*. This, as pointed out above, is used in the post-parturient animal to a great extent for the activation of ruminal fatty acids and is partly lost through milk secretion[6,7]. These considerations led us to envisage the possibility that the interference with the oxidation of pyruvate and of oxoglutarate in ketosis may be caused by a reduced availability of coenzyme *A*. The idea is supported by the work of Peeters *et al.*[8], in which the authors showed a diminished acetylating power of ketotic cows, as ascertained by their excretion of acetylated sulphanilamide. Moreover, Gallagher[9] has recently demonstrated a subnormal level of coenzyme *A* in the livers of ewes suffering from ketosis. The above hypothesis was tested by injecting into ketotic animals small quantities of cysteamine, which in certain reactions possesses coenzyme *A* activity[10]. From Fig. 4 it will be seen that this treatment caused a rapid fall in the serum-levels of pyruvate and oxoglutarate. On the other hand, treatment with fumarate proved to be ineffective in this respect, leading to an even greater increase in the levels of pyruvate and oxoglutarate. This was to be expected if one accepted the view that fumarate stimulated the cycle without, however, overcoming the interference with the oxidation of the two oxo-acids.

Both forms of treatment, as shown in Figs. 2 and 3, led to a disappearance of the other abnormal biochemical symptoms investigated—cysteamine treatment more rapidly than fumarate treatment. Among

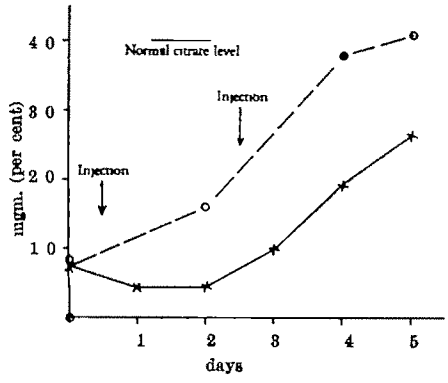

Fig. 2 Changes in the serum levels of citrate during treatment of cows suffering from ketosis with fumarate (20 gm. in 450 ml. water, injected subcutaneously), ———, and cysteamine (750 mgm. in 250 ml. water, injected intravenously), - - - -

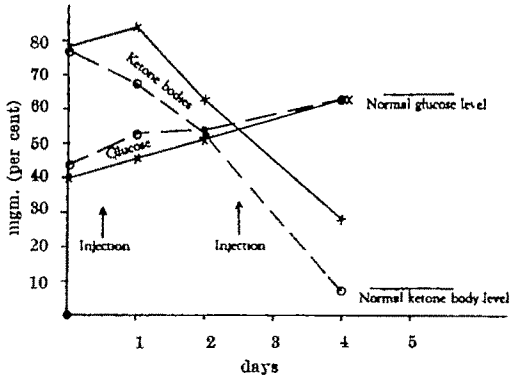

Fig. 3. Changes in the serum levels of glucose and ketone bodies during treatment of cows suffering from ketosis with fumarate, ———; cysteamine, - - - -. Dosages as in Fig. 2

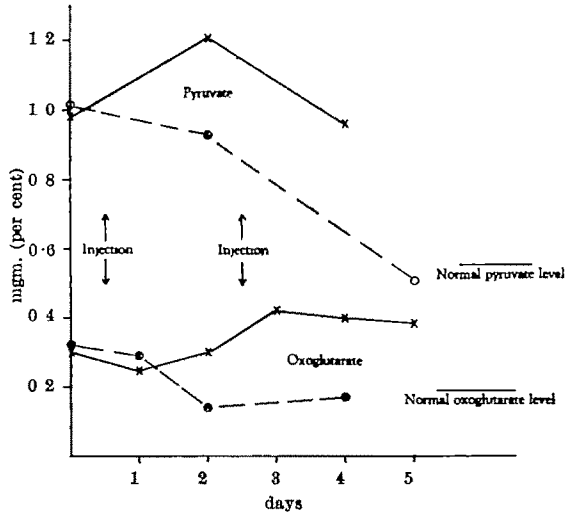

Fig. 4. Changes in the serum levels of pyruvate and α-oxoglutarate during treatment of cows suffering from ketosis with fumarate, ———; cysteamine, - - - -. Dosages as in Fig. 2

the symptoms of recovery was an immediate rise of the abnormally low level of glucose in the serum. These low levels may be caused by an interference with the adenosine triphosphate-requiring *synthetic* mechanism, since in bovine ketosis the *degradation* of glucose appears to be proceeding at a normal rate[11]. It can therefore be argued that an increase in the formation of adenosine triphosphate through stimulation of the cycle could raise the level of hepatic glycogen and that of blood glucose. Furthermore, with more glucose present for the purpose of degradation, more reduced pyridine nucleotides should become available for the reduction of acetoacetyl coenzyme *A*, which in turn would lead to a decrease in the level of ketone bodies, since an inverse relationship appears to exist between the degree of anaerobic degradation of carbohydrate and the accumulation of ketone bodies[12,13].

Therapeutic Experiments. Of 16 animals treated with sodium fumarate, 14 responded to the treatment and recovered within 7–10 days. All the 33 cases of primary ketosis treated with cysteamine responded rapidly and recovered within 3–6 days. Figs. 2–4 refer to pairs of animals which, for the sake of comparison, were selected for the similarity of the pre-treatment-levels of their serum components. However, the course of recovery shown in these graphs was very similar in all recorded cases, full details of which have been published elsewhere[14].

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SELF-DECOMPOSITION OF COMPOUNDS LABELLED WITH RADIOACTIVE ISOTOPES

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IT is quite evident that before an isotopically labelled compound can be profitably used its purity must be known. This will normally be determined following the preparation of the material and, if it is purchased, the information will be provided by the commercial supplier. However, if the material is not used at once, it may undergo significant decomposition under the influence of its own radiation, and there are some aspects of this problem of which we feel users of tracer compounds are insufficiently aware. It is true there is a substantial literature on radiation chemistry generally, but most of it is concerned with irradiation of solutions rather than of pure organic substances, while the actual phenomenon of radiation self-decomposition has been dealt with in relatively few papers[1-5]. The object of this article is to analyse the problem with particular reference to carbohydrates and to present some further quantitative information.

It is important to distinguish in what follows between a chemical and a radiochemical impurity, and to be clear what is meant by the latter. We define a radiochemical impurity as being any radioactive species other than the declared isotope in the stated position(s) of the given compound. In passing, we may note that it commonly happens that a small quantity of radiochemical impurity can be critical whereas a comparable amount of inactive impurity is unimportant.

Types of Self-decomposition

The decomposition of a compound labelled with a radioactive isotope can be due to one or more of four effects:

(i) Primary (internal) radiation effect, that is, the decomposition or transformation of a molecule caused by the disintegration of one of its unstable atomic nuclei. This atom, transformed into another element, might or might not be eliminated from the molecule. However, in either case, providing the daughter nuclei are stable, this will only give rise to a radiochemical impurity if the molecule contains a further radioactive atom.

(ii) Primary (external) radiation effect, that is, the decomposition or transformation of a molecule by interaction with a nuclear particle. If the molecule is a labelled one, this will contribute to the radiochemical impurity.

(iii) Secondary radiation effect, that is, the decomposition or transformation of a molecule of the labelled compound due to its reaction with reactive species, for example, free radicals, produced as a result of primary radiation decomposition. The reactive species may not necessarily be produced from the labelled compound but from its environment, for example, residual water in freeze-dried samples.

(iv) Chemical effect, that is, the decomposition or transformation of the radioactive material caused by chemical reactions which are not connected with radiation. Clearly, this is a hazard faced by any chemical compound, but it may be more probable in the case of a labelled one for several reasons. First, in an effort to obtain a good yield of material of high specific radioactivity, the highest chemical purity is not always achieved, and it is often difficult or expensive to determine this purity. The impurities may then react with the compound. Further, the small amount—possibly only a few micrograms—of radioactive material which is commonly synthesized or distributed by suppliers may suffer chemical decomposition in unexpected ways which would not normally be observed with larger quantities. It could be due, for example, to the atmosphere above a solid, or non-inertness of the container.

Magnitude of the Radiation Effects

The magnitude of the primary (internal) effect can be calculated in any particular case from the available data. Commonly it is a greater practical concern to know the amount of radiochemical impurity produced, and this can be calculated if the pattern of labelling is known. An example of this is given in the subsequent section on macromolecules.

One of the factors influencing the amount of decomposition due to primary (external) and secondary effects is the fraction of its own radiation energy absorbed by the labelled material. For a pure β-emitter distributed over a relatively large area in a layer of even thickness l (cm.) this fraction, F, is given by:

$$F = \frac{pl}{2r}\left(1{\cdot}5 + \ln\frac{r}{pl}\right)$$

where p is the density (mgm. cm.$^{-3}$) and r is the mean range of the particles, expressed in mgm.cm.$^{-2}$ units. In this it is assumed that $r \nless pl$ and that all particles have the energy corresponding to their mean energy. A more exact value may be obtained for definite values of p and l using a known beta-spectrum, but the error is generally small. No allowance is made for back-scatter from the container or for edge effects, though for a given area these latter will, of course, be of increasing significance with increasing energy of the β-particle. The calculation involves determination of the average range of a β-particle by a double integration, the first for the solid angle around a point in a layer of the material, and the second for the contribution of all layers throughout the thickness of the solid.

The magnitude of decomposition (per cent) due to the primary (external) radiation effect is $\{1 - \exp(- F\epsilon a s_0 t. 6{\cdot}14 \times 10^{-16}\} 100$, where F is the fraction of its own radiation energy absorbed by the compound, ϵ is the mean energy of the radiation in electron-volts, a is the number of molecules irreversibly damaged per 100 eV., s_0 is the initial specific radioactivity of the compound in curies/mole, and t is the time in seconds. For compounds labelled with relatively short-lived isotopes, the term t in this expression should, of course, be replaced by $1/\lambda \{1 - \exp(- \lambda t)\}$, where λ is the radioactive decay constant.

Remedial Measures

It is clearly desirable to reduce the magnitude of decomposition of labelled compounds to a minimum. Setting aside the decomposition due to the primary (internal) radiation effect as being beyond control, we can consider the possible remedies for the other three types of decomposition.

Considering decomposition due to the chemical effect first, it is evident that the highest possible degree of freedom from harmful impurities is desirable, consistent with the requirements for specific radioactivity. Storage under vacuum is a common and useful precaution. Attention should also be paid to the inertness of the storage vessels, particularly for liquids or freeze-dried syrups. In our experience the alkalinity of normally washed 'Pyrex' glass is detrimental to the stability of carbon-14 carbohydrate syrups. Storage at as low a temperature as possible can also help by reducing the rate of otherwise unavoidable chemical reactions.

The two fundamental methods for reducing the magnitude of primary (external) radiation decomposition are dispersion over a large area and dilution.

As already pointed out, the fraction of its own radiation energy absorbed by a radioactive compound distributed over a relatively large area is dependent on the thickness and density of the layer. Thus, the principle of such dispersion is to ensure that the nuclear particle escapes from the body of the radioactive material with the minimum interaction on the way. This method has been widely utilized in storage of labelled compounds—particularly for small quantities at high specific radioactivities—but frequently the material may need to be distributed over an area too large to be practical in order to reduce the self-irradiation to a satisfactory level.

The object of dilution is to interpose inactive molecules in the path of the radiation. This can be achieved either by adding the inactive form of the compound itself or by introducing other substances. The former avoids the necessity of subsequent isolation of the radioactive compound, but as it involves a drop in specific radioactivity it is not always acceptable.

It is not possible to suggest a universal method which will prevent the decomposition due to secondary radiation effects. However, it is evident that either dispersion over an area or dilution with the substance itself will reduce this type of decomposition, but the effect of dilution with a foreign substance will depend on the nature of that substance. On the credit side it will absorb radiation which might produce radioactive impurities, and in certain cases it may terminate chain reactions which would otherwise result in substantial decomposition following the radiolysis of a few radioactive molecules[6,7]. Conversely, if unwisely chosen, it may produce, by interaction with the radiation, reactive species which will interact with the labelled compound, and so do more harm than good. It is important to appreciate how wide is the range of susceptibilities to radiation for different compounds[4]. Storage of radioactive materials at low temperatures will usually reduce the decomposition due to secondary radiation effects, but will not, in general, completely prevent it. A high standard of chemical purity, already stressed for another reason, may also reduce this decomposition, since, although the impurity may not be harmful in itself, the products of its interaction with the nuclear particles may be. An example of such an impurity is water in the case of carbohydrates.

Observations on Carbon-14 Carbohydrates

The stabilities of samples of uniformily labelled [^{14}C]-sucrose and D-[^{14}C] glucose with relatively high specific radioactivities are shown in Table 1. The compounds were prepared by photosynthesis, purified by ion-exchange and paper chromatography and finally crystallized. No radiochemical impurity was detected in either case by reverse isotope dilution analysis, and their chromatographic radiochemical purities were both found to be 99·9 per cent. After being dispensed from aqueous solutions, samples were stored in the freeze-dried form or uniformly distributed on Whatman No. 3 paper. In either case they were contained in 'Pyrex' tubes which had been filled with water and autoclaved for 2 hr. at 15 lb./sq. in. to remove surface alkalinity. The tubes of those samples which were stored *in vacuo* were evacuated to a pressure of 0·01 mm. mercury for several hours before being sealed in order to reduce the moisture content to a minimum.

The radiochemical impurities produced during storage were determined by scanning of paper chromatograms. Spots with R_F values corresponding to those of glucose and fructose were the principal impurities in the case of sucrose.

Many other experiments covering a wide range of specific radioactivities have shown that, under given storage conditions, the amount of decomposition is proportional to the specific radioactivity, provided that the substance is not allowed to decompose too far.

A comparison of tubes 7–10 suggests that, in at least the first three of these, secondary radiation effects take a major role in the decomposition. This is perhaps not surprising, since freeze-dried glucose will retain non-bonded water as 'impurity'. Sucrose, on the other hand, can with efficient freeze-drying techniques be obtained anhydrous, and the small difference in magnitude of decomposition between tubes 1 and 2 suggests that in these cases decomposition is to a great extent due to primary radiation effects. This view is supported by the relatively high calculated value for the apparent energy required to disrupt one molecule (24 eV. for tube 2). By the same criterion the most stable freeze-dried glucose sample (tube 10) is probably still greatly susceptible to decomposition due to secondary radiation effects.

It is clear from the high $G(-M)$ values for tubes 3–6, 11, 12, that such decomposition as does occur when radioactive sugars are distributed on paper is due to secondary radiation effects, probably as a result of the moisture content of the paper. However, under optimum conditions, the overall magnitude of decomposition is markedly reduced by storage under such conditions and so, since it is easy to recover the sugar quantitatively, this method is now used to facilitate

Table 1. SELF-DECOMPOSITION OF [^{14}C]-SUCROSE AND D-[^{14}C] GLUCOSE

Compound	Tube No	Storage conditions: Form	Temp.	Pressure	Impurity observed (per cent)	Initial decomposition per year per mc./mM (per cent)	Average mass per unit area (freeze-dried) (mgm./cm.^{2})	Area of paper (cm.^{2}) (d)	Energy absorbed by sugar or sugar syrup ($F \times 100$) (per cent) (e)	$G(-M)$ value (f)
Sucrose (a, b)	1	Freeze-dried	Room	Vac	16·4	0 071	0 35	—	16	4·6
	2	Freeze-dried	−80° C.	Vac.	15·1	0 065	0 35	—	16	4 2
	3	On paper	Room	Atm.	15 7	0 068	—	21	0 3	234
	4	On paper	−80° C.	Atm.	4·9	0 020	—	21	0 3	68
	5	On paper	Room	Vac.	2·4	0 010	—	21	0 3	33
	6	On paper	−80 °C.	Vac	1 8	0 007	—	21	0 3	25
Glucose (c)	7	Freeze-dried	Room	Atm	18 9	0 77	0 2	—	10	79
	8	Freeze-dried	−80° C.	Atm.	6 0	0 23	0 2	—	10	23
	9	Freeze-dried	Room	Vac	13 1	0 51	0 2	—	10	53
	10	Freeze-dried	−80° C	Vac.	3·6	0·133	0·2	—	10	14
	11	On paper	Room	Vac.	1·2	0 044	—	47	0 05	900
	12	On paper	−80° C.	Vac	0 7	0 026	—	47	0 05	526

(a) Each tube of sucrose contained 500 μc in 1 16 mgm sucrose (149 mc. per m.mole, abundance of carbon-14 19·5 per cent) and was stored for 88 weeks. Calculation shows that primary (internal) radiation decomposition contributed 0 05 per cent to the observed impurity.

(b) Other experiments with samples of freeze-dried sucrose have shown that at −80° C. decomposition is considerably increased if the sugar is stored under atmospheric pressure instead of being sealed under vacuum. The difference is even greater with samples held at room temperature.

(c) Each tube of glucose contained 100 μc. in 0·43 mgm. glucose (42 mc. per m mole ; abundance of carbon-14 11·0 per cent) and was stored for 34 weeks. Calculation shows that primary (internal) radiation decomposition contributed 0 005 per cent to the observed impurity.

(d) The weight of the Whatman No. 3 paper was 18 mgm. cm.$^{-2}$.

(e) The fraction of the energy absorbed by the sugar or sugar syrup was calculated either (i) by using the relationship deduced above, although the geometry is some way from the ideal; or (ii) by assuming the compound and the paper to absorb all the radiation in the ratio of their weights.

(f) Defined as the number of molecules permanently altered or decomposed per 100 eV. absorbed by the sugar or sugar syrup.

the supply of carbohydrates with high specific radioactivities from the Radiochemical Centre.

An example of the varied decomposition by secondary radiation effects was recently observed by us. [^{14}C]-dextran sulphate containing c. 20 glucose units per molecule was prepared by sulphation of an appropriate [^{14}C]-dextran hydrolysate. It had the relatively low specific radioactivity of 22·4 mc. per gm. atom of carbon (c. 3 mc./m.mole dextran sulphate). It was stored in the freeze-dried form, but when inspected after three weeks it was charred and became a total loss, whereas inactive dextran sulphate did not decompose during storage for several months. The decomposition of the labelled dextran sulphate was presumably due to a secondary radiation effect arising from the prior liberation of sulphuric acid. The sulphuric acid, being fortified rather than diluted in the process, destroyed the rest of the material.

Macromolecules

We quoted earlier an expression for the magnitude of the primary (external) effect which includes a term for specific radioactivity, s_0, expressed in curies per mole. While it is, of course, true for all compounds, it is particularly important when dealing with macromolecules to appreciate that this term needs to be expressed on a molar, and not on a unit weight, basis. To illustrate this we may consider the case of some glucose, maltose and amylose (containing n glucose units), all prepared from [^{14}C]-carbon dioxide of the same specific radioactivity, and stored under identical conditions, so that the irradiation per unit mass is the same in each case. It is clear that for each destructive interaction between a β-particle and a carbohydrate molecule the impurity produced will contain x, $2x$, and nx atoms of carbon-14 respectively in the three cases. Nevertheless, if we hydrolyse such partially decomposed samples, the resultant glucose will have the same purity in each case, neglecting any effects due to other causes.

How secondary effects will vary with increasing chain-length will depend on what the result of the particular effect is. In some cases the above principle will hold, whereas in others—such as attack on reducing end-groups—it will not.

It is sometimes necessary to consider the contribution of the primary (internal) effect to the production of radiochemical impurity from a labelled macromolecule. This will depend, of course, on the pattern of labelling. For example, in a polysaccharide prepared directly from [^{14}C]-carbon dioxide, so that the labelling is statistically uniform throughout all its molecules, the number of radioactive atoms in the form of an impurity initially produced per nucleus disintegrating is the multiple of its isotopic abundance expressed as a fraction and $(n - 1)$, where n is the number of atoms of the given element in the molecule. Production of radiochemical impurity due to this cause, will, of course, fall exponentially with time, as nuclei in the resultant impurity themselves disintegrate; but it is important to appreciate that a similar compound, prepared from [^{14}C]-carbon dioxide at twice the specific radioactivity, and then diluted with an equal weight of inactive carrier, will produce a different amount of radiochemical impurity as a result of the primary (internal) effect, even though its pattern and degree of labelling appears superficially to be identical with the compound first mentioned.

The amount of radiochemical impurity arising as a result of this effect can be surprisingly large with macromolecules, even when the isotope has a long half-life. For example, a glucose polymer containing 1,000 glucose units, and prepared from [^{14}C]-carbon dioxide having the same isotopic abundance as that used to prepare the sucrose quoted in Table 1, would give rise to 0·28 per cent of radiochemical impurity in one week as a result of this effect.

Conclusion

We have not attempted to give a comprehensive review of this subject. We have rather aimed at

illustrating certain principles and have endeavoured to show that material of very high specific radioactivities can be used, and even stored, under certain conditions, but that a constant awareness of the phenomenon is called for on the part of all users of compounds labelled with radioactive isotopes.

We are indebted to Prof. E. J. Bourne, Dr. J. R. Catch, and Dr. J. S. Glover for helpful discussions.

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TRACE ELEMENTS IN AUSTRALITES

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THE chemical composition of tektites can provide much evidence about their origin. The concentrations of the major elements have been known within close limits for many years, although for some of the constituents present in low amounts, for example, sodium monoxide, the data are of poor quality[1]. A few determinations have been made of the elements present in trace quantities. Among the early investigations are those of Preuss[2,3] and Heide[4-6]. More recent determinations have been of rubidium[7,8], uranium[9,10], thorium[9], lithium, rubidium and cæsium[11] and of several elements by Cohen[12]. None of these data, except for the lithium and rubidium figures given by Cohen[12] (see Taylor[11]) is very different from terrestrial abundances, and gives any support to theories requiring an extra-terrestrial or extra-solar system origin for these interesting glassy objects. Many of the reported determinations have been carried out as a sideline to other work, or to provide evidence on a particular point, examples being the nickel and chromium determinations of Preuss[2,3]. No systematic study of one group appears to have been carried out.

In collaboration with R. D. Cherry of the Physics Department of this University, we have been studying the composition of a group of australites kindly provided by the South Australian Museum, Adelaide. The australites are a singularly suitable group for study. They cover a wide area (2×10^6 miles^2); occur, with minor exceptions, on the present surface; have been melted less than 10^6 years ago, on the basis of recent potassium–argon ages[13]; show well-preserved evidence of two periods of melting, and cover a wider range in chemical composition than any other group. Evidence is accumulating that they display a regional variation in composition[11,14].

Determinations have been completed of trace elements on 14 australites using emission spectrochemical methods of analysis following the methods outlined by Ahrens and Taylor[15]. Because of the current interest in the origin of tektites, averages of these results are presented here (Table 1) and briefly discussed in this preliminary account. The analytical techniques for the alkali elements have been described elsewhere[11]. Copper and gallium were determined using sodium as a variable internal standard, utilizing the similar volatilization behaviour of these elements in the d.c. arc. Anode excitation was employed throughout. The remaining elements, which are relatively involatile under these conditions, were determined using palladium as an internal standard. All determinations were made in duplicate, and the wave-length range of 2470–9600 Å. was covered, with a total of four exposures using Kodak 103-0 and *IN* plates. Spectrochemical determinations are particularly liable to systematic bias and it is mandatory to employ standard samples for calibration as close as possible in composition to the samples being analysed. The interlaboratory rock standards, *G*-1 (granite) and *W*-1 (diabase)[16], were selected as the most suitable. In general, they bracket the composition of the australites, and differ only in being composed of discrete minerals, in contrast to the glassy tektites. The effect of this difference has not been evaluated, but is believed to be small. Most difficulties due to matrix difference in spectrographic analysis using the d.c. arc arise from the presence of different anions in samples and standards. In fact, the d.c. arc emission spectra of the australites over the entire wave-length range bear a general resemblance to a mixture of these standards, which represent, of course, the two common igneous rock types.

The results are given in Table 1. The average of all the fourteen samples is given, with the extremes of the range in composition. The spread in composition is also expressed as a relative deviation, *C* (per cent standard deviation), and this should be compared with the analytical precision for individual determinations, given in the same units. It can be seen that the range in composition is greater than the precision of individual determinations, indicating that there are real differences in composition between individual samples[11]. The detection limits for the spectrochemical methods used are also given. Those elements for which no data are given were sought, but if present, are below the detection limits given. Table 1 also contains figures for the average abundances of the elements in igneous rocks (commonly referred to as the crustal abundance) from Ahrens and Taylor[15], in chondritic meteorites from Goldschmidt[17] (with later additions) and in shales. We wish to direct attention to the general similarity between the abundances of the trace elements in australites, and the average abundance of these elements in the Earth's crust.

Cherry and Taylor[18] suggested that the average major element composition of tektites can be closely matched by a mixture of one part quartz with three parts of the non-volatile constituents of shales. It is

TABLE 1. A COMPARISON OF THE ABUNDANCES OF TRACE ELEMENTS IN CHONDRITIC METEORITES; IGNEOUS ROCKS, AND SHALES WITH AVERAGES FROM FOURTEEN AUSTRALITES

Element	Chondrites (17) p.p.m.	Igneous rocks (15) p.p.m.	Shales (19) p.p.m.	Australites				Spectrographic detection limit p.p.m.
				Average p.p.m.	Range p.p.m.	Relative deviation C(%)	Analytical precision C(%)	
Ag	0.09	0.08	—	—				0.5
As	2	2	—	—				100
Au	0.10	0.002	—	—				10
B	1.5	3	—	—				10
Ba	8	1,000	570	655	570–805	9.5	7.7	3
Be	1	2	—	—				30
Bi	0.002	0.2	—	—				10
Cd	0·5	0.15	—	—				10
Ce	0.52	46	—	—				100
Co	800	20	18	16	13–20	10.4	9.2	2
Cr	2,200	100	110	52	35–73	22.4	9.5	1
Cs	0.13	5	5[18]	2.7	1·4–4.2	34.6	9.9	1
Cu	90	55	18	7.0	5.2–8.6	15.4	13.2	0.5
Ga	5.3	19	13[24]	8·6	6.7–11.4	16.5	7.0	3
Ge	10	1.1	—	—				5
Hg	0.10	0.08	—	—				100
In	<0.001	0.11	—	—				1
La	0.33	18	—	—				50
Li	2·7	32	55	42	37–52	11.0	7.6	0.5
Mn	1,900	1,000	620	800	670–955	11.6	7.1	5
Mo	1.5	1	—	—				10
Nb	0.5	24	—	—				30
Nd	0.63	24	—	—				10
Ni	13,400	35	64	30	25–50	22.1	4.1	5
Pb	0.65	15	20[21]	—				20
Pd	1.5	0.004	—	—				10
Pt	2.0	0.005	—	—				50
Rb	3.7	115	140[22]	84	65–99	12.1	8.3	1
Sb	0·1	0.1	—	—				20
Sc	9.4	20	14	12	8.9–16	15·6	12.5	2
Sn	1	2	—	—				20
Sr	10	450	300[20]	195	150–265	16.8	10.8	5
Th	0.03	10	—	—				100
Ti	790	4,400	4,920	4,280	3,040–5930	21.4	7.5	10
Tl	0.0014	0.8	—	—				1
U	0.05	3	—	—				100
V	39	110	120	75	58–94	14.6	5.4	5
W	—	2	—	—				20
Y	5	28	45	—				20
Yb	0.19	3	—	—				10
Zn	180	40	—	—				100
Zr	33	156	160[23]	470	370–555	12.6	7.9	10

difficult to establish average values for trace elements in shales, but Shaw[19] has considered many of the problems and his data are used, except where indicated. More recent data for strontium[20], lead[21], zirconium[22], rubidium and caesium[23], and gallium[24] are used to supplement Shaw's results. In general, the trace element data in australites are consistent with derivation from a quartz-shale mixture in which shale is the major component. The relatively higher amount of zirconium in the australites in comparison with shales may well be derived from small quantities of the resistant mineral zircon accompanying the quartz.

In conclusion, the data for chromium, nickel and cobalt given here lend no support to a derivation of tektites from meteorites, or from meteorite collisions with the Earth, or from the Moon. From considerations of the structure and density of the Moon, its overall composition is probably close to that of the chondrites. Material from the lunar surface is probably similar to that in the interior, since there seem to be no selenological processes comparable to geological ones. In addition, the surface material can be expected to be rather rich in nickel and cobalt from meteoritic collisions, and hence rather easily distinguished from terrestrial rocks. Extra-terrestrial theories for the origin of tektites must provide for the duplication of many geological processes to account for the overall pattern of trace element distribution.

Data for the individual samples, together with details of the analytical methods and determinations of the major elements by Dr. H. B. Wiik, will be discussed at length in a subsequent paper.

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A MATHEMATICAL MODEL FOR GAS-LIQUID PARTITION CHROMATOGRAPHY

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THE widespread adoption of gas-liquid partition chromatography for the separation of complex mixtures has led to much speculation with regard to the mechanism of separation. Plate theories of separation have been considered by Martin and Synge[1], Mayer and Tompkins[2], and Glueckauf[3], while continuous or rate theories have been developed by Boyd, Adamson and Myers[4], Lapidus and Amundson[5], Glueckauf[6], Klinkenberg[7], Tunitskii[8], Giddings and Eyring[9] and by van Deemter, Zuiderweg and Klinkenberg[10]. Keulemans[11] has summarized the major results obtained by both theories of chromatography. The model discussed in this article essentially includes most of the previous continuous models with the further inclusion of the effects of non-linear solubility and column pressure drop. The use of arbitrary overall mass transfer coefficients has been avoided by separating the resistance to mass transfer into two parts, one due to the gas film and the other due to the liquid film. The describing partial differential equations are:

$$\frac{\partial X}{\partial t} = E\frac{\partial^2 X}{\partial z^2} - \left(u - \frac{2E}{P}\frac{\partial P}{\partial z}\right)\frac{\partial X}{\partial z} - \frac{k_G RTA}{\varepsilon}(X - X_i) \quad (1)$$

$$c_i = K_1 X_i P + K_2 X_i^2 P^2 \quad (2)$$

$$\frac{\partial c}{\partial t} = D_L \frac{\partial^2 c}{\partial y^2} \quad (3)$$

where $X(z,t)$ is the mole fraction of solute in the gas phase, $X_i(z,t)$ the mole fraction at the gas-liquid interface, $c(y,z,t)$ the concentration of the solute in the stationary liquid phase, $c_i(z,t)$ the concentration at the gas-liquid interface, z the axial distance along the column, y the distance in the liquid film, t is time, $u(z)$ is the average gas velocity through the voids in the packed bed, $P(z)$ the total pressure, T the uniform column temperature, R the gas constant, k_G the 'Whitman' gas-film coefficient[12], E the longitudinal dispersion coefficient (cf. Taylor[13]), ε the void fraction, D_L the diffusivity of the solute in the liquid phase, and A is the area of the gas-liquid interface per unit volume of packed bed. The constants K_1 and K_2 are empirical constants in the solubility relationship.

Equation (1) accounts for diffusion in the gas phase, equation (2) represents a nonlinear equilibrium relationship between the gas and liquid phases, and equation (3) is a statement of molecular diffusion in the partitioning liquid. If the liquid film is thin and $c_m(z,t)$ is the concentration at a point midway in the liquid film, then equation (3) can be approximated by the following differential-difference equation:

$$\frac{\partial c_m}{\partial t} = \frac{D_L}{\Delta y^2}(c_i - c_m) \quad (4)$$

where Δy is half the liquid film thickness.

Numerical Solution of Equations

Equations (1), (2) and (4) have been solved numerically on the IBM 704 digital computer using finite difference techniques. The inset of Fig. 1 shows the conditions for an initial value problem in which a slug of solute of mole fraction $\bar{X}$ and length L_1 is suddenly introduced into a carrier gas stream at time $t = 0^+$ by simultaneously opening two gates. The initial conditions for this case are then:

$$X(z,0) = \begin{cases} \bar{X}, & 0 < z < L_1 \\ 0, & z > L_1 \end{cases} \quad (5)$$

$$\left.\begin{aligned} X(z,0) &= X_i(z,0) = 0 \\ c(z,0) &= c_m(z,0) = 0 \end{aligned}\right\} L_2 < z < L_3 \quad (6)$$

and the boundary conditions are:

$$\text{gas velocity} = \begin{cases} u, & L_2 < z < L_3 \\ u\varepsilon, & z < L_2 \text{ and } z > L_3 \end{cases} \quad (7)$$

$$\text{gas film coefficient} = \begin{cases} k_G, & L_2 < z < L_3 \\ 0, & z < L_2 \text{ and } z > L_3 \end{cases} \quad (8)$$

A study of the parameters that affect gas-liquid chromatography has been made using the computer programme and considering the particular case of the elution of a pure *iso*butylene slug with argon using dinonyl phthalate as the stationary phase, the column temperature and pressure being 25° C. and 1 atm. throughout. The data were as follows: $L_1 = 5$ cm., $L_3 - L_2 = 50$ cm., $L_2 - L_1 = L - L_3 = 1$ cm., $u = 5$ cm./sec., $A = 131{\cdot}2$ cm.^{2} per cm.^{3}, $\Delta y = 7{\cdot}0 \times 10^{-5}$ cm., $K_1 = 1{\cdot}14 \times 10^{-3}$ gm.-mole per cm.^{3} atm., $D_L = 6{\cdot}7 \times 10^{-7}$ cm.^{2} per sec. (cf. Funk[14] and Kesten[15]), $k_G = 10^{-5}$ gm.-mole per cm.^{2} sec. atm. Unless otherwise specified, E was taken to be equal to the molecular diffusion coefficient of *iso*butylene in argon (0·0674 cm.^{2} per sec.) as calculated by the method of Hirschfelder, Bird and Spotz[16].

Below a value of about 10^{-5} gm.-mole per cm.^{2} sec. atm., k_G was found to affect strongly both the retention time and the shape of the elution curve. However, above a value of 10^{-5}, k_G has no effect on the elution curve, indicating that in order to effect good separations, diffusion-rates through the gas film must be high. Fig. 1 clearly demonstrates that the effect of large longitudinal dispersion coefficients is to broaden the elution curve and therefore reduce the resolution without affecting the retention time.

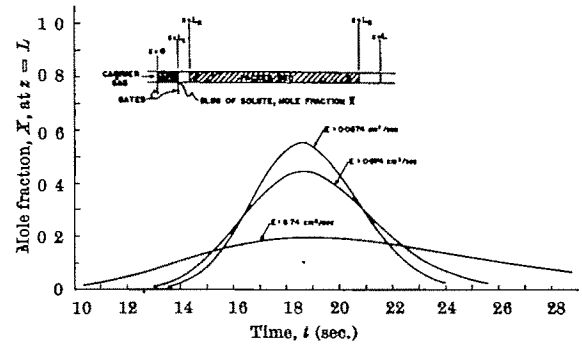

Fig 1. Effect of longitudinal dispersion coefficient

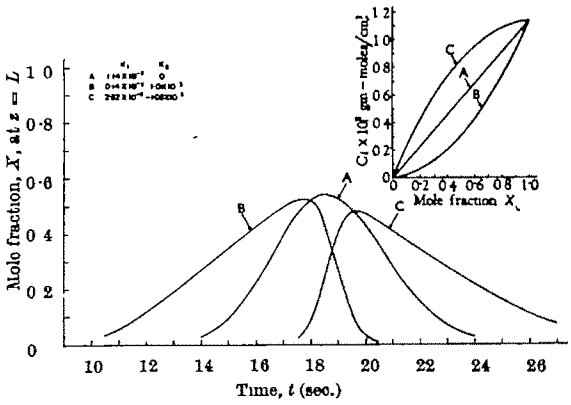

Fig. 2. Effect of non-linear solubility

Fig. 2 demonstrates that the effect of a nonlinear solubility relationship is to induce considerable skewness and tailing in the elution curve with a consequent displacement of the peak. The direction of tailing is obviously coupled to the nature of the nonlinearity.

Analytical Solution of Equations

For the special case of uniform column pressure ($\partial P/\partial z = 0$) and linear solubility ($K_2 = 0$), equations (1), (2) and (4) have been solved analytically by a transform method similar to that of Lapidus and Amundson[5]. The result, however, was found to be unwieldy; in this respect the numerical solution is easier to use and also accounts for the effects of nonlinear solubility and pressure drop.

Since the numerical solution shows that longitudinal diffusion has no effect on the retention time but only affects the sharpness of the band, the effect of physical properties on the retention time may be obtained by solving equations (1), (2) and (4) with the assumptions that $E = 0$, $\partial P/\partial z = 0$ and $K_2 = 0$, subject to the initial conditions (6) and the following boundary conditions:

$$X(0,t) = \begin{cases} 0, & 0 < t \\ \overline{X}, & b > t > 0 \\ 0, & t > b \end{cases} \tag{9}$$

A solution to this boundary value problem was obtained by Laplace transform methods and reads:

$$\frac{X(L,t)}{\overline{X}} = \begin{cases} 0, & 0 < t < L/u \\ \displaystyle\int_{t-b}^{t} \exp\left(-\alpha\left(\tau - \frac{L}{u}\right)\right) \exp\left(-\frac{L}{u}\beta\right)\sqrt{\frac{\alpha\beta L/u}{\tau - \frac{L}{u}}}\, I_1\left[2\sqrt{\alpha\beta\frac{L}{u}\left(\tau - \frac{L}{u}\right)}\right] d\tau, & t > \frac{L}{u} \end{cases} \tag{10}$$

where

$$\alpha = \frac{D_L}{\Delta y^2}\left[\frac{k_G}{\frac{D_L K_1}{\Delta y} + k_G}\right] \text{ and}$$

$$\beta = \frac{k_G RTA}{\varepsilon}\left[\frac{D_L K_1/\Delta y}{\frac{D_L K_1}{\Delta y} + k_G}\right] \tag{11}$$

The modified Bessel function of first order, I_1, can be approximated by an asymptotic expansion if $2\sqrt{\alpha\beta\frac{L}{u}\left(\tau - \frac{L}{u}\right)} > 10$ so that equation (10) becomes:

$$\frac{X(L,t)}{\overline{X}} \frac{(\alpha\beta L/u)^{\frac{1}{2}}}{2\sqrt{\pi}} \int_{t-\left(\frac{L}{u}+b\right)}^{t-\frac{L}{u}} \frac{\exp\left(-\left(\sqrt{\alpha}\sqrt{\tau - \frac{L}{u}} - \sqrt{\beta\frac{L}{u}}\right)^2\right)}{\left(\tau - \frac{L}{u}\right)^{\frac{1}{2}}} d\tau, \quad t > \frac{L}{u} \tag{12}$$

Investigation of equation (12) has shown that it is valid for most conditions experienced in gas-liquid chromatography. Since we are only interested in the retention time a further approximation can be made by reducing the duration of the pulse, b, when equation (12) becomes:

$$\frac{X(L,t)}{\overline{X}} = \frac{b(\alpha\beta L/u)^{1/4}}{2\sqrt{\pi}\left(t - \frac{L}{u}\right)^{3/4}} \exp\left(-\left(\sqrt{\alpha}\sqrt{t - \frac{L}{u}} - \sqrt{\beta\frac{L}{u}}\right)^2\right) \tag{13}$$

The retention time, t_R, is the time at which the above function maximizes, so that:

$$t_R = \frac{L}{u}\left[1 + \frac{K_1 RTA\,\Delta y F}{\varepsilon}\right] \tag{14}$$

where:

$$F = \frac{1}{2} - \frac{3u}{4\beta L} + \frac{1}{2}\sqrt{1 - \frac{3u}{\beta L}} \tag{15}$$

In cases where the liquid film is thin and the column is long, F has a value very close to unity and the volume V of stationary liquid per unit volume of column is $2A\Delta y$ so that:

$$t_R = \frac{L}{u}\left[1 + \frac{K_1 RTV}{2\varepsilon}\right] \tag{16}$$

The so-called 'apparent' retention time, t'_R, can be obtained by subtracting the transport time L/u from (16), therefore:

$$t'_R = \frac{LK_1 RTV}{2u\varepsilon} \tag{17}$$

Furthermore, if the liquid solution is ideal, K_1 can be calculated by Raoult's law and the vapour pressures of the solute represented by the Clausius–Clapeyron equation, so that:

$$t'_R = \frac{L\rho_m RTV}{2p^0 u\varepsilon} = \frac{L\rho_m RTV \exp(\Delta H/RT)}{2Bu\varepsilon} \tag{18}$$

where p^0 is the vapour pressure of the solute at the column temperature, ρ_m the molal density of the liquid phase, ΔH the latent heat of vaporization of the solute and B is a constant in the Clausius–Clapeyron equation.

Equation (18) predicts that the 'apparent' retention time is proportional to the volume of stationary liquid and the column length, inversely proportional to the vapour pressure of the solute, and independent of the absolute column pressure provided the carrier

gas velocity is constant. The retention time should also be inversely proportional to the carrier gas velocity. Furthermore, according to (18), a plot of $\ln(t'_R/T)$ against $1/T$ will be a straight line. All the above predictions are observed experimentally and discussed by Keulemans[11]. The detailed comparison of the above theory with experiment will be discussed in further communications.

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EFFICIENCY OF SEPARATION IN BUFFERED PAPER CHROMATOGRAPHY OF ORGANIC ELECTROLYTES

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In chromatographic methods the efficiency of separation of a system in respect to a given binary mixture depends mainly on two parameters: (1) the number of theoretical plates, which determines the spread of a zone; (2) the selectivity, which determines the distance between two zones.

The latter parameter is usually expressed by the separation factor, which may be defined, for example, as the ratio of the distribution coefficients of the two substances to be separated (liquid–liquid extraction), or the ratio of the retention times (gas–liquid partition chromatography), etc. In paper chromatography it is most conveniently expressed as the difference between the R_F values of the substances under study ($\Delta R_F \geqslant 0$).

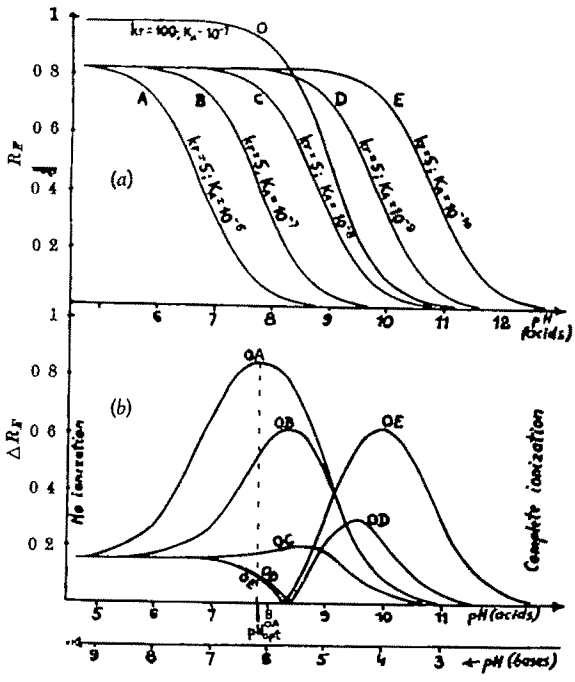

Fig. 1

In the case of organic electrolytes which in un-ionized form give high R_F values (near 1), improved separation may often be obtained by changing the pH of the water phase[1]. Fig. 1*a* illustrates the variation of the R_F values of a number of substances; in Fig. 1*b*, curves for ΔR_F as a function of pH are presented, which were obtained by subtracting the ΔR_F values of different pairs of substances at the same pH; for example, curve OA shows the variation of the ΔR_F of components O and A with change of pH of the water phase. It can be seen that often a maximum occurs on $\Delta R_F = f(p\text{H})$ curves; the pH value at which this maximum is obtained may correspond to conditions of optimum efficiency of separation (highest possible differences in R_F values) for the pair of components considered. This optimum pH may be calculated by equating the derivative $d\Delta R_F/dp\text{H}$ to zero; thus, taking into account the formulæ derived by Waksmundzki and Soczewiński[2]:

$$\frac{d\Delta R_F}{dp\text{H}} = \frac{d}{dp\text{H}}\left(\frac{\dfrac{k'r}{K'_A}}{\dfrac{k'r+1}{K'_A}+10p\text{H}} - \frac{\dfrac{k''r}{K''_A}}{\dfrac{k''r+1}{K''_A}+10p\text{H}}\right) = 0 \quad (1)$$

where k is partition coefficient of un-ionized substance; r is ratio of volumes of mobile and fixed phases; (kr is partition number of un-ionized substance[3]); K_A is ionization constant of acid. The indices $'$ and $''$ denote first and second component, respectively.

Solution of (1) gives:

$$p\text{H}_{\text{opt}} = \log \frac{\dfrac{k'r+1}{K'_A}\sqrt{\dfrac{k''r}{k''_A}} - \dfrac{k''r+1}{K''_A}\sqrt{\dfrac{k'r}{K'_A}}}{\sqrt{\dfrac{k'r}{K'_A}} - \sqrt{\dfrac{k''r}{K''_A}}} \quad (2)$$

The case for $kr \geqslant 100$. In buffered paper chromatography, the partition numbers kr of the un-ionized substances to be separated often are high, for example, 100 or more; hence the limiting R_F values (when

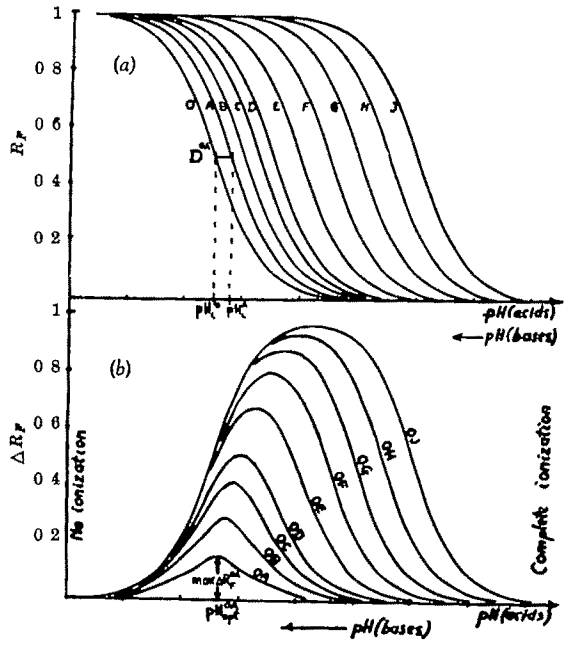

Fig. 2

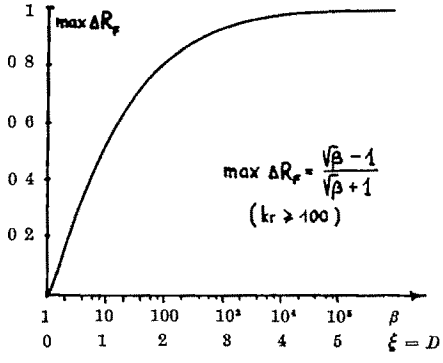

Fig. 3

substances are un-ionized) are greater than 0·99—the substances migrate with the front of the developing solvent. In those cases the shapes of the R_F vs. f(pH) curves are invariable and independent of the parameters K_A and kr, which influence only the positions of the curves. The inflexion point, which lies at the half-height of the curve (R_F about 0·5) and is the centre of axial symmetry of the curve, lies then at the pH value given by the formula:

$$pH_i = pK_A + \log(kr + 1) \approx pK_A + \log kr = \log \frac{kr}{K_A} \quad (3)$$

Thus the horizontal distance between two inflexion points (and owing to almost identical shapes, between whole curves as well, excluding asymptotes) is:

$$D = \log \frac{k'r}{K'_A} - \log \frac{k''r}{K''_A} = \log \frac{K''_A \cdot k'}{K'_A \cdot k''} = \log \beta = \xi \quad (4)$$

or, expressing it in another way, the horizontal distance between a pair of R_F vs. f(pH) curves, when $k'r, k''r \gg 100$, is equal to the logarithm of the separation factor of the substances to be separated, as defined by Golumbic[4]; or it is simply equal to the selectivity ξ (a term introduced by Kemula and Buchowski[5]) of the system with respect to the two substances, provided that (H) $\ll K_A$. Vice versa, an expermentally determined horizontal distance between two R_F vs. f(pH) curves gives directly log β for the solvent with respect to the two substances. This is illustrated in Fig. 2*a*, where a number of R_F vs. f(pH) curves is plotted ($kr \geqslant 100$) with different horizontal distances from the arbitrarily chosen reference curve 0. The relation (2) in this case simplifies considerably (by omitting the 1's from relations 1 and 2), becoming:

$$pH_{opt} = \frac{1}{2} \log \frac{k'r \cdot k''r}{K'_A \cdot K''_A} \quad (5)$$

The resulting error will not exceed 0·01 R_F, which lies within the experimental error of the method. Comparing (5) with (3), it can be easily seen that optimum pH value lies in the centre of the line connecting the pH_i values of a pair of components. In Fig. 2*b* the ΔR_F of different pairs of components at corresponding pH values are given.

Introducing pH_{opt} into ΔR_F (expression in brackets in formula 1, units omitted) we can calculate the maximum obtainable difference of R_F values between the two components considered:

$$\max \Delta R_F = \frac{\sqrt{\beta} - 1}{\sqrt{\beta} + 1} \quad (6)$$

Fig. 3 presents a plot of function (6), that is, it shows what maximum difference of R_F values may be obtained (at pH_{opt}) with a given separation factor β, as defined by Golumbic[4]. At other pH values the differences of R_F are smaller. Thus formulæ 5 and 6 permit the theoretical prediction of the optimum pH value and the maximum resolution, expressed in terms of ΔR_F, from partition numbers and ionization constants of the substances which are being separated.

Since R_F vs. f(pH) curves for bases are mirror reflexions of those of acids (axis of symmetry at pH = 7), some of the relations deduced above must be altered if the substance under consideration is a base. Thus:

(1) $$\frac{d\Delta R_F}{dpH} = \frac{d}{dpH}\left(\frac{k'r/K'_B}{\frac{k'r+1}{K'_B} + 10^{14-pH}} - \frac{k''r/K''_B}{\frac{k''r+1}{K''_B} + 10^{14-pH}}\right) = 0$$

(2) $pH_{opt.}$ (base) = 14 − $pH_{opt.}$ (acid); K_A replaced by K_B.

(3) $pH_i = 14 - \log \frac{kr}{K_B}$

(4) unchanged, only K_A replaced by K_B

(5) $pH_{opt.} = 14 - \frac{1}{2} \log \frac{k'r \cdot k''r}{K'_B \cdot K''_B}$

(6) unchanged.

Figs. 1 and 2 can also be adapted to bases by replacing pH values by 14−pH (as shown in Fig. 1).

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LETTERS TO THE EDITORS

RADIOPHYSICS

Radio Detection of the Planet Saturn

DETECTION of 3·45-cm. radiation from the planet Saturn has been accomplished with an X-band ruby maser radiometer[1,2] installed on the 85-ft. (26 m.) diameter, paraboloidal antenna at the University of Michigan's Radio Astronomy Observatory[3].

The initial detection on August 25–26, 1960, resulted from seven drift curves, one of which is shown in Fig. 1. The average of the seven drift curves indicates a peak antenna temperature of 0·10 ± 0 028° K. Although the increase at the predicted position of the planet is visible on a single drift curve, the observation was repeated five days later to eliminate any possibility of confusion with radiation from other extra-terrestrial sources. At the time of the second observation, the predicted average change in Saturn's right ascension was 37·3 sec., westward; the measured average change was approximately 36·5 sec., westward. The average of the seven drift curves of the second observation indicates a peak antenna temperature of 0·09 ± 0·028° K. These results are summarized in Fig. 2.

The total of fourteen drift curves, with a 'superimposed epoch' reduction technique, yields a peak antenna temperature of 0·095 ± 0·02° K. This value indicates an equivalent black body disk temperature of 106 ± 21° K., neglecting the effect of radiation from the rings. A correction factor of 2 per cent has been applied for terrestrial atmospheric absorption. This equivalent black body disk temperature is in reasonable agreement with that predicted from optical measurements[4].

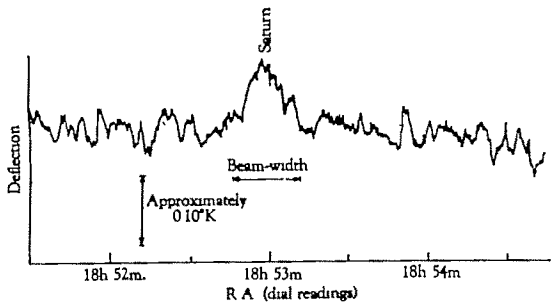

Fig. 1. Drift curve of the planet Saturn obtained with the maser radiometer. $\lambda = 3$ 45 cm. Peak antenna temperature is about 0 10° K.; integration time, 12 sec.

The peak antenna temperature of Saturn is about 350 times less than that measured from the standard source Cassiopeia *A* with the same system. In 1957, Drake and Ewen[5], using a 28-ft. antenna and a *TWT* radiometer at 3·75 cm., reported an antenna temperature for Saturn of 0·04° K. This reported detection was from one observation of 'off-on-off' type. This same paper reports an antenna temperature of 2° K. from Cassiopeia *A*. Their ratio of 50 could predict an antenna temperature of about 0 7° K. from Saturn, with the 85-ft. antenna of the University of Michigan, as opposed to our measured 0·10° K. The solid angle subtended by the planet during our measurements was the same as during the Drake and Ewen measurement of 1957.

The ruby maser radiometer developed by us is being described fully elsewhere[2]. Stated briefly, it is a modified Dicke system[6] with a switching input which is balanced off source on 'cold' sky. The maser preamplifier is a four-level ruby maser operating at 8·72 kMc./s. with push–pull magnetic field of approximately 4,000 gauss. The voltage-gain band-width product is typically 300 Mc./s., with a maser band-width of about 30 Mc./s. System band-width is at present intermediate-frequency limited at 8 Mc./s. The total equivalent system noise temperature is about 100° K., including antenna spill-over and back-lobes. These parameters result in a root mean square fluctuation of about 0·012° K. with a 12-sec. integration time. In Fig. 1 the root mean square fluctuation, taken as 1/4 the peak-to-peak off-source noise, is about 0·015° K. Thus the signal to peak-to-peak noise ratio for Saturn is about 2 to 1, on a single drift curve.

In this observation the modified Dicke system consisted of two identical horns pointed at the antenna surface, but physically separated so as to displace their beams by about 3 5 beam-widths in declination. Thus in all fourteen drift curves the comparison is between two discrete areas of the sky, one of which contains the planet. For small sources such as this, problems of balance and stability of gain are greatly reduced.

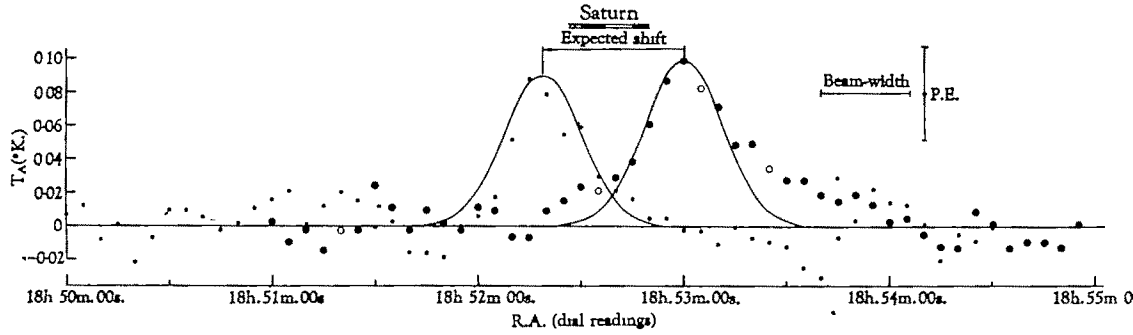

Fig. 2. Drift curves of planet Saturn, taken five days apart with the maser radiometer; ○, August 25–26, ●, August 30–31. Each is the average of seven individual drift curves. Solid lines are gaussian representation, at the expected shift of the planet

We are grateful to Prof. F. T. Haddock, A. H. Barrett, G. Makhov and W. E. Howard for their advice and support; to J. L. Talen, R. Yorks, R. W. Banta, F. Alred and W. Flowers for technical assistance.

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GEOPHYSICS

The Outer Radiation Belt and Auroræ

Rees and Reid[1] have found a diurnal variation in the latitude of the hydrogen lines in auroræ observed at College, Alaska. The variation is approximately sinusoidal with latitude minima at local midnight. They explain the phenomena by assuming that auroræ are produced by energetic protons and electrons which are sporadically scattered out of the outer radiation belt and showing that a day-side compression of the geomagnetic field by a continuous solar wind[2] could produce the latitude shift. The magnitude of the shift during geomagnetically quiet periods requires the solar wind to penetrate to within 4–5 Earth radii from the centre of the Earth. This corresponds to a translational kinetic energy density of about 300–600 keV./cm.^{3} for the wind, which is within the energy-range suggested by other measurements[3].

There is additional evidence which seems to corroborate this model. The position of the belt must have a diurnal variation such that the tips are always over the auroral regions at night and the day-side is slightly compressed from the usual dipole shape by the solar wind. The meagre space-probe observations of the belt[2–6] listed in Table 1 tend to

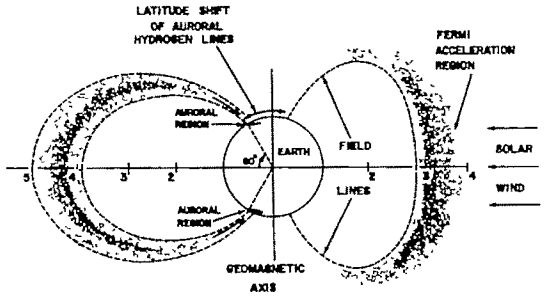

Fig. 1. Cross-section of the outer radiation belt in the geomagnetic meridian plane of the solar wind

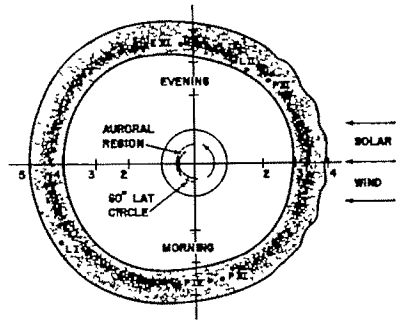

Fig. 2. Cross-section of the outer radiation belt in the geomagnetic equatorial plane. The labelled points are observed maxima listed in Table 1

support this unsymmetric model. In Table 1, φ is geomagnetic latitude; τ is local time; r is the geocentric radial distance in Earth radii; r_e is the radial distance of the dipole projection of r in the geomagnetic equatorial plane; and r_{ec} is r_e taking into account the day-side solar wind compression. Figs. 1 and 2 are schematic diagrams of the belt in meridian and geomagnetic equatorial planes. The seasonal variation of the direction of the solar wind and the difference between the geographical and geomagnetic axes have been omitted. In Fig. 2 the labelled points correspond to the space probe measurements listed in Table 1.

Table 1. GEOMAGNETIC CO-ORDINATES OF THE MAXIMUM OF THE OUTER RADIATION BELT

Space probe	Date	φ	τ	r	r_e	r_{ec}
Pioneer III (out, ref. 3)	Dec. 6, 1958	5° N.	0650	3·6	3·6	3·6
Pioneer III (in, ref. 3)	Dec. 7, 1958	15° S.	1510	3·3	3·6	3·4
Lunik I (refs. 4, 5)	Jan. 2, 1959	20° N.	0200*	4·2	4·8	4·8
Pioneer IV (ref. 6)	Mar. 3, 1959	0°	0630	3·6	3·6	3·6
Explorer VI (out, refs. 7, 8)	Aug. 9, 1959	7° N.	1820	3·6	3·6	3·6
Lunik II (ref. 5)	Sept. 12, 1959	33° N.	1600*	2·7	3·8	3·2

* The longitudinal logs of these trajectories are unavailable. The numbers were obtained assuming trajectories similar to that of *Pioneer* IV.

The agreement of the space-probe observations with the model may be fortuitous in view of the limited observations. However, all the probes listed in Table 1 passed through the region during geomagnetically quiet periods when *Explorer* VI has shown that the position of the outer belt is relatively stable. The theory could be tested by a single satellite in a highly eccentric orbit with a large rate of longitudinal precession.

Additional characteristics of auroræ might be explained with this model. The compression of the solar wind on the day-side will increase the magnetic field-strength and cause the mirror points of the trapped particles to be shifted nearer the geomagnetic equator. The day-to-night variation in the position of the tip of the belt shown in Fig. 1 was obtained assuming a 75 per cent increase in field-strength. This effect would prevent trapped particles in the belt from reaching auroral altitudes and explain the lack of day-time auroræ during geomagnetically quiet periods. The auroral $H\alpha$ profile maximum indicates that a large number of primary auroral protons have energies near 2 keV. (ref. 9), which is the same order of magnitude as the average solar wind proton energy. Parker[10] has shown how instabilities at the interface of the wind and the magnetic field result in Fermi acceleration of the particles (Fig. 1) and could pro-

duce the high-energy component of the auroral proton energy spectrum.

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PHYSICS

Observations of the Emission of Light on Dissolution of Irradiated Solids in Certain Liquids

Ahnström and Ehrenstein have observed the emission of light on dissolution of some organic solids in water[1]. We have been concerned with measurements of stored radiomimetic energy in solids treated with ionizing radiation. This problem has been approached partly by dissolution in liquids typical for dosimetry by the methods of radiation chemistry and partly by attempts to excite, during dissolution, liquid scintillators[2]. Some results of the latter kind will be summarized here. Most of the experiments were concerned with fine-grained sodium chloride which was given doses up to 200 Mrads of cobalt-60 γ-radiation and 2-MeV. electrons from a Van de Graaff machine.

Emission of light was observed by a photomultiplier (*EMI* 6255 *B*) and current recordings[3]. The solid is poured mechanically, using a manipulator, into a liquid contained in a quartz glass cup (Ekco's design for liquid scintillation counting). The liquid may be water, aqueous solutions, organic solvents or organic solutions.

It was noted that irradiated sodium chloride gave light pulses on dissolution in (aerated) water. The first part of the effect is very fast (rise-time about 0·5 sec.) and thus a fast recorder (Mingograf 230 *B* from the Elema-Schonander Co.) was selected. Emission of light was observed also for lithium fluoride, potassium iodide, glucose, saccharose and alginic acid. (The shape of the light-pulse of the latter was, however, flatter.)

Dissolution in the liquid scintillator described by Kallman and Furst[3] containing dioxane, diphenyloxazole, naphthalene and water gave less light than water itself, although it responds well to an external cæsium-137 source.

It was therefore decided to select solutes, known to be fluorescent to ultra-violet light or X-rays, that are either surface active, that is, exhibiting naturally a rather high concentration within the dissolution zone, or very slightly surface active, that is, having nearly the same concentration in the bulk solution and dissolution zone. Some simple inorganic ions approximate to the last case.

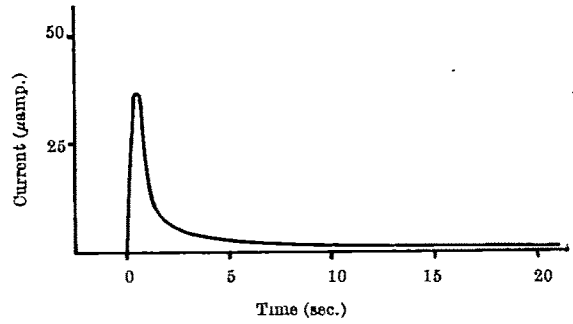

Fig. 1. Record of light emission on dissolution of 10 mgm. fine-grained sodium chloride (*pro analysi*) given a dose of 50 Mrads with 2-MeV. electrons 12 months before experiment (stored at + 4° C.). Solvent is $4 \cdot 2 \times 10^{-5}$ thallium chloride in water. The sodium chloride is dissolved within 1 min. The ordinate is anode current of the photomultiplier tube and well within its linear region. The system is quantitatively calibrated by tritium-water in the same apparatus

Following up these ideas, it was noted that a strong light emission is obtained with diphenyloxazole dissolved in water and with a commercial naphthalene sulphonic acid condensed with formaldehyde also in aqueous solution ('Belloid TD', a product of the Geigy Co.). Both systems should be regarded as surface active and the solutes as fluorescent. The total light output (found by measuring the total area of the light output pulse) was now nearly a thousand times greater than in the case of water. In a dark-room, the light flash occurring during dissolution is quite clearly seen. Fig. 1 shows a typical record in which the time-scale is also seen.

Similar experiments were performed with solutions of thallium chloride in water. This system is known to be fluorescent[4]. It seems to be somewhat surface-active. Here also, a large light output was observed —about a thousand times greater than that for water. Also this light flash is readily observed in the dark-room. It was found that the light output has a pronounced maximum at about 0 01 gm./litre thallium chloride.

A comparison with the luminescence of tritium water (~100 mc./ml.) containing thallium chloride was made. This solution exhibited a small but easily measurable fluorescence. Assuming that the stored energy acts like radiation and excites the thallium ion electronically, we found that, using 0·01 gm./litre thallium chloride, the energy stored was about $1 \cdot 5 \times 10^{8}$ ergs/gm. or 3 per cent of the primary absorbed dose. This figure is of the same order as that found by using chloroform as a detector[2].

It was further observed that irradiated alginic acid gave a light-pulse; but, after storage in humid air (98 per cent relative humidity, 20° C.) for one day, no light emission was observed.

Irradiated polystyrene samples gave rise to luminescence when dissolved in the liquid scintillator *NE* 213 (xylene, *POPOP*, from Nuclear Enterprises, Ltd.). Samples treated by electrical a.c.-corona discharges (by Dr. A. Kelén, ASEA Co.) gave similar light pulses, thus yielding a qualitative indication of the equivalence between the action of ionizing radiation and electrical discharges.

Further observations showed that lanthanide ions known to be fluorescent, namely, gadolinium, neodymium, samarium, terbium and europium, did not amplify the water light-pulse for sodium chloride. It is not clear at present why the lanthanide ions do

not give large luminescence effects whereas thallium ions and organic fluorescent solutes do.

These results might be of some significance for health problems which may eventually be encountered in food preservation by irradiation[1,2]. They show that dry substances store energy but that hydrophilic materials lose this energy on sorption of water. No strict proof of radiation-equivalence is obtained because the average wave-length emitted is around 4000 Å. Nevertheless, the results indicate that the phenomenon of stored energy has to be carefully examined, at least for dry solids, before preservation of food by irradiation is adopted on a large scale. For further details, see ref. 2 and a more complete paper given elsewhere. The work on ionic crystals has some relation to the discussion of stored energy and volcanism[5].

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Aberration of Plane Waves

BY 'aberration' is meant the change in the apparent angular position of a source (usually at infinity) due to a change in the velocity of the observer.

In elementary treatments of this phenomenon, the source is considered as a source of particles and the required formula is obtained by applying the rules for addition of velocities. It will be shown here that the result obtained in this simple way is also valid for plane waves with velocity c, but is not valid for plane waves having other velocities. For example, the aberration of sound in Newtonian mechanics is zero, whereas a misapplication of the addition of velocities rule would lead one to think that there should be an aberration of the order of the change in velocity of the observer divided by the velocity of sound.

The fact that there is no classical aberration for sound may be realized by thinking of the following experiment:

A sound-direction finder or sound telescope is made from several small microphones attached to a rigid structure so that they are coplanar; the signals from the microphones are received without appreciable delay by an integrating apparatus which is also part of the rigid structure. When this telescope is activated by the sound from a far distant source, the total signal received is maximum when the signals from the individual microphones are in phase, that is, when the plane of the microphones is parallel to the planes of the oncoming waves. If a change in velocity is now imposed on the telescope, it is clear that the above condition of parallelism will not be destroyed. Hence, no re-orientation of the telescope for maximum signal is necessary, which means that there is no aberration.

Consider two observers O and O' moving with respect to one another, so that O sees O' moving with velocity v in the positive direction of their common x-axis. Let the y and z axes of O be parallel respectively to those of O'. The Lorentz transformations which relate the measurements of these observers are:

$$x = \gamma(x' + vt')\,;\quad y = y'\,;\quad z = z'$$

$$t = \gamma\left(t' + \frac{vx'}{c^2}\right),\ \text{where}\ \gamma = 1/\sqrt{1 - v^2/c^2}$$

Suppose O observes the plane wave:

$$\chi = \exp 2\pi i\left(\frac{lx + my + nz}{\lambda} - ft\right)$$

that is, he observes it as moving in the direction (l, m, n) with velocity $f\lambda$.

The manner in which O' observes the same wave can be obtained by substituting for x, y, z and t in terms of x', y', z', and t' giving:

$$\chi = \exp 2\pi i\left(\frac{l'x' + m'y' + n'z'}{\lambda'} - f't'\right)$$

where $\dfrac{l'}{\lambda'} = \dfrac{\gamma(l - vf\lambda/c^2)}{\lambda'}$

$$\frac{m'}{\lambda'} = \frac{m}{\lambda}\,;\quad \frac{n'}{\lambda'} = \frac{n}{\lambda}$$

$$f' = \gamma\left(f - \frac{lv}{\lambda}\right) = \gamma\left(1 - \frac{lv}{f\lambda}\right)f$$

From these equations one obtains the general aberration formula:

$$l' : m' : n' = \gamma\left(l - \frac{vf\lambda}{c^2}\right) : m : n$$

A common case of aberration is when the oncoming wave is moving roughly at right angles to the relative velocity of the two observers. Let its direction of motion as observed by O be in the direction of the negative y axis, that is: $(l, m, n) = (0, -1, 0)$.

The direction of motion as observed by O' will differ from that of the negative y axis by an angle θ where $\tan\theta = \dfrac{l'}{m'}$. From the general formula above it is evident that:

$$\tan\theta = \gamma\frac{vf\lambda}{c^2}$$

This formula becomes the usual one $\left[\tan\theta = \dfrac{v}{c}\right]$ for the case of astronomical aberration. It also explains why the aberration of waves vanishes in non-relativistic mechanics, that is, as $c \to \infty$.

Even though the apparent direction of a distant sound source does not depend on the motion of the observer it does, nevertheless, vary with the velocity of the medium relative to the source. This effect may be understood classically as follows:

When a signal is emitted by the source, it progresses as a spherical wave the radius of which grows with the velocity of sound and the centre of which remains fixed in the medium (that is, moves with the wind). The sound telescope of any observer (regardless of his velocity) at a point P must for maximum signal be aimed at the position of the centres of the waves as they pass P. From this it follows that, if s is the unit vector in the direction of the sound telescope at

maximum signal and V the velocity of sound in still air and $\mathbf{w}$ the velocity of the wind with respect to the source, the vector $V\mathbf{s} - \mathbf{w}$ points in the true direction of the source.

This latter phenomenon should not be treated as aberration because it is not associated with the motion of the observer, and because the direction of the effect is opposite to what one gets from the over-simplified application of the law of addition of velocities referred to at the start of this paper.

I wish to express my thanks to Prof. J. L. Synge for a very stimulating discussion on this topic.

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Forces on Charged Particles of a Plasma in a Cavity Resonator

FOLLOWING the methods adopted by Boot *et al.*[1], we have recently undertaken an analysis of the conditions required for the containment of an ionized plasma by electromagnetic waves at high frequency, taking collisions and space-charge forces in the plasma into account. During this work, now being prepared for publication, one of us (H. G.) directed attention to the fact that two types of confining force are present when the plasma interacts with the wave in the presence of large field gradients. One is due to the electric, or induced electric, field acting directly on the electrons, as analysed by Boot *et al.* For this force to be unidirectional, certain relations between amplitude, gradient and frequency of the electric field and electron density must be fulfilled. We call this the Mathieu force, since these relations may be obtained by examining the differential equation which is of the Mathieu type[2]. The other unidirectional force we call the electromagnetic force. This force results from the interaction of the electron current set up by the electron moving in the electric field with the magnetic field component of the electromagnetic wave. This is the force considered by Volkov[3].

The nature of the solution of the Mathieu equation may be deduced from an examination of the stability chart (Fig. 1). The operating point (a, q) appropriate to a particular region of the plasma is dependent on the plasma parameters, the generator frequency, and the square of the electric field gradient $(\mathrm{d}E_0)/(\mathrm{d}x)^2$. For a cylindrical cavity excited in the TM_{010} mode:

$$a = \frac{\omega_p^2}{\omega^2} - \frac{2\cdot 75e^2}{m_e^2c^2}\cdot(\omega^2 - \omega_p^2)\times \frac{2\omega_p^4 - 3\omega^2\omega_p^2 + \omega^4 + \omega^2\nu^2}{\{\omega^2\nu^2 + (\omega^2 - \omega_p^2)^2\}^{3/2}}\left(\frac{dE_0}{dx}\right)^2 - \left(\frac{\nu}{2\omega}\right)^2$$

$$q = \frac{1\cdot 375\, e^2}{m_e^2c^2}\cdot\frac{2\omega_p^4 - 3\omega^2\omega_p^2 + \omega^4 + \omega^2\nu^2}{\{\omega^2\nu^2 + (\omega^2 - \omega_p^2)^2\}^2}\left(\frac{\mathrm{d}E_0}{\mathrm{d}x}\right)^2$$

where ω_p is $2\pi\left\{\frac{ne^2}{\pi m_e}\right\}^{1/2}$; ν is the collision frequency for momentum transfer between electrons and atoms or ions; $\omega/2\pi$ is the generator frequency; and E_0 is the electric field in the cavity.

Solutions for points (a,q) which lie below a_0 or between a_2 and b_2, etc., correspond to a unidirectional force on the electrons. Those for points which lie between a_1 and b_1, a_3 and b_3, etc., correspond to exponentially increasing amplitudes of oscillation of the electrons. Although this latter condition is not effective for containment, yet, if collisions between atoms and electrons are appreciable in number, it will result in conversion of the radio-frequency energy into plasma heating.

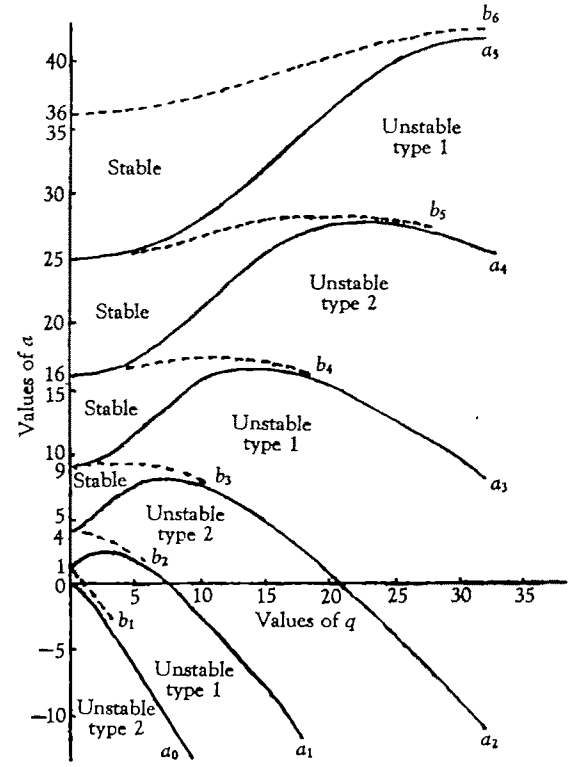

Fig. 1. Stability chart. This diagram is symmetrical about the a-axis

The Mathieu force and the electromagnetic force both originate from the electric field gradient, although for different reasons, and this makes it difficult to separate them mathematically. However, the role of the Mathieu force may be illustrated by putting $\omega = \omega_p$, when the electromagnetic force disappears.

In general, it may be said that, in the region below a_0 in Fig. 1, the electromagnetic force predominates, while between a_2 and b_2 the Mathieu force predominates; but it should be noted that this is not always true, and the electromagnetic force may oppose confinement for certain values of plasma parameters. It can be shown that concentration of the ionized portion of a partially ionized gas is also feasible. The relevance of this to the experiments of Self and Boot[4] has not yet been examined in detail, but they would appear to support our conclusions.

In practice, under the most general plasma conditions, it seems unlikely that containment of a fully ionized plasma will be obtained by operating in the (a_2b_2) region where the Mathieu force predominates, partly due to the large field gradients required, and partly due to the difficulty in obtaining the correct relative values for a and q. Our analysis does show, however, that when the special conditions of plasma resonance as defined by Dutt and Stainsby[5] are satisfied, and when $\nu \ll \omega_p$, the operating point (a,q) can lie between a_2 and b_2 for moderate input

powers, resulting in a unidirectional Mathieu force on the plasma of appreciable magnitude.

Since completing this analysis we have seen a letter from C. M. Haaland[6] in which he distinguishes between the Mathieu and electromagnetic forces; but seems not to have noticed the phase-dependence of the latter.

The forces considered above are additional to those due to the pinch effect, considered by N. J. Phillips (private communication) for high-frequency currents, which will be present at the surface of a contained plasma.

It may be of interest to note that our analysis resembles that of Prof. W. K. R. Watson[7] in his theory of fire-ball formation, except that he apparently omits the space-charge terms and does not consider the electromagnetic force as defined by us. His statement that the charge tends to concentrate at the voltage nodes is supported by the analysis and experiments of Boot *et al.*, Volkov's analysis, the experiments of Glagolev *et al.*[8], and our own analysis.

Our thanks are due to Mr. J. K. Brown, director of research, for permission to publish this communication.

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A New Micrometer Microscope

THE usual method of measuring the dimensions of microscopic objects is to compare them against an eye-piece scale or to use a calibrated filar micrometer eye-piece. Such methods are not capable of great accuracy and are inherently slow and poorly adapted to statistical problems. In order to plot the size distribution of a large number of particles, it is necessary to bring each in turn to the centre of the field and to set it against the scale.

These difficulties can be avoided by means of a double-image system in which two images, sheared by a controlled amount, are viewed. If the separation of the two images of a particle is less than its diameter, they will overlap. If the separation is greater than the diameter, a clear space will be seen between them, and if the separation is equal to the diameter they will just touch. The position of contact can be observed with great precision, and theoretical calculations by J. Dyson (unpublished work) have shown that the accuracy of setting may be considerably better than the resolving power.

Only two double-image micrometer microscopes appear to have been described. McGinn[1] used birefringent elements which introduced some aberration and gave only a small amount of shear. Timbrell[2] used a mirror vibrating at 50 c./s. phased with an interrupted light source. The shear was controlled by varying the amplitude of vibration of the mirror. This system requires relatively complicated electrical accessories and cannot readily be used with any type of microscope. A purely optical instrument similar to the Mach-Zehnder interferometer has been constructed in the workshop of this Department by Mr. A. B. Charters and is shown diagrammatically in Fig. 1. P_1 and P_2 are two beam-splitting prisms; M_1 and M_2 are two surface-metallized mirrors. The instrument is constructed as an attachable body that fits just above the objective carrier. M_2 can be rotated through a small angle by means of a differential screw micrometer mechanism, producing a sheared image in one azimuth. Shears equal to the diameter of the entire field of view can be obtained at any power. The direction of shear can be altered by rotating the whole attachment about the optical axis of the microscope; an angular scale is provided. It is thus possible to plot the shape and dimensions of an irregular object in polar co-ordinates.

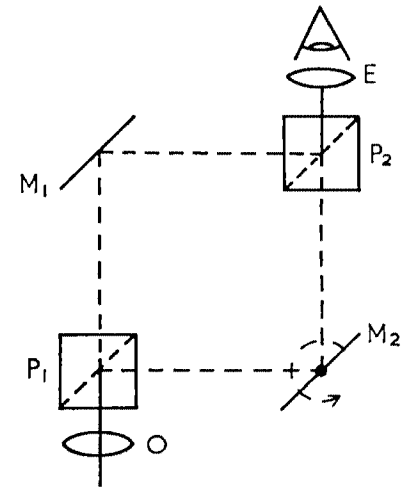

Fig. 1

A special advantage of this system is its use for plotting statistical size-distribution curves. For this purpose the micrometer is set at a known value. On observing the field of particles, those with diameters greater than this value will give overlapping images, those with diameters less than this value will give two separated images and a few may give images that just touch. The number in each category can easily be determined. The micrometer is then set to another value and the process is repeated. In this way an integrated distribution curve can be obtained without making an actual measurement on a single particle. The instrument can be used with almost any method of microscopy, including phase contrast, and it can be readily applied to living cells, including motile ones.

Many modifications of the basic system are possible. Colour filters can be inserted into one or both paths and are sometimes helpful in distinguishing the sheared from the unsheared image. The three elements, P_1, P_2 and M_1, could be incorporated into a single solid block of glass. A modified version in the form of a convenient eye-piece attachment with a different mechanical system, but giving a smaller

total shear, has been designed by Dyson (unpublished work).

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METALLURGY

Hydrogen Diffusion in Mild Steels

DESPITE evidence in the literature that hydrogen diffusion in steels does not obey Fick's laws, experimental data continue to be analysed in their terms. A further deviation from these laws is presented here, and its relation to Fick's laws are discussed. An explicit statement of the inapplicability of Fick's laws to hydrogen in steels, at least below 100°, is desirable.

The solution of Fick's laws for the evolution of a diffusing species from a cylinder of radius a, length l in which the species is at uniform concentration at time $t = 0$ and the surface concentration is zero for $t > 0$ is given[1] by :

$$\frac{Q}{Q_0} = \left[4\sum_1^\infty \frac{1}{\beta_n^2} \exp\left(-\frac{\beta_n^2 Dt}{a^2}\right)\right] \left[\frac{8}{\pi^2}\sum_1^\infty \frac{1}{(2m-1)^2} \exp\left(-\frac{(2m-1)^2\pi^2 Dt}{l^2}\right)\right] \quad (1)$$

where Q and Q_0 are the total quantities of the species in the cylinder at times t and zero respectively, β_n is the nth root of the equation $J_0(X) = 0$, and D is the diffusion constant. After a comparatively short time, the first term in the series in the left-hand bracket becomes dominant, and the practice[2-5] is to assume that after $\frac{Q}{Q_0}$ is less than approximately 0·5, the equation followed is :

$$\frac{Q}{Q_0} = \frac{32}{\pi^2\beta_1^2} \exp\left[-\left(\frac{\beta_1^2}{a^2} + \frac{\pi^2}{l^2}\right)Dt\right] \quad (2)$$

If the evolution of hydrogen from a steel cylinder is measured by following the increase in pressure in a constant volume apparatus with time,

$$\frac{Q}{Q_0} = 1 - \frac{p}{p_f} \quad (3)$$

where p and p_f are the pressures at time t and infinity respectively and $p = 0$ at $t = 0$.

Hence after an initial period, from equations (2) and (3) :

$$y = \frac{32 p_f}{\pi^2\beta_1^2} \exp(-Kt) \quad (4)$$

$$\frac{dy}{dt} = -\frac{32Kp_f}{\pi^2\beta_1^2} \exp(-Kt) \quad (5)$$

where $y = p_f - p$ and $K = \left(\frac{\beta_1^2}{a^2} + \frac{\pi^2}{l^2}\right)D$

Hence if Fick's laws are obeyed, plots of both log y and log $\left(\frac{dy}{dt}\right)$ against t should yield, after an initial period, straight lines of slope $-K$ from which D can be obtained.

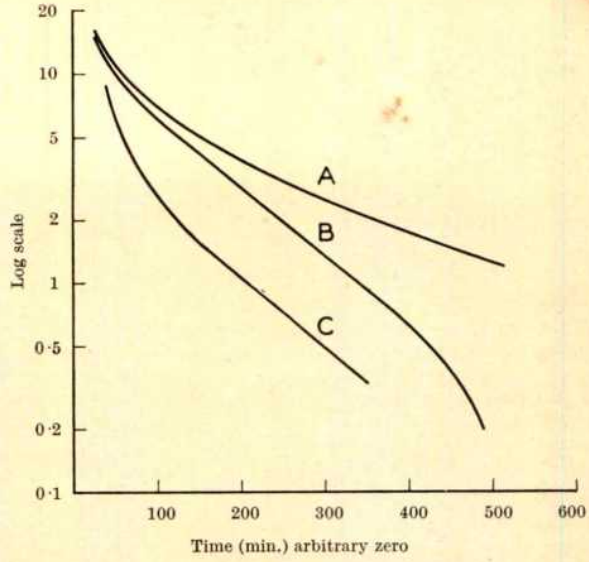

Fig. 1. Evolution results for ⅜-in. diameter cylinder. *A*, log y versus t. *B*, log $(y - y_1)$ versus t. *C*, log $\left(\frac{dy}{dt}\right)$ versus t

Evolution experiments have been carried out on mild steel cylinders, 4 in. long and with nominal diameters of ½ in., $\frac{7}{16}$ in. and ⅜ in., which were saturated with hydrogen by immersion in 3 per cent sodium chloride solution saturated with hydrogen sulphide at 25°. Hydrogen evolutions at 65° C. were studied by following changes in pressure in an initially evacuated constant volume gas burette with a mercury manometer until constant pressure was attained. In each case, values of y were calculated, and values of $\frac{dy}{dt}$ were obtained graphically from plots of y versus t.

The results for a ⅜-in. diameter cylinder are given as semi-logarithmic plots in Fig. 1. Curve *C*, displaced vertically for clarity, shows that equation (5) is obeyed to the extent of giving, after an initial period, a line which is straight within experimental error throughout the range in which slopes could be determined graphically. Curve *A*, however, has curvature over its length and thus shows that equation (4) is not obeyed. This length corresponds to the evolution of 90–95 per cent of the total. Indications so far are that the evolution thereafter is exponential.

It is necessary to show that the results reported here are a measure of the movement of the hydrogen within the steel and not a measure of any surface processes. This can be done by using specimens of different dimensions, and showing that some measured property of the system is a function of the specimen volume, and not of the specimen surface area[6]. The slope of the log $\left(\frac{dy}{dt}\right)$ versus t plot was found to be a reproducible property and could be characterized by $t_{1/2}$, the time required for log $\left(\frac{dy}{dt}\right)$ to halve its value. $t_{1/2}$ was determined using cylinders of different radius (a) and Table 1 shows that $t_{1/2}$ varies as a^2 as required.

Table 1

a^2 (in.^{2})	0·0622	0·0475	0·0350
$t_{1/2}$ (min.)	155	113	90
$10^3 a^2/t_{1/2}$	4·0	4·2	3·9

The behaviour of curves A and C is due to the fact that y decays exponentially within experimental error over a limited range ; but this decay requires a finite value of y at infinite time, that is, the relation $y - y_1 = A \exp(-Bt)$, where y_1, A and B are constants, holds during a substantial portion of the evolution. Thus within this range of applicability, log $\left(\frac{dy}{dt}\right)$ versus t is linear, but log y versus t is not. Curve B shows that y_1 can be chosen to give a linear plot of log $(y - y_1)$ versus t with the same slope as log $\left(\frac{dy}{dt}\right)$ versus t. Curve B shows the deviation from the linear relation at large values of t, when y is approaching y_1 in value. It follows that curve C would show deviations over the same range but with opposite curvature to curve B. Direct measurement of this was precluded by the sensitivity of the apparatus used.

This deviation in a plot of log $\left(\frac{dy}{dt}\right)$ versus t has been reported previously for evolutions at higher temperatures[2], and attributed to the appearance of "residual or slowly-diffusing hydrogen . . . a real component or effect detectable only after the removal of the rapidly diffusing or 'diffusible' hydrogen".

Now for valid diffusion constants to be obtained for a given system, it is essential that all equations derived from Fick's laws be obeyed. There are already important experimental data obtained below 100° which do not obey the appropriate equations derived from Fick's laws[7,8]. The division of the hydrogen in solution into 'diffusible' and 'residual' fractions in the present case would therefore be based on deviations from an equation which would not be expected to apply.

The present results provide more evidence against the applicability of Fick's laws and additional data to be explained by a comprehensive theory of the behaviour of hydrogen in steels.

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Crucible Material for the Growth of Palladium Single Crystals

INVESTIGATIONS in this laboratory of the catalytic activity of palladium indicated that it was desirable, during a particular measurement, to limit the active surface to a single crystallographic plane. For such experiments large single crystals of palladium were required. This resulted in the development of a crystal-growing apparatus (to be described elsewhere) in which the Bridgman[1] method was utilized, and in an investigation of crucible materials suitable for containing molten palladium. The results of this latter work are reported here.

Although metals of the platinum group are quite inert under most conditions, they react with many common substances when molten. The molten platinum metals will dissolve appreciable quantities of carbon, most of which will be rejected as graphite on slow cooling. Palladium and silicon form the compounds Pd_2Si and PdSi (ref. 2). Palladium and Pd_2Si form a eutectic mixture at 6 per cent silicon, melting at 670° C. Aluminium oxide has been reported to be stable in contact with molten nickel at 1,800° C. in an inert atmosphere[3]. From the foregoing considerations, pure aluminium oxide was selected as the crucible material (E. M. Wise, International Nickel Co., states in a private communication that he has used aluminium oxide for containing palladium melts). A crucible of morganite (99·7 per cent aluminium oxide), 8 mm. internal diameter, 12 mm. external diameter, 8 cm. long with a rounded, closed end was used.

Fig. 1. Palladium ingot—side view

The crystals were grown by the following technique. Chemically pure-grade palladium moss was compressed in a steel die to small pellets slightly less than 8 mm. in diameter. Approximately 25 gm. of palladium pellets were inserted in the crucible and the crucible placed in the crystal-growing apparatus. This was flushed with argon at room temperature and again at 500° C. The final argon pressure was 3 lb./sq. in. gauge. The palladium was brought to 1,650° C., approximately 95° above its melting point. The crystals were grown at a dropping rate of 3 cm. per hr. No attempt was made to determine the optimum growing-rate.

Crystals 8 mm. × 40 mm. were easily grown under these conditions. A typical ingot is shown in Fig. 1. Except for a 3-mm. region at the top, the entire ingot is a single crystal. The small zone at the top consists of four small crystals of different orientation (Fig. 2). The orientation of the crystal axes of the large crystal with respect to the direction of growth was determined by Laue back-reflexion photographs : a cube edge forms an angle at about 20° with the axis of the ingot.

Liquid palladium does not wet aluminium oxide, and any gas entrapped in the melt tends to adhere to the crucible walls. This gas is difficult to remove. Even when the pressure is reduced to the point where a considerable amount of palladium distils to the cooler parts of the furnace, small surface bubbles occur on the palladium ingot. The surface bubbles which formed at the molten palladium–aluminium oxide interface are clearly visible in Fig. 1.

Aluminium oxide is satisfactory from the point of view of purity. No evidence of reaction between the crucible and molten palladium was found. Spectroscopic analysis indicated 100 p.p.m. of silicon and iron in the crystal—no more than in the starting material.

The results of this investigation show that pure aluminium oxide is satisfactory as a crucible for molten palladium. As no reaction is detectable between the crucible and the melt, the finished crystal can easily be removed from the crucible

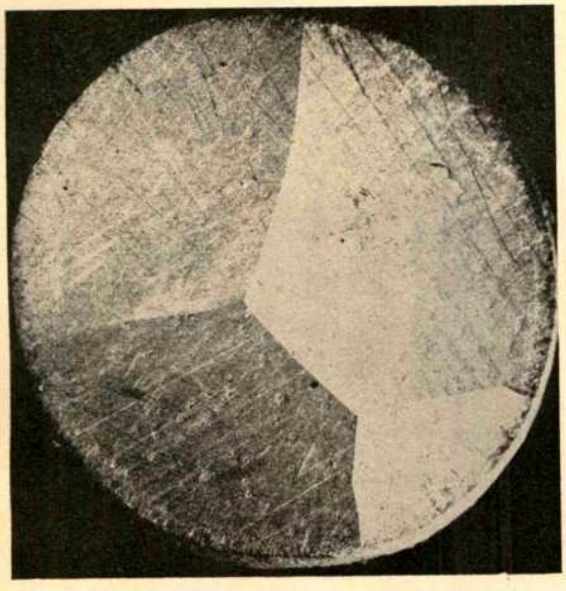

Fig. 2. Palladium ingot—top view

because the melt does not wet its container. When aluminium oxide is used as the container in growing palladium crystals, the diameter of the single crystal ingot should exceed the diameter of the crystal desired because of the gas bubbles, which collect at the crystal-container interface.

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CHEMISTRY

A Photoionization Detector for Gases and Vapours

SENSITIVE ionization methods for the measurement of low gas and vapour concentration require the ionization of the test gas or vapour under conditions where an inert carrier gas is unionized. Such methods as the ionization of carbon compounds in a hydrogen flame[1] and the reaction between gases and vapours and rare gas metastables[2] are well established and successful for this purpose. An alternative method is to irradiate the gas mixture with ultra-violet radiation of such a frequency that photoionization of the test gas occurs without any accompanying ionization of an inert carrier gas. In practice an electrical discharge in one of the rare gases or in nitrogen or hydrogen generates photons of energy sufficient for the ionization of almost all polyatomic compounds, but with insufficient energy to ionize simple diatomic gases.

A practical photoionization detector is illustrated in Fig. 1, together with the details of its construction. The gas supply to the discharge which generates the ultra-violet radiation is led through the tube (A); this tube also serves as a cathode for the discharge, and in use a current of a few m. amp. is maintained between this cathode and the anode (B). The test gas is introduced through the tube (D); this also serves as the collecting electrode for the ions liberated within the chamber enclosed by the second cathode (C). When the discharge is supplied with hydrogen, nitrogen or argon it is necessary to reduce the pressure within the detector to 100 mm. or less; at higher pressures a stable discharge is difficult to maintain. With helium however a stable discharge is possible at atmospheric pressure particularly if the detector is supplied with radiofrequency energy instead of d.c.[3]. The carrier gas in which the test sample is introduced into the sensing chamber (C) can be almost any gas which is not itself ionized by the radiation from the discharge. Water-saturated air, for example, gives entirely satisfactory results.

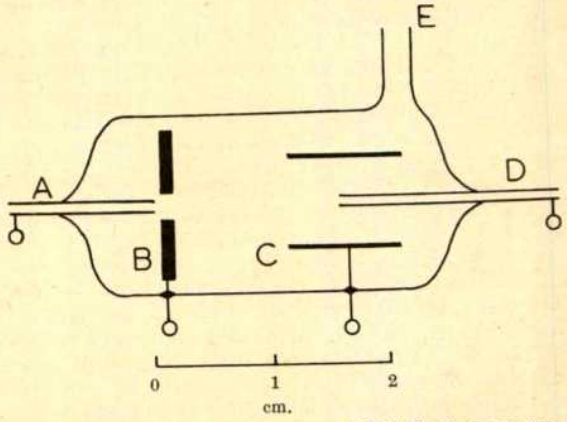

Fig. 1. Construction of the detector. A, Inlet for discharge gas and cathode connexion; B, discharge anode; C, measuring chamber anode; D, sample inlet and cathode; E, outlet to water pump. The detector body is of glass, the cathodes of platinum tubing and the anodes are of copper

The detector illustrated gave a current of approximately 10^{-10} amp. in the absence of ionizable vapour, possibly due to the photoelectric emission of electrons from the surfaces of the measuring chamber (C). In the presence of ionizable vapour, a substantially linear response to vapour concentration was observed up to a signal current of 10^{-7} amp. The efficiency of ionization of propane as a test substance was approximately 0·01 per cent. The response of the detector appeared to be unaffected by gross contamination of its surfaces with dirt or decomposition products and was stable over long periods and on repeated operation. The stability of this device, unlike that of other discharge methods of measuring vapour concentration, is probably due to the fact that the discharge takes place within the hollow cathode (A), which contains only a clean and uncontaminated supply of inert gas. The design shown should not be considered as final, but rather to illustrate the potentialities of this method.

I am indebted to Mr. P. Simmonds for technical assistance.

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Absorption Spectra of Copper(II) and Nickel(II) Complexes

IT has been demonstrated that there is a definite relation between the basicity of ligands and the stability of the complexes[1-3]. There are, however, few data in the literature dealing with the relation between these two factors and the absorption spectra; as an example may be mentioned the work of Jones *et al.*[4].

It is known[5] that the bands appearing in the absorption spectrum of the electrovalent, normally paramagnetic copper(II) and nickel(II)-complexes, belong to the transition $^2E_g \rightarrow {}^2T_{2g}$ and $^3A_{2g} \rightarrow {}^3T_{2g}$, $^3A_{2g} \rightarrow {}^3T_{1g}(F)$, $^3A_{2g} \rightarrow {}^3T_{1g}(P)$ respectively. If the distance between the sub-levels, due to the effect of the electrostatic field of the ligands, increases, then the bands corresponding to these transitions appear shifted to shorter wave-lengths. The polarization of the ligands plays an important part in the formation of the electrostatic field[6]. The short-wave shift observed with the different ligands means increase of the field and simultaneously that of the polarization[7]. The increase of the covalent character of the bonds results also in a shift of similar direction; and further, the intensity of the bands increases with the σ-donor properties of the ligands[8].

Our experimental results show that the intensity of the bands in the copper(II) complexes increases in the order ammonia–ethylenediamine–1,2 propylenediamine – trimethylenediamine – triethylenetriamine – tetraethylenepentamine (see, for example, ref. 8), whereas in nickel(II) complexes the order is ethylenediamine–ammonia – trimethylenediamine – tetramethylenepentamine–triethylenetriamine. The extinction value of the bands in general increases with the length of the polyamine chain (trimethylenediamine–triethylenetriamine–tetraethylenepentamine) and with the increase of the size of the chelate rings produced (see Table 1).

In copper(II) complexes there are increases not only in the intensity but also in the width and splitting of the bands with the length of the polyamine chain[9]. The change of the extinction value of the bands is not so regular in the case of nickel(II) as in that of copper(II). The λ(water)/λ(complex) values (that is, the shift in relation to the hydrated ions) compared with the log β_n values, in both the copper(II) and nickel(II) complexes, is in good agreement with a linear relationship (Fig. 1).

In the case of the nickel(II) complexes, the distance between the red band and blue band is considerably changed ($\lambda_{II}-\lambda_{III}$; $\Delta\lambda$). As the stability increases, these bands get nearer to each other, indicating the approach of the terms $^3T_{1g}(F)$ and $^3T_{1g}(P)$. The λ_{II} and $\Delta\lambda$ values give a straight line in good agreement (Fig. 2). The log β_n and λ(water)/λ(complex) values change in almost the same way in the case of both metal ions.

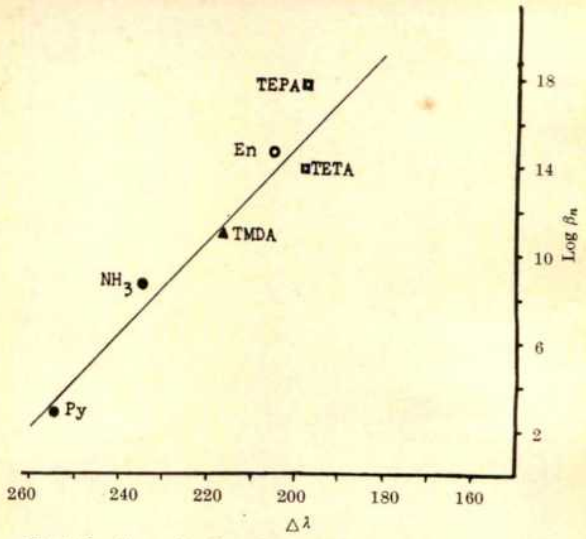

Fig. 1. Log β_n as a function of $\Delta\lambda$. ●, log β_4; ▲, log β_3; ○, log β_2; □, log β_1

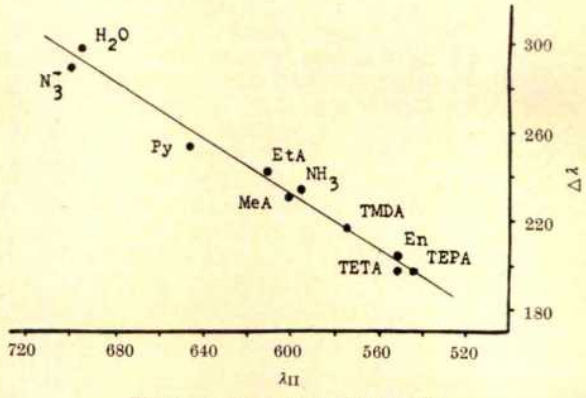

Fig. 2. A plot of $\Delta\lambda$ against λ_{II} (Ni)

According to the D_q values in the nickel(II) complexes the order may be as follows:

$$NO_2^- > NO_3^- > N_3^- > H_2O = Py > NH_3 = EtA > MeA > TMDA > TEPA > TETA > En$$

Table 1

Ligand	mμ and log ε Ni(II)			Cu(II)		Ligand	Ni(II)			Cu(II)	
H_2O	1,150	695	395	792	—	MeA	1,000	600	368	—	—
	0·24	0·28	0·68	1·12			0·72	0·90	1·11		
NO_2^-	1,175	700	383	754	—	TMDA	930	574	357	574	—
	0·30	0·27	0·91	1·61			0·66	0·79	0·93	2·01	—
NO_3^-	1,170	710	397	820	—	DETA	—	—	—	710	—
	0·28	0·26	0·66	1·09	—					2·01	
N_3^-	1,160	700	410	750	—	En	890	550	345	555	—
	0·99	0·94	1·48	2·23			0·79	0·71	0·89	1·69	—
Py*	1,150	645	390	688	—	TETA	920	550	352	850	587
	0·47	0·75	1·07	2·22			1·01	0·86	1·10	1·30	2·12
NH_3	1,010	595	360	605	—	TEPA	922	545	347	860	656
	0·56	0·76	0·94	1·68			1·10	0·82	1·30	2·00	2·22
EtA	1,010	610	368	—	—	1,2-Pn	—	—	—	540	—
	0·72	0·90	1·10							1·80	

* Py, Pyridine; EtA, ethylamine; MeA, methylamine; TMDA, trimethylenediamine; DETA, diethylenetriamine; En, ethylenediamine; TETA, triethylenetetramine; TEPA, tetraethylenepentamine, 1,2-Pn, 1,2-propylenediamine.

while the order of stability[10] is:

$$Py < NH_3 < TMDA < TEPA < En$$

In the copper(II) complexes:

$$NO_3^- > H_2O > NO_2^- > N_3^- > Py > TEPA > NH_3 > TETA > TMDA > En > 1,2\text{-}Pn$$

which differs slightly from the stability order.

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A Technique for pyrolysing or vaporizing Samples for Gas Chromatographic Analysis

A TECHNIQUE was recently reported where rapid heating by induction was used to sublime solid inorganic, organic, and metal complexes[1]. The fine powdered sublimate was collected on salt plates and infra-red spectra were determined. The results indicated that very small particle size was obtained, as well as very little decomposition even for organic compounds, although the sublimation technique consisted of heating a platinum dish containing the compound from room temperature to white heat in a few seconds.

It occurred to us that the gaseous products of such a sublimation could be introduced into a gas chromatograph and thus separated for further study.

Normally, a fixed-temperature vaporization block is used on gas chromatographs, so that all possible gaseous products are produced instantaneously; however, it is difficult to choose a temperature which is satisfactory for all components. It was hoped that the rapid heating by induction would result in a series of gaseous products being produced as the temperature rose, each vaporizing at an optimum temperature. Since the time required to reach very high temperatures is only a few seconds, each component would be introduced into the vapour state almost instantaneously, and no broadening of peaks should be seen on the chromatograph.

Two advantages were sought for. First, some separation of volatile from less-volatile components should take place by virtue of the slight time required to pass from low to high temperatures; second, the possibility of reducing cracking of materials unstable at high temperatures, since they will volatilize before cracking temperatures are reached. It should also be possible to use this heating technique for vaporizing viscous or high-boiling liquids which cannot be handled by the usual chromatographic techniques. Pyrolysis of polymers can also be done, since extremely high temperatures can be reached. We have concentrated on this latter work at present and would like to report the results. Some results concerning the other advantages listed were obtained during the work on polymers.

A chromatographic instrument of our own design[2] was modified so that one loop of a gas valve passed through the induction coil of a Leco model *IH*-15 furnace. In our instrument it is possible to make this loop part of the column-detector circuit, or place it under vacuum, or make it part of a loop not entering the instrument. Using the first loop it is possible first to pyrolyse a polymer in a vacuum and then introduce the resulting gases into the column-detector circuit. The second loop can be used to pyrolyse while the helium-flow brings the gases through the column-detector circuit. By comparing chromatographs obtained by both techniques, it is possible to see if better separation of components is obtained by rapidly changing the temperature of the sublimation apparatus or by holding it constant. We are assuming here that the technique of pyrolysing into a helium stream gives chromatographs indicative of a changing temperature sublimation apparatus, whereas the technique of introducing the gases into the chromatograph after pyrolysis is complete gives similar results to a constant-temperature sublimation technique. We also cut out the sample loop after a fixed time so that tarry materials cannot enter the column-detector circuit.

It is possible to use a metal sample holder for the polymers and induce heat in it to pyrolyse samples or, alternatively, mix a metal with the polymer and use it to pyrolyse. The latter technique was chosen because it allows a very intimate mixture of metal and polymer to be obtained and therefore homogeneous heating of the sample. Plaskon metal, commonly used for induction heating of steel samples, was used. In addition, in some runs a very fine iron powder was added to obtain very intimate mixtures. A 10/30 ground-glass sample tube was used with the metal sample mixture. The sample was held by glass wool plugs at a fixed geometry.

The chromatographs for a polyurethane polymer pyrolysis is shown in Fig. 1. The upper curve represents the technique of pyrolysing while the helium stream passes over the sample; the lower is that where the pyrolysis is done in a vacuum and then the products are introduced in the helium stream. The point where the furnace is 'fired' gives a mark on the chromatograph, the width of it being a measure of the firing. The first peak is an air peak since some air is always trapped in the solids and released when they are heated. We note a similar pattern is obtained for both techniques, but slight peak displacement is obtained. Sufficient polymers have been run to show this displacement always occurs. For the first technique discussed above, the peaks appear at slightly longer times. It appears better separation of components is also obtained by this first technique as illustrated by the lack of tailing in the long-time peaks of the upper chromatographs.

While more work will be required to establish the best conditions for pyrolysing samples, work to date suggests the first technique has a good deal of promise. A number of variables must be tested, including length of pyrolysis, column packing and temperature, sample geometry and preparation.

A number of interesting experiments suggest themselves for this system. For example, catalytic effects could be studied by introducing catalysts into the sample. Oxidizers could also be introduced to give oxides of the pyrolysis products and these

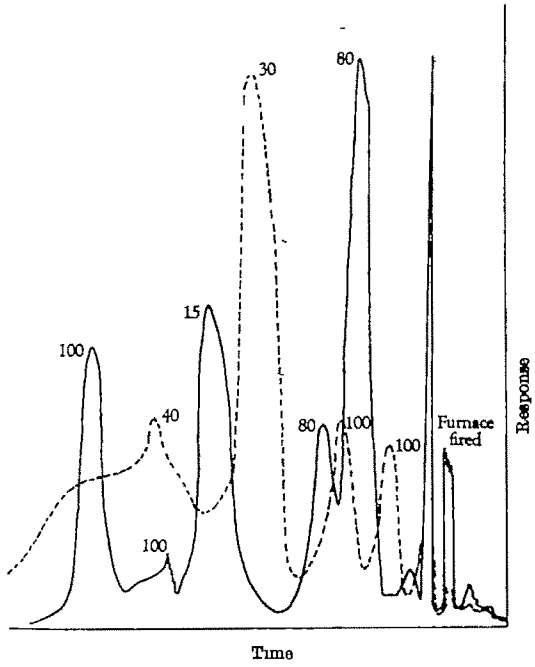

Fig. 1. Upper curve is the chromatograph of a polyurethane pyrolysate using the technique of introducing the gaseous products into the helium stream during pyrolysis. Lower curve is a similar pyrolysate which was introduced into the helium stream after pyrolysis is complete. Silicon rubber column; 130° C.; chart paper ½ in. per min.; flow-rate 100 c.c. per min. Attenuator readings are given at each peak; 100 being equivalent to full gain setting.

could be studied. Solids, high-boiling and viscous liquids will also be attempted in later work. Kinetic studies on polymer ageing, as well as other systems could also be done.

Harns has reported how the infra-red spectra of pyrolysates can be used for identification[3]. By standardizing our technique a similar identification could be done.

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Heterogeneous Catalysis in Hydroformylation

THE original observers of the hydroformylation (Oxo) reaction assumed heterogeneous catalysis. Subsequent workers have attributed, either by specific hypothesis or apparent assumption, both hydroformylation and concurrent hydrogenation (of aldehyde) to homogeneous catalysis by dicobalt octacarbonyl or cobalt hydrocarbonyl. Our recent results, which indicated a heterogeneous character of hydroformylation via cobalt catalysis[1], made it appropriate to wonder if hydrogenation under these conditions were not also in reality heterogeneously catalysed.

The evidence on which arguments for homogeneous catalysis of hydrogenation have been based consists of observations that sulphur compounds and carbon monoxide, which are known to be poisons for metallic hydrogenation catalysts, do not poison this hydrogenation[2]. It is now proposed that these previous observations can be rationalized in terms of a heterogeneous mechanism if the dynamic equilibrium between metallic cobalt and the cobalt carbonyls is taken into account. It has been pointed out that if cobalt carbonyl is subjected to hydroformylation conditions, a precipitation of cobalt occurs in the reactor, and conversely that cobalt carbonyl is formed if metallic cobalt is subjected to these conditions[3]. Also, it has been observed that in the presence of organic materials cobalt hydrocarbonyl decomposes to the metal, tetracobalt dodecarbonyl, carbon monoxide and hydrogen rather than to hydrogen and dicobalt octacarbonyl[4]. Applying this concept of the nature of the catalyst to the mechanism of hydrogenation, it becomes readily understandable that surface poisons should not be effective on a cobalt surface in such a dynamic equilibrium system, since the metal is constantly being solubilized and re-deposited. Each such creation of fresh surface allows the aldehyde to compete with the poison for this surface.

It is thus evident that in order to test adequately the heterogeneity of this hydrogenation catalysis, it is necessary to study poisons which affect metallic catalysts in a fashion more fundamental than blocking of surface adsorption. Such poisons are the heavy metals, which enter into the solid catalyst phase and poison its activity for hydrogen reactions by filling the *d*-band holes with the outer electrons of the poison[5,6]. Experiments in which ions of lead, mercury and bismuth are added in oil-soluble form to a hydroformylation reaction indeed show the anticipated poisoning effect (Table 1).

Table 1. HEAVY METALS AS HYDROGENATION POISONS IN HYDROFORMYLATION MEDIA*

Run No.	Metal ion added	Metal ion (gm. atom/l.)†	$Cobalt^{2+}$ (gm. atom/l.)†	Olefin conversion (mole per cent)	Hydrogenation of aldehyde (per cent)
1–5	None	—	0·020	81·8	90 0
6	$Lead^{2+}$	0·0040	0·020	72 1	22·8
17	$Mercury^{2+}$	0 0040	0·020	80·5	70·8
29	$Thallium^{3+}$	0 0040	0·020	78 8	91·0
40	$Bismuth^{3+}$	0·0018	0 020	76·6	43·0

* Conditions were C_7 olefin (mixed isomers), 177° C., 6 hr. reaction time, 3,000 *g* lb./sq. in. maximum pressure, hydrogen partial pressure varied as the run proceeded from 1,750 to as low as 1,230 *g* lb /sq. in., depending on the amount of hydrogenation which occurred in the given reaction.

† All metals were added in ionic form. Undoubtedly the bulk of metals do not remain in ionic form, hence concentrations are recorded in gm. atom/l.

Conversely, thallium does not poison the hydrogenation. The oxidation-reduction potentials are such that ions of lead, mercury and bismuth should be reduced to the metallic state when brought into contact with metallic cobalt, whereas the thallic ion should be reduced only to the thallous state.

This experimental demonstration of poisoning of hydrogenation by a recognized class of poisons for metallic catalysts, together with a rationalization of the inactivity of the class of poisons previously studied[2], indicates that hydrogenation under hydroformylation conditions in reality proceeds via a heterogeneous mechanism in which metallic cobalt is the catalyst.

A full report on this work will be published elsewhere in the near future.

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BIOPHYSICS

Thermal and Electrical Properties of Nucleic Acids and Proteins

IN 1955, Duchesne and Monfils[1] discovered absorption lines in the frequency-range of 30 Mc./sec. in the sodium salts of deoxyribonucleic acid and nucleoprotein of yeast and of ribonucleic acid of *Escherichia coli*, all in the dry state, when these substances were inserted in the condenser of a super-regenerative oscillator.

It was clear from a detailed study of the whole question[2] that the main factor determining the occurrence of these lines was the piezoelectric character of the substances, and that they originated from mechanical movements of large groups of particles inside the crystals, or perhaps, in the case of large systems such as those under consideration, inside the molecules themselves. This same remarkable piezoelectric property has recently been observed and analysed by Polonsky, Douzou and Sadron[3] using deoxyribonucleic acid of different origins, and it was further discovered by these authors that these substances were ferroelectric, with a Curie point at about 50° C.

In our method[1,2], it was shown that the lines are reversibly shifted by temperature and that the displacements called Δ are given by:

$$\Delta = -\frac{1}{\nu}\frac{d\nu}{dT} = \alpha\gamma$$

where α is the thermal expansion coefficient (in volume) of the substance, and γ the Gruneisen constant. On applying this formula to the deoxy- and ribo-nucleic acids and nucleoprotein already mentioned, it was found that the Δ's reached a remarkably low value comparable to that known for quartz and metals, and in fact a hundred times less than those we had measured for ordinary organic compounds.

We have now extended our earlier investigation to include deoxyribonucleic acid of various other kinds, and also some proteins. Further, as a consequence of the low values of the Δ's, it was possible to infer, according to well-known empirical relationships[4], that thermal and, perhaps, electrical conductivities ought to be exceedingly high. With the view of verifying this inference, it was also decided to perform experiments designed to measure the latter properties.

Calf thymus and herring sperm deoxyribonucleic acid on one hand, and rabbit myosin and actomyosin, as well as collagen, on the other hand, were studied in the form of pellets which were prepared at a pressure of 700 kgm./cm.^{2}. All the compounds were characterized by a few lines especially in the region 33–35 Mc./sec., so that piezoelectricity seems to be a rather general property not only of the nucleic acids but also of the proteins. The frequency shifts which were measured over a temperature range 77–296° K., led to Δ's the approximate values of which were respectively 50, 56, 85, 100 and 47 $\times 10^{-6}$ unit. It was found that the absorption lines disappear around 323°K. in the case of the deoxyribonucleic acid. It is to be noted that the accuracy of the measurements was excellent for the herring sperm deoxyribonucleic acid, in which absorption lines were intense and well defined. In all other cases, it was much less satisfactory because the lines were considerably broader. The order of magnitude of the Δ's is unmodified in the deoxyribonucleic acid series, including those which were measured earlier, and among the proteins the values corresponding to myosins seem to be the highest. In this connexion, the nucleoprotein measured previously was characterized by a Δ definitely greater than in the corresponding deoxyribonucleic acid, and this may result from the influence of the combined protein.

We have also measured the electrical conductivities. As single crystals were not available, we used specimens in the powdered or fibrous state. The samples were generally in the form of a pellet of about 0·3 cm. thick and 1·3 cm. in diameter. The average value of the pressure used to prepare the pellets was 700 kgm./cm.^{2}. The specimens were then compressed between brass electrodes. The system was placed in a closed tube filled with dry air and was heated in a thermostat. The electrical resistance was measured using a commercial megohmmeter (B.P.L. *RM*-175), the applied voltage being 500 V.

In the series of biological substances examined, the variation of the d.c. electrical conductivity with temperature was found to follow the well-known equation for semi-conductors:

$$\sigma = \sigma_0 \exp(-E/2kT)\ \Omega^{-1}\ \text{cm.}^{-1}$$

The activation energies found in the range 273–313° K. were: herring sperm deoxyribonucleic acid 1·80 eV., calf thymus deoxyribonucleic acid 1·80 eV., myosin 1·75 eV., collagen 0·9 eV. Despite the fact that the two samples of deoxyribonucleic acid were not only of different origins but were also in different forms (calf thymus deoxyribonucleic acid was not compressed and was used in its natural fibrous state), they were found to have practically equal E. The constant σ_0 of the herring sperm deoxyribonucleic acid, which was less reproducible than the activation energy, was of the order of magnitude of 10^8 Ω^{-1} cm.$^{-1}$. The activation energies must not be considered as very accurate not only because of lack of homogeneity of pellets but also because they are presumed to depend to a certain extent on the quantity of adsorbed water. A sample of herring sperm deoxyribonucleic acid was irradiated with a dose of 10^8 roentgens of gamma-rays of cobalt-60 and no noticeable change was measurable in its semi-conductivity. As the current through the substances reaches a steady value in a few seconds, it seems that the main contribution to the conductivity should be

due to the motion of electrons. This would indeed be in agreement with recent discoveries of Blumenfeld *et al.*[5], according to which the anomalous magnetic characteristics of nucleic acids found by electron spin resonance are largely connected with the electric anisotropy of the systems.

On the other hand, it seems that the activation energy of myosin is particularly small in comparison with the other proteins, for which values as high as 3·0 eV. are fairly commonly found[6]. The values obtained for σ_0 were about 5×10^2, which is exceptionally low when compared with that for deoxyribonucleic acid. For collagen, the constant σ_0 may be estimated at $4 \times 10^{-3}\ \Omega^{-1}\ \text{cm.}^{-1}$.

We believe that all these remarkable and very intimately related properties characterizing nucleic acids and nucleoproteins, as well as proteins, must play a large part in the specific biological behaviour of these substances. Indeed, as a result of their well-known peculiar structure, the individual molecules as such may be responsible for most of the properties described here. Experiments now in progress in our laboratory have been devised to test these views.

We thank Dr. G. Hamour for generously supplying us with samples of myosin.

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BIOCHEMISTRY

Identification of the Black Sub-Unit of the Crystallographic Model of Horse Hæmoglobin with the Valyl-Glutaminyl Polypeptide Chain

THE three-dimensional Fourier synthesis of horse hæmoglobin showed four sub-units which were identical in pairs[1]. In the model of the molecule, these two kinds of sub-units were painted black and white for distinction, the chief difference being the presence of one reactive sulphydryl group in each of the two black sub-units and their absence from the white ones.

Chemical and physico-chemical methods have shown that horse globin consists of two types of polypeptide chains and each chain is equivalent to one-quarter the molecular weight of hæmoglobin[2-4]. Procedures for the separation of these two types have been devised[3,5]. One type has the N-terminal sequence valyl-leucyl (*vl*-chains) and the other valyl-glutaminyl (*vg*-chains)[6,7]. Each of the two types of chain contains one residue of cysteine[8], but only in one type is the cysteine reactive in the native protein. By determining whether the *vl*- or the *vg*-chain carries the reactive cysteine, we have now been able to correlate the chemical sub-units with those found by X-ray analysis.

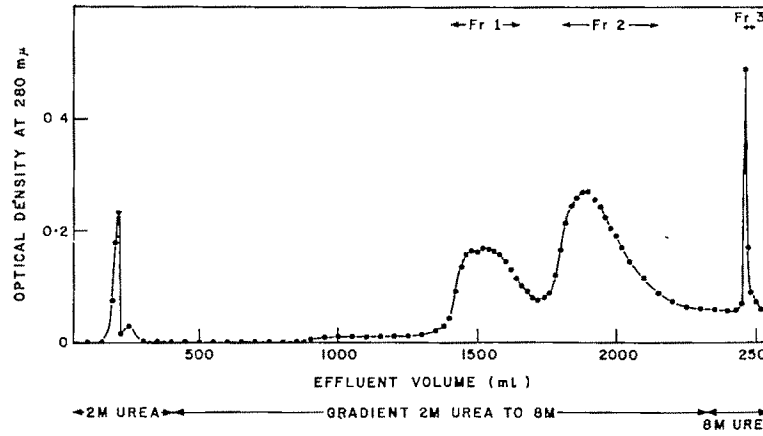

Fig. 1. Elution pattern of globin from horse oxyhæmoglobin treated with iodoacetamide. Column, 60 cm. × 2·2 cm. of 'Amberlite CG-50' type 2 resin. Elution with urea gradient, 2–8 *M*, *p*H 1·9

Treatment of native hæmoglobin with iodoacetamide should affect cysteine residues on the black sub-units only and give rise, after acid hydrolysis, to S-carboxymethyl cysteine. Riggs and Wells[9], by a similar method involving N-ethyl maleimide, have located the more reactive sulphydryls of human hæmoglobin on the β- or valyl-histidyl-chains.

The red cells of fresh oxalated horse blood were washed several times with saline and lysed by dilution with water. After removal of cell debris by centrifugation, a ten-fold excess of iodoacetamide was added. After 1 hr. at room temperature, excess reagent was removed by dialysis against 0·01 *M* ammonium phosphate, *p*H 7. The oxyhæmoglobin was crystallized by the addition of ammonium sulphate to 2·0 *M*. The crystals were filtered off, washed with ammonium sulphate solution, packed wet in a plastic vial and sent across the Atlantic by air mail. On arrival they were put in a refrigerator, but transformation to methæmoglobin had occurred.

The methæmoglobin was reduced in 0·01 *M* phosphate buffer *p*H 7 with a five-fold excess of ammonium ferrotartrate and dialysed against water. Globin was precipitated with acid-acetone[3] and fractionated by the chromatographic procedure of Wilson and Smith[5]. The preliminary slurrying of globin solution with a portion of resin before addition to the column was omitted. Fig. 1 shows the elution pattern and the fractions selected.

Amino-acid analyses of samples hydrolysed in 5·7 *N* hydrochloric acid in sealed tubes for 24 hr. at 105° C. were made, using a Beckman-Spinco amino-acid analyser and the procedures of Spackman, Moore and Stein[10]. The averages of duplicate analyses (uncorrected for decomposition or incomplete hydrolysis) are listed in Table 1 as μmoles of amino-acid relative to aspartic acid = 14·0.

Table 1. RECOVERIES OF AMINO-ACIDS FROM 24-HR. HYDROLYSATES OF GLOBIN FRACTIONS

Amino-acid	Fraction 1 (μmoles)	Fraction 2 (μmoles)	Fraction 3 (μmoles)
Lysine	11·3	10·8	—
Histidine	10 4	8·8	—
Arginine	3·1	3 9	—
Cysteic acid	0·5	0·1	0·1
S-carboxymethyl cysteine	0	0 6	0·4
Aspartic acid	14 0	14 0	14 0
Threonine	8 7	3·4	4·5
Serine	11 2	5·4	7·0
Glutamic acid	4·8	12 7	12 2
Proline	6·2	5·1	5·5
Glycine	10 6	13 0	12·9
Alanine	16 5	13·8	14·3
Valine	12·8	14 1	14·9
Methionine	1·0	0 9	1 0
*Iso*leucine	0	0	0 8
Leucine	22 3	19 2	19·5
Tyrosine	2 8	2·9	2 6
Phenylalanine	7·1	7·7	7·7

Except for the presence of cysteic acid, fraction 1 has the composition of 24-hr. hydrolysates of the *vl*-chain, and excepting S-carboxymethyl cysteine and cysteic acid, fraction 2 that of the *vg*-chain. The small amount of *iso*leucine in fraction 3 is likely to be due to some contaminating protein; otherwise its composition is similar to that of the *vg*-chain.

S-carboxymethyl cysteine was present in fractions 2 and 3 only; none could be detected in the hydrolysate of fraction 1. The valyl-glutaminyl chains must then correspond to the black sub-units of the crystallographic model.

The yield of S-carboxymethyl cysteine, about 0·6 mole/mole polypeptide, is similar to that found earlier[8]. The nature of the oxidation that converted oxyhæmoglobin to methæmoglobin and unreacted cysteine to cysteic acid is being investigated. The occurrence of this oxidation, however, does not invalidate the identification of the black sub-unit with the valyl-glutaminyl polypeptide.

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Production of Acid Mucopolysaccharides by Fibroblasts in Cell Cultures

ACID mucopolysaccharides characteristic of connective tissue ground-substance are produced in tissue culture by fibroblasts from a variety of tissues of mesenchymal derivation[1-4]. It would appear that in the conditions of growth in tissue culture the spectrum of acid mucopolysaccharides typical of a given tissue[5] is not reproduced. Rather the results suggest that the cultured cells, whatever their tissue of origin, revert to a similar pattern with respect to production of acid mucopolysaccharides in that all secrete into the medium a major fraction of hyaluronic acid and a smaller component of sulphomucopolysaccharide, presumably chondroitin sulphate *C* [2,3]. Moreover, the present experiments show that production of acid mucopolysaccharides by 'stock' strains of fibroblasts may continue in tissue culture for long periods of time, up to years.

In order to assess the effects on synthesis of acid mucopolysaccharides of different conditions of growth and nutrition, it was first necessary to devise reliable methods of measuring accurately the amounts of acid mucopolysaccharides produced per cell during any given interval. Only in this way would it be possible to gain information about such issues as the relationship between the rate of cellular proliferation, cell concentration and composition of medium to the formation of a specific product, the acid mucopolysaccharides.

To this end, series of replicate cell cultures were prepared. Cell suspensions derived from trypsinization of the primary outgrowth of osteogenic fibroblasts from explants of stripped new-born rat calvarium were rendered uniform and dispensed in identical aliquots into *T*-15 culture flasks, each of which then contained approximately the same initial number of cells. Cultures were washed and fed with fresh medium usually every 72 hr. (except as otherwise indicated), each interval constituting a feeding period. 'Used' media withdrawn at each feeding were saved for analysis. The cells grew well on the glass floors and preserved a uniform appearance. They were collected at intervals from groups of flasks for determination by deoxyribonucleic acid (by the diphenylamine method as adapted by Zamenhof[6] and modified by Burton[7]), and acid mucopolysaccharides (by carbazole determination of uronic acid content from fractions obtained either after exhaustive hyaluronidase digestion, or a protamine precipitation method modified from Bollet[8]). Results were expressed as a ratio of the amount of acid mucopolysaccharides or acid mucopolysaccharides-uronic acid per μgm. of deoxyribonucleic acid per flask, the specific production, and as a rate, the specific production per hour. The mean amount of deoxyribonucleic acid present over a given period was calculated whenever possible as a more representative value than either the initial or terminal deoxyribonucleic acid values for that period.

Production of acid mucopolysaccharides on growth media. At moderate rates of growth in a 'biological' medium consisting of 20 per cent human cord serum, 50 per cent beef amniotic fluid, and 30 per cent Earle's balanced saline solution, the acid mucopolysaccharides uronic acid: deoxyribonucleic acid ratio ranged from 1·6 to 4·0 (mean = 2·75 ± 0·18). This average corresponds to approximately 47×10^{-12} gm. acid mucopolysaccharides per average cell, if it is assumed that each cell is equivalent to a diploid rat cell containing $6{\cdot}8 \times 10^{-12}$ gm. of deoxyribonucleic acid (Leslie, 1955), and that its uronic acid content constitutes 40 per cent of the acid mucopolysaccharide molecule.

Analysis of specific production and its rate by intervals revealed that within 20 hr. after the first feeding following set-up (that is, Period II of Table 1) a specific production of 1·83 μgm. acid mucopoly-

Table 1. RATES OF GROWTH AND PRODUCTION OF ACID MUCOPOLYSACCHARIDES BY CULTURES OF FRESH RAT CELLS IN THE INTERVAL BETWEEN SUCCESSIVE CHANGES OF MEDIUM
(Exp No. 50—Medium No. 5)

Period	Hours from last feed	Net supernate AMPS–uronic acid μgm /flask	DNA μgm./flask	Cell-bound AMPS–UA	Specific AMPS–UA production (μgm /μgm. mean DNA)	Rate constant spec. prod /hr
I	50*	3 98	1·13	—	—	
II	20	3·07	—	—		
		2 32	1 81	0 7	1 83	0 092
	79	5 72 (± 0 63)	2 62	0 4	3 10	0 023
			2·50	0 55		
III	12	1·61	2·26	0 8	0 79	0 066
		2·00	2·30	0 8		
	34	5·37	3·12	0 6	2 07	0 062
		5·42	2 90	0 65		
	50	6 72	2 93	0 65	2 46	0·029
		6 92	3 05	0·55		

* Refers to hours after initial set-up
AMPS, acid mucopolysaccharides, UA, uronic acid; DNA, deoxyribonucleic acid.

saccharides–uronic acid/μgm. mean deoxyribonucleic acid had occurred, while the deoxyribonucleic acid had increased 60 per cent, its maximal rate of increment. The amount of acid mucopolysaccharides released in this time was 47 per cent of the total produced over the whole (79 hr.) feeding period. In the next 59 hr. of this period, deoxyribonucleic acid increased an additional 41 per cent, during which time specific production was 1·4 μgm. acid mucopolysaccharides–uronic acid/μgm. mean deoxyribonucleic acid and the production-rate was 0·023, a decrease of 75 per cent. The acid mucopolysaccharides–uronic acid/final deoxyribonucleic acid ratio for the whole 79-hr. feeding period was 2·24; specific production for the whole period on the basis of the mean deoxyribonucleic value was 3·1. Within period III, that is, the subsequent period following the second feeding, the same relationships obtained, so that in the segment of this period during which the rate of increase of deoxyribonucleic acid was greatest, that is, the first 34 hr., production-rate was also greatest. Such results suggested a direct, rather than a reciprocal, overall relation between rate of cell population increase and synthesis of acid mucopolysaccharides in a relatively rich medium promoting moderate growth. With still higher rates of growth (obtained on a low-serum growth-stimulating medium consisting of 5 per cent cord serum, 75 per cent Eagle's medium and 20 per cent whole egg ultrafiltrate) the increment of acid mucopolysaccharides produced did not keep pace with the increase in deoxyribonucleic acid; specific production was generally not as high as that measured during comparable periods of moderate growth on high serum media with amniotic fluid instead of whole egg ultrafiltrate.

Conversely, when cultures nourished on these growth media became 'crowded', that is, as the cells of the monolayer became contiguous, the rate of cell proliferation declined. This reduced growth was accompanied by a decreased specific production of acid mucopolysaccharides.

Production of acid mucopolysaccharides on maintenance media. Maintenance media consisting of 2 per cent dialysed cord serum, Earle's balanced saline and variable proportions of Eagle's medium supported seemingly healthy cell life, but with little or no growth, for six or more feeding intervals. Increased proliferation could be effected in such media by augmenting the proportion of Eagle's medium. Acid mucopolysaccharides continued to be produced by cells in maintenance media, in some instances attaining a specific production ratio as high as 1·0; but in no case was specific production greater than 1·0; more usually it was less (Fig. 1). Addition of glucose, known to be a substrate for synthesis of acid mucopolysaccharides, in concentrations of 0·04–0·3 per cent in maintenance medium has no appreciable effect on specific production.

Distribution and kind of acid mucopolysaccharides produced in cell culture. A fraction of the total amount of acid mucopolysaccharides synthesized in any culture remained bound to the cells after washing with either warm or cold saline. This cell-bound acid mucopolysaccharide usually amounted to about 10 per cent of that secreted into the medium. However, in conditions of crowding, the proportion of cell-bound acid mucopolysaccharides to the total increased markedly and reached high levels in extremely dense 'stock' cultures. In some series of analyses of very crowded non-growing stock cultures, specific production tended to be stabilized at about 0·6.

The acid mucopolysaccharides produced by both stock strains of rat osteogenic fibroblasts and recently isolated cell lines was predominantly non-sulphated, and had the properties of hyaluronic acid. After addition of sulphate labelled with sulphur-35 to the

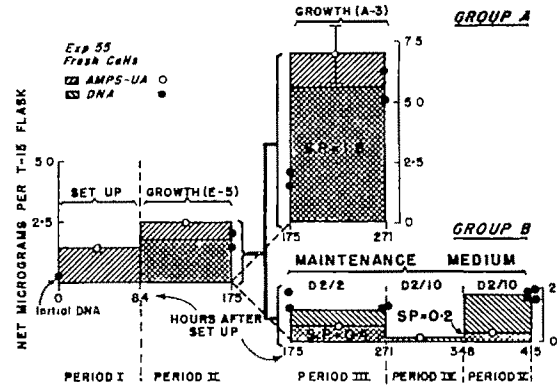

Fig. 1. Growth and production of soluble acid mucopolysaccharides over successive feeding periods by cell cultures of recently isolated rat fibroblasts. Cultures were grouped at random and transferred to either growth or maintenance medium at the end of period II. Differences in growth and total and specific production of acid mucopolysaccharides (see text) 96 hr. later are graphed. Slight growth and production of acid mucopolysaccharides continued on maintenance medium
AMPS, acid mucopolysaccharides; UA, uronic acid; DNA, deoxyribonucleic acid

medium, sulphate was fixed in not more than 5–10 per cent of the acid mucopolysaccharides secreted by the fibroblasts. Chemical fractionation and analyses of the acid mucopolysaccharides produced by cultured fibroblasts are in progress.

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A Rapid Dialyser for Small Samples

WHILE purifying enzymes, it became necessary to dialyse small amounts of a suspension with maximum efficiency, without allowing the precipitate to settle. This led to the design of a rapid dialyser of simple construction, which we call a 'flat dialyser'.

The dialysis cell consists of a frame (Fig. 1) cut from a 1-mm. thick 'Plexiglas' sheet. This is slipped into previously moistened Visking seamless cellulose tubing (2⅜ in. wide: for sizes of tubing mentioned later only the inflated diameter will be given), inside which it fits snugly, leaving about 5 cm. of tubing on each side. One of the ends of the tubing is then wound on a 'Plexiglas' strip (0·3 × 0·7 × 7 cm.) and fastened on to the frame with a wide rubber band *F* (Fig. 2). If the length of the tubing has been correctly chosen, in the last turn some tension will be applied to the membrane, thus stretching it over the frame. The solution to be dialysed (up to 1·5 ml.) is then introduced from the open end with a Pasteur pipette, and most of the excess air is driven out by pressing the cellulose tubing between the fingers. The open side of the cell is then closed in the same way as the other

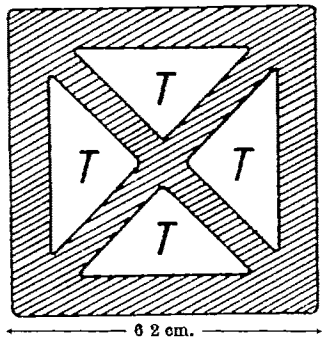

Fig. 1

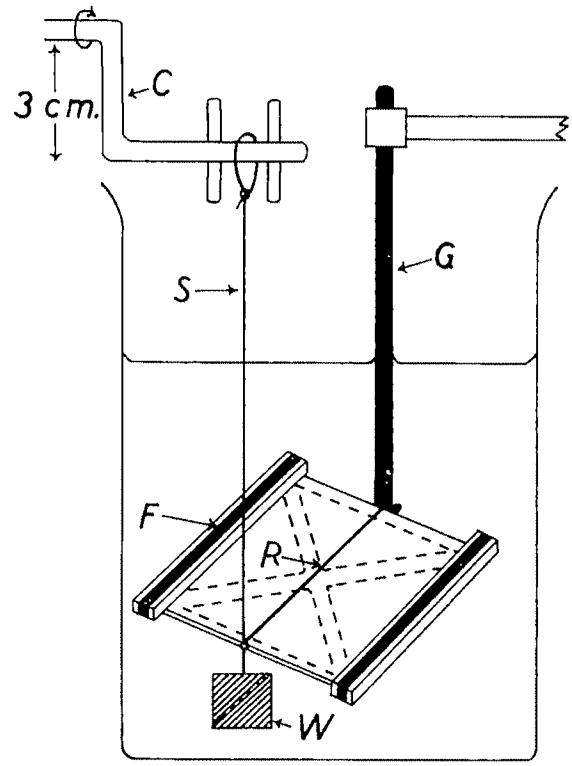

Fig. 2

one. The assembled dialysis cell is inserted into a rubber band *R*, which is tied on one side to a glass rod *G*, supported by a clamp, and on the other side to a weight *W* and to a length of string *S*. The other end of *S* is made into a loop and hooked from the glass crank *C*, which is driven by a motor at about 60 r.p.m., thus imparting an up-and-down motion to the dialysis cell. The air bubbles entrapped, together with the liquid in the triangular spaces *T*, help to stir the solution. The whole apparatus is placed in a 1,000-ml. beaker, containing at least 600 ml. of liquid. When the dialysis is completed, one side of the cell is unrolled, the cell is held in an oblique position and the liquid is sucked out with a Pasteur pipette.

This arrangement was compared with other methods by dialysing 1 ml. samples of 0·1 *M* sucrose at 1° C. against 800 ml. of water for different times, and analysing the solution that remained in the bag. The results, corrected for changes of volume during dialysis, are shown in Fig. 3. Most of the points are average values of duplicate, and in somes cases triplicate, experiments. Under condition *A*, 8/32 in. cellulose tubing containing the sample was tied on both ends, leaving a small bubble of air inside and placed in a beaker provided with a magnetic stirrer. Condition *B* was similar but the diameter of the tubing was larger (18/32 in.) and about three-fourths of the inner space were occupied by air under a slight pressure. When the magnetic stirrer was set at a high speed, the bag revolved on its vertical axis so rapidly, that the liquid rose on to the sides, thus increasing the useful surface for diffusion and probably the internal agitation. In order to eliminate possible discrepancies arising from variations in permeability of the different sizes of cellulose tubing used[1], condition *A* was repeated with the 18/32 in. tubing. This arrangement is called condition *C*. Condition *D* refers to an 8/32 in.

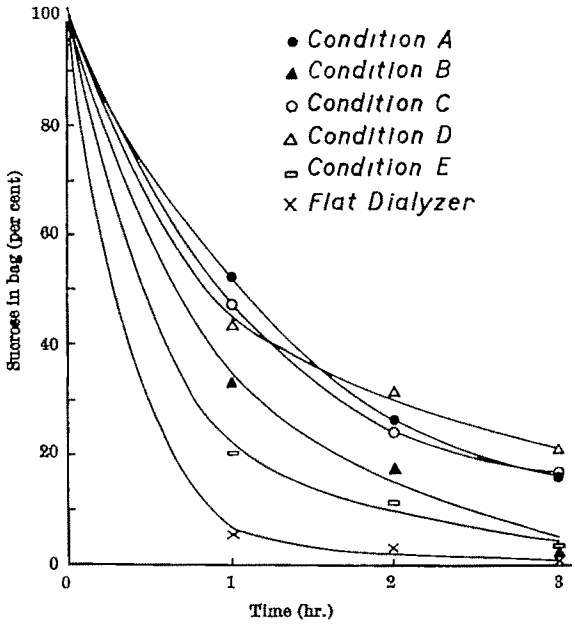

Fig. 3. Time-course of dialysis with different methods

tubing, containing an air bubble and a glass bead and placed in a rocking dialyser. Finally, condition *E* was the arrangement first proposed by Seegers[1,2], where a glass tube closed at both ends was placed in the cellulose bag, thus confining the solution to be dialysed to a thin layer in the annular space formed. In this case also the bag was placed in a rocking dialyser.

It can be seen in Fig. 3 that conditions *A*, *C* and *D*, with a membrane surface about a quarter that of the flat dialyser, gave similar results, while condition *B* was appreciably superior. The flat dialyser was the most efficient, followed by condition *E*. Since in the last two cases the membrane surface in contact with the inner liquid was about the same, the difference was probably due to the internal stirring obtained in the flat dialyser. It should be noted that condition *E* was unsuitable for our particular purpose, because the precipitate sedimented during the run.

In another experiment 2 *M* ammonium sulphate was used. After 30 and 60 min. dialysis under condition *A* the amount of salt remaining in the bag was 40 and 13 per cent respectively. The corresponding values for the flat dialyser were 3·8 and 0·6 per cent.

We are indebted to our colleagues of the Instituto de Investigaciones Bioquímicas 'Fundación Campomar' for many useful discussions. This work was supported in part by a research grant (No. *G*-3442) from the National Institutes of Health, U.S. Public Health Service and by the Rockefeller Foundation.

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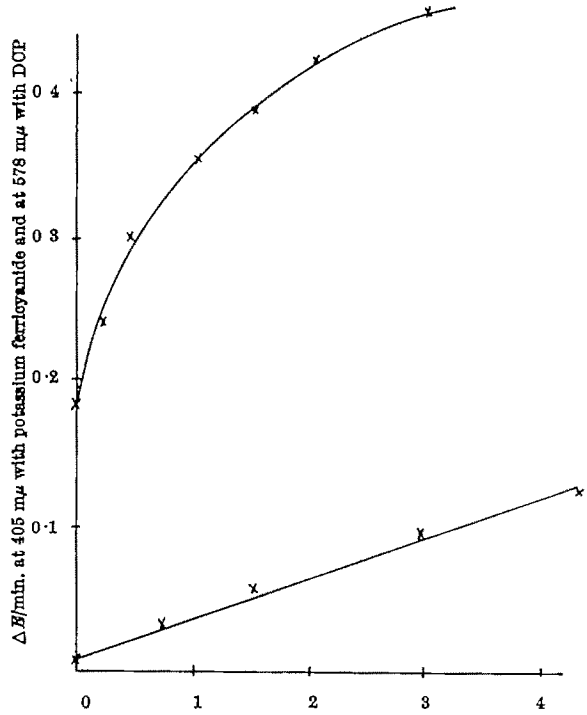
Phenazine Methosulphate as a Mediator in the Oxidation of Pyruvate by Pyruvate Decarboxylase from Brewer's Yeast

PURIFIED pyruvate decarboxylase from brewer's yeast[1] is not only capable of decarboxylating pyruvate to acetaldehyde and carbon dioxide[2], but can also catalyse the oxidation of pyruvate to acetate with 2,6-dichlorophenolindophenol as artificial hydrogen acceptor[3]. Ferricyanide cannot act as a hydrogen acceptor with pyruvate decarboxylase irrespective of whether the enzyme is prepared from yeast[3] or wheat germ[4].

We now find phenazine methosulphate to be an excellent electron carrier for the oxidation of pyruvate by pyruvate decarboxylase from brewer's yeast. Although phenazine methosulphate is not reduced to any measurable extent as no extinction changes were observed at 366 and 405 mμ, it accelerated the reduction of 2,6-dichlorophenolindophenol by some 120 per cent and made possible the otherwise scarcely measurable reduction of ferricyanide (Fig. 1).

The reaction-rate is not dependent on the concentration of ferricyanide. At *p*H 7·4 there is significant non-enzymatic reduction of 2,6-dichlorophenolindophenol and ferricyanide respectively, but under the conditions of our experiments (*p*H 6·0) the non-enzymatic reaction is negligible. That phenazine methosulphate works only as a carrier, and is not itself reduced to a measurable extent could be related to its negative redox potential[5].



Phenazine methosulphate concentration in gm./ml. × 10^2 with DCP and gm./ml. × 2 10^3 with potassium ferricyanide

Fig. 1. Acceleration of reduction of DCP and potassium ferricyanide by addition of varying concentrations of phenazine methosulphate. In cuvette (d = 1 cm) 1 0 ml. *M*/20 pyruvate, 1 8 ml *M*/6 citrate/sodium hydroxide buffer *p*H 6 0, 0 01 ml. purified yeast carboxylase[1] (protein content as above), and DCP or potassium ferricyanide as detailed above; total volume 3 0 ml. Upper curve, 40 μgm. DCP/ml.; 30 μgm. enzyme protein/ml.; lower curve, *M*/300 potassium ferricyanide; 300 μgm. protein/ml DCP = 2,6-dichlorophenolindophenol

In recent experiments with pyruvate labelled with carbon-14, compounds of pyruvate and acetaldehyde with thiamine pyrophosphate (activated pyruvate and activated acetaldehyde) were found to be intermediates of pyruvate decarboxylation[6]. Considering these findings and other previous experiments on the oxidation of pyruvate with 2,6-dichlorophenolindophenol[3] a possible reaction sequence which would account for the effects illustrated in Fig. 1 would be: pyruvate → α-lactyl-thiamine pyrophosphate (activated pyruvate) → α-hydroxy-ethyl-thiamine pyrophosphate (activated acetaldehyde) → α-oxoethyl-thiamine pyrophosphate (acetyl-thiamine pyrophosphate) → acetate, the penultimate step being brought about by phenazine methosulphate and 2,6-dichlorophenolindophenol or ferricyanide.

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Elution of Alkaloids from Citrate-buffered Paper Chromatograms

ONE of the most satisfactory methods of paper chromatography of alkaloids is the butanol–citrate system introduced by Curry and Powell[1]. It suffers, however, from the disadvantage that if one attempts to elute the alkaloid with chloroform for subsequent confirmatory tests, a certain amount of citrate is also extracted. This interferes with certain important colour tests, as the yellow colour which it gives with concentrated sulphuric acid modifies any colour given by the alkaloid. For example, morphine with the Marquis reagent gives a muddy brown instead of a clear violet.

This drawback can be overcome by converting the citrate to the barium salt, which is much less soluble in organic solvents. The chromatogram spot is cut out and, if the paper has been sprayed with iodoplatinate or iodobismuthate, decolorized with a drop of 10 per cent sodium sulphite solution. It is then dried, treated with a drop of a 10 per cent solution of barium chloride, re-dried and the free base liberated by the addition of a drop of concentrated ammonium hydroxide solution. After again drying, the alkaloid is eluted with chloroform[2,3], and its identity confirmed by suitable colour and micro-crystal tests[4].

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Production of D-Araboascorbic Acid by *Penicillium*

WE have found that some species of *Penicillium* produce D-araboascorbic acid. Rarely has this acid been found in biological material or products. Isherwood *et al.*[1,2] have found it in cress seedlings in D-altrono-γ-lactone solution and in the urine of a rat injected with D-mannono-γ-lactone.

P. decumbens, *P. chrysogenum*, *P. chrysogenum* mut. *fulvescens* Takashima Arima and Abe, *P. notatum*, *P. meleagrinum* and *P. cyaneofulvum* produced D-araboascorbic acid from sucrose.

The following medium was used (per cent): glucose or sucrose, 2; sodium nitrate, 0·1; ammonium sulphate, 0·1; urea, 0·1; potassium dihydrogen phosphate, 0·25; crystalline magnesium sulphate, 0·1; crystalline manganese sulphate (trace); and crystalline zinc sulphate (trace); *p*H 5·2. The *Penicillium* was incubated for five or seven days at 25–27° C. The broth showed strong reducing activity to 2,6-dichlorophenol indophenol. The contents in the broth were up to 3 mgm. per ml. After the broth was cleared of impurities, the supernatant was run through the anion resin '*IR-4B*' column[3]. 1 *N* hydrochloric acid solution was used in elution. The effluent was evaporated *in vacuo* to a syrup at 25–30° C. under an atmosphere of carbon dioxide. After the syrup was dried in a vacuum desiccator for three or five days, white crystals were obtained. These were recrystallized from methanol dioxane mixture. The 2,4-dinitrophenyl hydrazone was prepared from the resin effluent[4]. The chemical properties of the free crystal and the osazone are shown in Table 1 and their infra-red absorption spectra in Figs. 1 and 2.

D-Araboascorbic acid was produced from D-glucose, D-gluconate and sucrose only; but not from other carbon sources, for example, glycerin, 2-ketogluconate, glucuronate and galacturonate. These observations make it seem possible that the conversion of carbon source into D-araboascorbic acid occurs without rupture and inversion of the carbon chain. The stereochemical relation between glucose and D-araboascorbic acid was studied by means of isotopes. The replacement culture by the intact cells

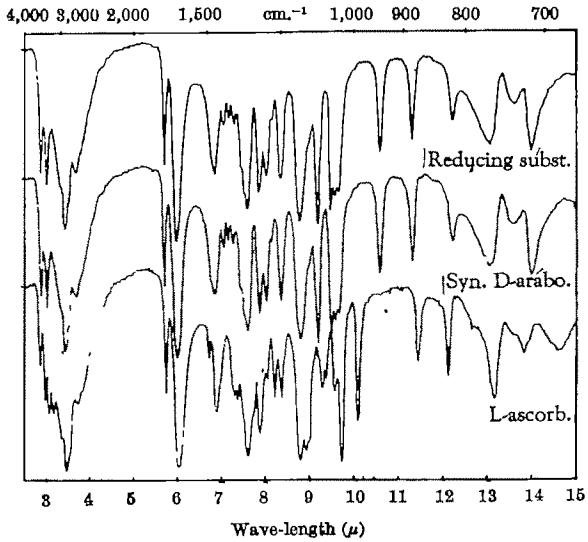

Fig. 1. Infra-red absorption spectra of free crystal

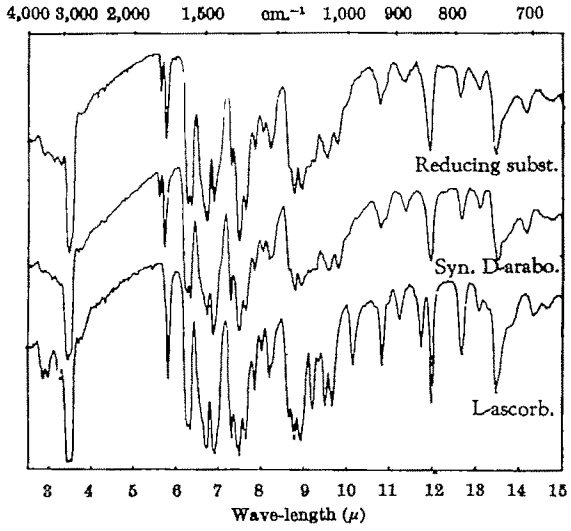

Fig. 2. Infra-red absorption spectra of 2,4-dinitrophenyl hydrazone

of *P. notatum* was carried out with D-glucose-1-^{14}C as a tracer. The D-araboascorbic acid was isolated by paper chromatography from the broth and crystallized. In order to determine the distribution of the isotopic carbon, the crystals were decarboxylated in 8 *N* sulphuric acid at 100° C. for 3 hr., and the residual, furfural, was burned and the radioactivities measured in barium carbonate[3]. It was found that D-glucose-1-^{14}C was converted to D-araboascorbic acid with 80 per cent of its activity in the carbon 1.

Table 1. CHEMICAL PROPERTIES OF THE REDUCING SUBSTANCE

(1) Free crystal			
m.p. 172° C. (uncorr.)			
Anal.	Calcd. for $C_6H_8O_6$	C 40 92%	H 4 58%
	Found	C 41 27%	H 4 66%
$[\alpha]_D^{26.5}$ −23° (1% in water)			
Maximum absorption in ultra-violet spectrum		245 mμ (in 2 per cent hydrogen phosphate)	
		265 mμ (in water)	
(2) 2,4-dinitrophenyl hydrazone			
m.p. 238–242° C. (uncorr.)			
Anal.	Calcd. for $C_{12}H_{14}O_{12}N_6$	C 40 44%	H 2 64% N 20 97%
	Found	C 41·55%	H 2·84% N 21 15%

Investigations of the intermediates between glucose and D-araboascorbic acid have been carried out which indicate the following possible scheme:

D-Glucose → D-gluconate → 3-keto-D-gluconate → D-araboascorbic acid
D-gluconate → D-glucono-γ-lactone → D-araboascorbic acid

We wish to express our thanks to Prof. T. Asai and Prof. K. Yamada, University of Tokyo, and Dr. H. Okazaki, Sankyo Co., Ltd., for their kind advice.

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RADIOBIOLOGY

Prevention of the Lethal Effect of the Decay of Incorporated Phosphorus-32 by Growth at 45°

IN recent years there has been a growing conviction that understanding the effects of radiation on bacterial cells requires distinguishing between the primary radiation targets on one hand and the metabolic events which ensue, on the other[1]. Even if the primary target is, or includes, deoxyribonucleic acid, as is the case for irradiation with ultra-violet light of wave-length 2537 Å. and for X-irradiation, the probability of survival can be increased by such post-irradiation treatments as exposure to visible light[2], incubation at elevated temperature[3], antibiotic-induced inhibition of protein synthesis[4], etc.

Inactivation of bacteria by the decay of incorporated phosphorus-32 represents another instance where the targets include deoxyribonucleic acid[5]. It is therefore of interest to report that here too the lethal chain of events may be modified after primary damage has presumably occurred. Cells of *Escherichia coli* strain *B* containing phosphorus-32 which fail to form colonies if incubated at the usual temperature of 37°, will do so if incubated at 45° instead.

Carrier-free phosphorus-32 in the form of orthophosphate was obtained from E. R. Squibb and Sons, New Brunswick, New Jersey. The techniques employed to incorporate the isotope and to measure survival have been described by Fuerst and Stent[5]. The only deviation from their procedure was to freeze and store the radioactive and control aliquots at − 78° instead of − 196°. After thawing, cells were spread on the surface of two sets of nutrient broth agar plates. One set was incubated at 37° and the other at 45°. The numbers of colonies appearing were counted after 24 hr.

Non-radioactive control cells tested immediately after growth and after various periods of storage in the cold did not show a difference in colony count between plates incubated at 45° and at 37°. Cells containing phosphorus-32 also showed no difference when plated immediately after the incorporation of the isotope. The effect of 45° incubation on *B* cells tested during the course of decay is illustrated in Fig. 1. A long plateau in the curve for 45° incubation was observed in repeated experiments and a short plateau was observed occasionally in the curve for 37° incubation.

It has been shown that the cellular processes which determine the lethal and genetic effects of ionizing and ultra-violet radiation are completed in a time corresponding to less than one division[6]. By means of temperature-switch experiments[6], it was found that this generalization also applies to the lethal effect of decay of phosphorus-32. As shown in Fig. 2, when thawed and plated cells are incubated first at 37°, recovery decreases rapidly if transfer to 45° is made at later than ½ hr. Conversely, if the first incubation is at 45°, recovery begins immediately and 50 per cent of potentially reactivable cells can be rescued by 1 hr.

Fuerst and Stent[5] found that radioactive cells of *E. coli* strain 15_T^-, a thymine-less mutant, exhibited an increased lag before division at 37°. Control cells started to divide almost immediately, but cells containing phosphorus-32 did not begin until 1½–2 hr.

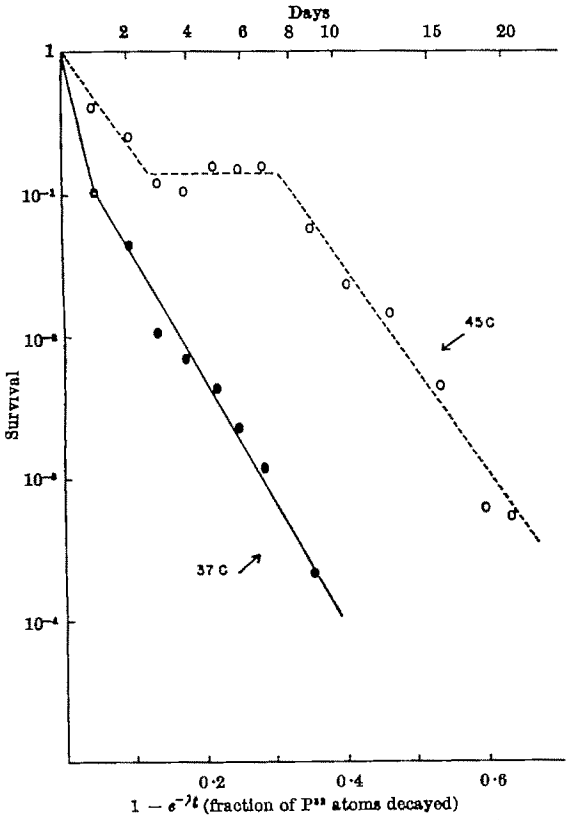

Fig. 1. Survival of phosphorus-32-containing *E. coli B* as measured by incubation at 37° and at 45°. Specific activity, 10 mc. phosphorus-32 per mgm. total phosphorus

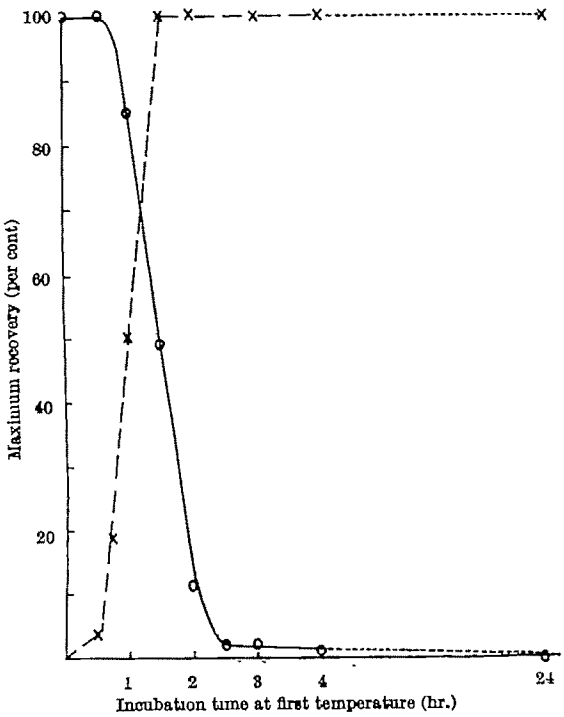

Fig. 2. Effect of changing incubation temperature at various times after plating. O, First temperature = 37°; ×, first temperature = 45°. The data were obtained when 17 per cent of the phosphorus-32 atoms had decayed. At this time, no recovery corresponded to 0 5 per cent survival and maximum recovery to 12 per cent survival

(depending on the amount of phosphorus-32 decay that had occurred). By re-spreading experiments[7], a lag of ½-hr. was found for control *B* cells at 45° and 1 hr. for radioactive *B* cells at 45° (1 per cent survival at 37°). A point of interest is that the growth of the cells containing phosphorus-32 at 45° was synchronized, in agreement with previous observations at 37°[5].

Reduction of the lethal effect of phosphorus-32 incorporated into strain *B* could not be obtained by other treatments which are effective after irradiation with ultra-violet. Photo-reactivation was attempted by diluting thawed cells into physiological saline and exposing to light of wave-length 3650 Å. (ref. 8) for 1 hr. before plating. No increase in survival was obtained. Substitution of *M*9–agar[9] for nutrient broth agar also had no effect, that is, the colony counts on the two media were identical after 37° incubation and also after 45° incubation.

The effects of phosphorus-32 decay on the bacterial cell resemble the effects of X-rays and ultra-violet radiation in the following particulars: prolongation of the lag[10], 'reactivability' and the existence of a sensitive period during which 'reactivation' can be obtained. Although the initial physical events are quite different for these three agents, it would appear that the biological events which they trigger must have some features in common.

I wish to thank Miss Eva Simson for technical assistance.

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Effects of X-irradiation on Papillary Muscle of the Cat

A NUMBER of investigations have been carried out on the influence of X-rays on the electrophysiological and mechanical properties of striated muscle[1-5]. Most of these experiments have been performed on frog's sartorius muscle, and have revealed the fact that striated muscle generally shows a high X-ray insensitivity. Only minor changes of the membrane resting potential could be recorded during the first few hours following a heavy X-irradiation (80–250 kr.). Similar results were obtained by us (Schliep, H. J., Kraupp, O. and Pillat, B., unpublished results). A 1-mV. decrease of resting potential was produced by an average of 160 kr. (50 kV. 25 m.amp.). Further investigations on the same preparation showed that doses between 300 and 500 kr. practically did not influence intracellular action potentials recorded at

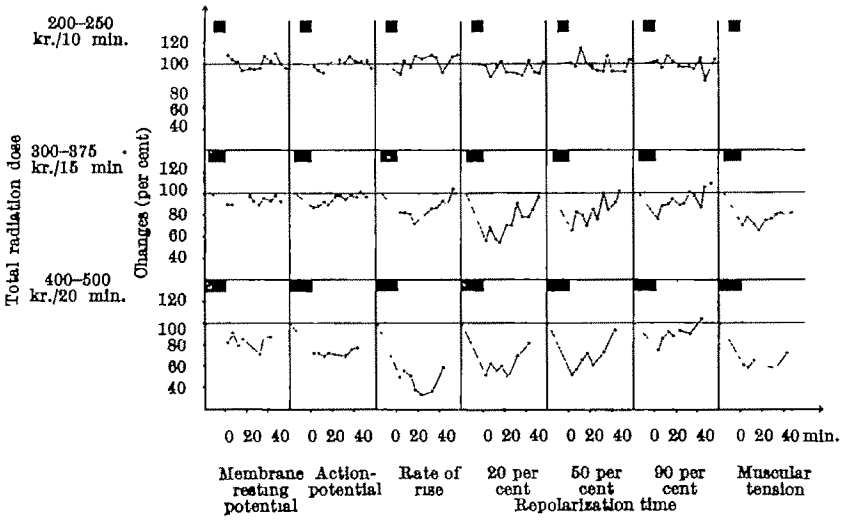

Fig. 1. Ordinate: Average percentage changes of membrane resting potential, action potential, rate of rise, 20, 50, and 90 per cent repolarization time and mechanical tension compared with the average control values of all experiments performed (100 per cent). Abscissa, Time in min. post-irradiation. Upper row, 200–250 kr./10 min; middle row, 300–375 kr./15 min.; lower row, 400–500 kr./20 min. Black bars indicate exposure to irradiation

5-min. intervals before, during and after irradiation (Kraupp, O. and Pillat, B., unpublished results).

However, no electrophysiological work concerning the effect of X-irradiation on heart muscle fibres has so far been reported. For that purpose membrane resting and action potentials were recorded with the intracellular micro-electrode technique from papillary muscles of cats. The method has been described in detail elsewhere[6]. An unfiltered X-ray source (50 kV., 25 m.amp.) was used at dose-rates between 20 and 25 kr./min. at an approximate distance of 10 cm. from the preparation.

In this way, three groups of experiments were carried out. Keeping the dose-rate constant (20–25 kr./min.), the duration of X-irradiation was varied. In four experiments the exposure to X-rays lasted 10 min., in six 15 min. and in two further experiments, 20 min.

In all these experiments measurements of membrane resting potential, action potential, rate of rise of the action potential, 20, 50 and 90 per cent repolarization time and of the mechanical tension were performed at 5-min. intervals for at least 1 hr. before and after X-irradiation.

To give a clear demonstration of our results the experiments of each group irradiated were combined. Changes of each parameter were expressed as percentages of the mean control values. As can be seen from Fig. 1, X-ray doses between 200 and 250 kr. had no significant influence on any of the parameters recorded. If the total X-ray dose was increased to 300–375 kr. definite changes of all parameters could be seen. These changes consisted in a decrease of the membrane resting and action potential, in a reduced rate of rise, and in a shortening of the 20, 50 and 90 per cent repolarization time. At the same time the muscular tension was diminished. At total radiation doses between 400 and 500 kr., the changes of all recorded parameters were even more pronounced. Two facts of interest were observed at total X-ray doses above 300 kr.: (1) The observed effects were most pronounced immediately after X-irradiation. (2) All irradiation-induced effects were reversible, at least to some extent, within 1 hr. Almost complete restitution of the normal repolarization time was found (Pillat, B., Kraupp, O., and Heistracher, P., unpublished results).

All the changes described are illustrated by a sequence of action potentials recorded before and following X-irradiation in a typical experiment (Fig. 2).

The above-described radiation-effects on heart muscle fibres resemble to some extent those obtained with 2,4-dinitrophenol or iodoacetate after incubation of rat's atrium in a solution of these substances[7]. Similarities between the effects of X-irradiation and of 2,4-dinitrophenol on striated muscle fibres have been reported by Woodbury[8]. This points to the possibility that reversible inhibition of some essential metabolic steps might be involved in the mechanism underlying the

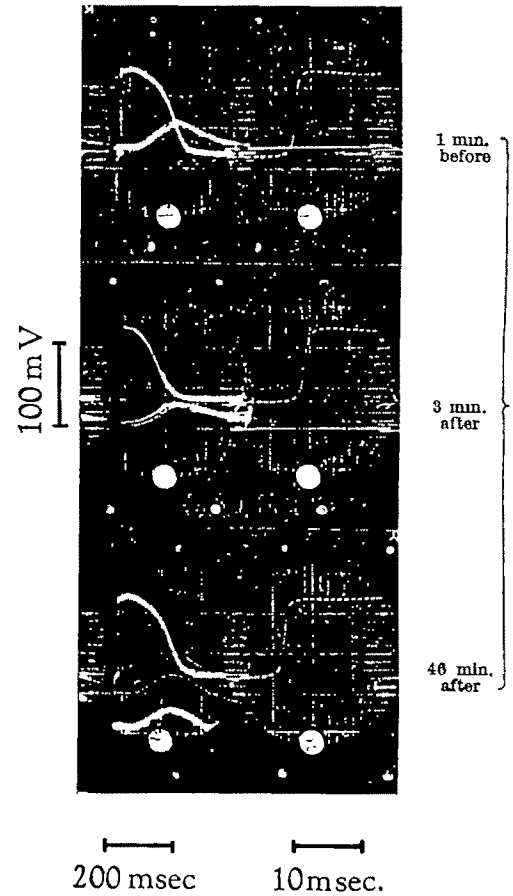

Fig. 2. Action potentials recorded in a typical experiment (total irradiation: 345 kr./15 min.) before, immediately after, and about 1 hr. after irradiation. Left column: slow sweep record. Right column: fast sweep record. Ordinate 10 squares represent 100 mV.

observed radiation effects as reported in this communication. The question arises whether the changes are due to a direct influence of radiation on the cell membrane or to a radiation-produced chemical substance; such a primary radiochemical step could be the formation of hydrogen peroxide.

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Sensitization of *Escherichia coli* to Gamma-Radiation by N-Ethylmaleimide

WITH the exception of oxygen and nitric oxide, chemical agents which enhance the effect of radiation on bacteria have received little attention. In the experiments to be described, N-ethylmaleimide is shown to be a sensitizing agent for *Escherichia coli* strain *B/r*. A sensitizing agent is taken here to be one which enhances radiation-damage when added before or during irradiation but not after irradiation.

N-ethylmaleimide was obtained from the Aldrich Chemical Co.; it was dissolved in sterile 0·067 *M* phosphate buffer to make a 0·01 *M* stock solution which was kept at 3° C. diluted as required. Sterilization of this solution was not found to be necessary. 20–24 hr. cultures on nutrient agar slopes were washed off with 10 ml. of 0·067 *M* phosphate buffer (*p*H 7) and 1 ml. was diluted into a further 10 ml. buffer before use. N-ethylmaleimide was added 4–6 min. before irradiation except where otherwise stated. The suspensions were irradiated at room temperature under aerated or anoxic (nitrogen bubbling) conditions with gamma-rays from a 1,000-curie cobalt-60 source. The dose-rate was approximately 300 krads/hr. Surface plate counts on 'Oxoid' nutrient agar were made before and after irradiation, and the colonies were counted after 48 hr. incubation at 30° C.

The survival curves in the presence and absence of 0·001 *M* N-ethylmaleimide are shown in Fig. 1, and it can be seen that a pronounced sensitization occurred. Under nitrogen there was approximately a two-fold difference in the sensitivity of control and treated cells, although under air sensitization was not so marked especially at the lower levels of irradiation. Incubation with 0·001 *M* N-ethylmaleimide for a period of 20 min. immediately after irradiation did not enhance radiation damage, nor was it toxic to unirradiated cells at this concentration, indicating that it is a true sensitizing agent. The shape of the aerobic curve suggested that pre-incubation with the sensitizing agent for several minutes might be necessary for the attainment of the full effect (under nitrogen there was always 6 min. incubation before

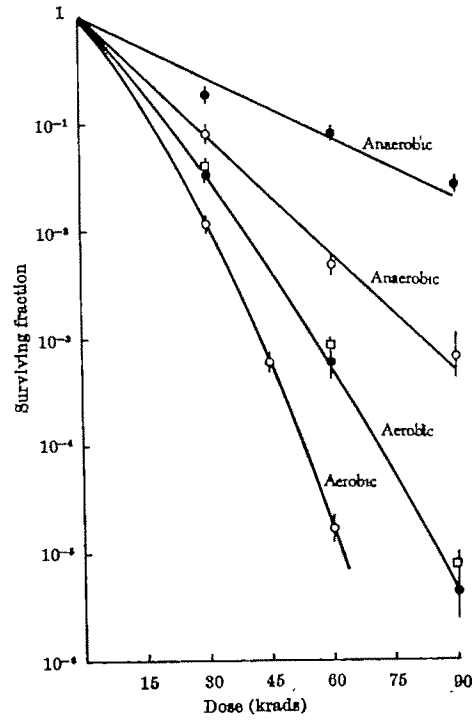

Fig. 1. Effect of 0·001 *M* N-ethylmaleimide on the inactivation of *Escherichia coli* strain *B/r* by gamma-radiation. ●, Control; ○, N-ethylmaleimide added before irradiation; □, N-ethylmaleimide added after irradiation for 20 min.

irradiation while oxygen was removed). Various times of pre-incubation were therefore tried, and it was found that a definite sensitization was observed with pre-incubation for as little as 1 min. The full effect was attained within 5 min. and there was no increase in sensitization when the pre-incubation period was increased from 5 to 15 min.

The sensitizing action of this compound might be due to its ability to combine with sulphydryl groups. Compounds with this property do not appear to have been reported before as sensitizers of bacteria to irradiation under controlled gas conditions, although halogen acetates which also combine with sulphydryl groups have been reported as sensitizing agents for mammals[1-3]. Kiga and his co-authors[4] reported that maleic acid enhanced the effect of X-rays on *Saccharomyces ellipsoideus*. If, however, the inhibitory action of maleic acid on respiratory enzymes influenced the concentration of dissolved oxygen, then the observed enhancement in this instance could be due to an effect of oxygen rather than to maleic acid directly. It may be significant that experiments in this Laboratory under controlled gas conditions have failed to show any sensitizing action of maleic acid on *E. coli* strain *B/r*.

I wish to thank Mr. M. J. Ashwood-Smith for discussions during the early part of this work.

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PHYSIOLOGY

Analysis of the Junction Potential of a Small Nerve

Fatt and Katz[1] demonstrated with the aid of an intracellular microelectrode that the end-plate potential was produced in the region of the motor end-plate by a sudden and transient reduction in the membrane potential as a result of neuromuscular transmitter action. They further pointed out that the prolonged decline of the end-plate potential was almost exponential and was determined by the electrical properties of the resting muscle membrane. An equivalent circuit of the resting muscle membrane is represented as a condenser in parallel with a battery (membrane potential) with a series resistance (membrane resistance). In the active phase of the end-plate potential, the membrane resistance at the junctional region is suddenly reduced by the transmitter action, that is, the muscle membrane is shortened by a shunting resistance[1]. To demonstrate the active process of the end-plate potential, Takeuchi and Takeuchi[2] and Oomura and Tomita[3,4] recorded a current flowing through the end-plate region of the muscle membrane by stimulating the nerve under conditions where the membrane potential was kept at the resting level, using the voltage-clamp technique[5,6]. On the other hand, the small motor nerve fibres which innervate the slow muscle fibres and relate to the tonic function in the maintenance of posture, also produce the junction potential of the small nerve at the junction region by its stimulation[7]. A distinctive feature of this junction potential is that it displays two phases with a terminal phase of hyperpolarization[7]. In the present work an attempt has been made to analyse the mechanism of production of the junction potential of the small nerve, using the voltage-clamp technique.

Two microelectrodes were inserted (within 50μ of each other) into a slow muscle fibre, one for recording the membrane potential and the other for passing current through the membrane. For the voltage-clamp experiment, a negative feedback amplifier system was connected to the microelectrodes to keep the membrane potential constant at the resting level. Junction potentials were evoked by selectively stimulating the small motor axons[8]. All experiments were carried out on isolated biceps muscles of bullfrogs (*Rana catesbiana*), in a cold room at 7° C. in summer.

The membrane potential of the resting slow muscle fibre ranged between 40 and 70 mV., the inside of the muscle being negative. In this experiment the time-constant of the resting muscle membrane, resistance multiplied by capacity, ranged from 500 to 1,000 m.sec. Occasionally after the insertion of the recording electrode at the region of the junction of the muscle a simple monophasic form of the small-nerve junction potential (see Figs. 1 and 2) was obtained. The time-course of the falling phase of this potential was roughly exponential, the $1/e$ decay time being approximately 800 m.sec. (note that this value is comparable with that of the time constant of the resting muscle membrane). The simple monophasic form soon (within 1 or 2 sec.) changed into the diphasic decay form (Fig. 3), which is characteristic of hyperpolarization, being accompanied by a 10 per cent reduction of the membrane potential. When the negativity of the membrane potential was increased by a steady inward current before applying a stimulation, the junction potential of the small nerve with the diphasic form (Fig. 3) changed to the monophasic form (Fig. 2). We therefore think that the small-nerve junction potential is of the monophasic form (Figs. 1 and 2), where the decline of the potential is determined by the electrical properties of the resting membrane as is the end-plate potential, and that the diphasic decay is due to a mechanism developed by injury of the muscle membrane at the junction region caused by impalement by the electrode.

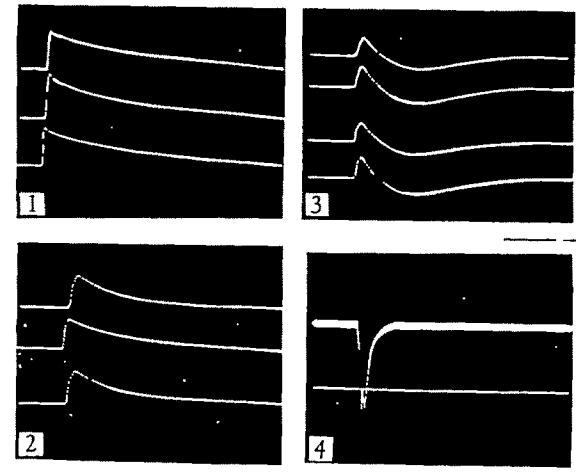

Fig. 1. Junction potentials of small-nerve with the monophasic form recorded intracellularly from a biceps muscle of a bullfrog (membrane resting potential, −66 mV.). Fig. 2, the same as 1, but from a different fibre (resting potential, −60 mV.). Fig. 3, junction potentials of small-nerve with a diphasic form (resting potential, −54 mV.). This characteristic form was changed from the monophasic one of Fig. 2. Upward deflexion shows the depolarization and downward one the hyperpolarization. Fig 4, the current (upper oscilloscope tracing) obtained at the same junction from which Fig 3 was taken under the clamped condition The membrane potential was kept at the resting level (−54 mV.) as shown by the lower tracing. Calibrations are 40 mV. for potential, 2×10^{-8} amp. for current. Horizontal bar . 500 m.sec. Temperature, 7° C.

The current showing the active phase of the small-nerve junction potential of the small nerve was obtained by the voltage-clamp experiment. The upper tracing of Fig. 4 shows the clamped current flowing through the junction of the muscle at the same junction where the record in Fig. 3 was taken. This current was obtained by stimulating the nerve under the condition where the membrane potential was kept at the resting level, as shown by the lower oscilloscope tracing of Fig. 4. It declined monophasically with an almost exponential time course, although the small-nerve junction potential on Fig. 3 decayed diphasically, and the current corresponding to the phase of hyperpolarization of the junction potential was not shown in the current observed. The clamped current represents the active phase, that is, the temporal change of the shunting resistance across the muscle membrane at the junction region (similar to the case of the current obtained at the end-plate region). The time-course of the clamped current was not altered significantly by making the membrane potential more negative, while the time course of the small-nerve junction potential changed from the diphasic to the monophasic form.

The intensity and the time-course of the clamped current and the amplitude of the small-nerve junction potential were increased by adding a small amount

of tetraethylammonium chloride or eserine to the Ringer solution bath. However, the intensity of the clamped current was not altered by excess calcium ions, while the amplitude of the small-nerve junction potential was increased. Since the clamped current represents the active process at the junction region, increases of both potential and current may indicate an increase in the amount of the transmitter substance liberated and the prolongation of its action. The increase of the junction potential without increase of the clamped current may not involve these mechanisms, but may be due to the increase of the resistance of the resting muscle membrane by calcium.

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Cell Proliferation in Precancerous Liver: Linear Growth Curve

IN extending our recently published work on cell growth and the development of tumours[1], we have observed that in the livers of rats fed 2-acetylaminofluorene the cell proliferation continues at a constant rate during the pre-cancerous period and does not decrease as we had at first supposed. Such continuous increase in a cell population at a constant rate constitutes a most unusual form of growth, and it affords an important insight into the dynamics of cell proliferation in a pre-neoplastic tissue.

As in the previous experiments[1], male rats of the Holtzman and Sprague–Dawley strains were fed continuously a commercial grain diet containing 2-acetylaminofluorene. In several of our experiments we have measured the consumption of 2-acetylaminofluorene, and have found it to be quite constant throughout the experiment. Eight similar experiments have been carried out to date, involving a total of about 400 rats; from these experiments, one has been selected for presentation in Figs. 1–3. In this experiment the initial body-weight of the animals was 135 gm., and the concentration of 2-acetylaminofluorene in the diet was 0·06 per cent. For each experimental point, 4 rats were chosen with body-weights representative of the average and range of body-weights of the whole experimental group. They were killed with ether, and the livers were removed and perfused immediately. Then the livers were pressed through a plastic tissue mincer and the mince from 4 livers was mixed carefully; an aliquot of this mixed mince was then homogenized in 0·88 *M* sucrose. The nuclei were counted in a hæmacytometer after

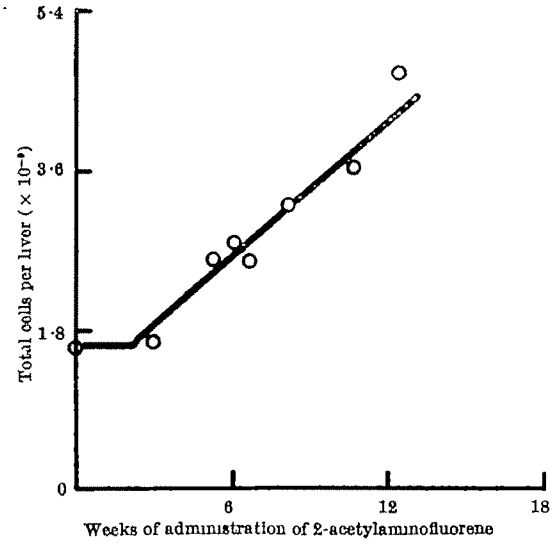

Fig 1. Changes in the total number of liver cells during the continuous administration of 2-acetylaminofluorene in the diet

dilution of the sucrose homogenate 1 : 40 in 3 per cent acetic acid containing a nuclear stain; under these conditions the nuclei are well dispersed and easily counted. From the known concentration of liver in the homogenate and the known dilution of the homogenate in the counting fluid, the number of nuclei per gram of fresh liver and per whole liver was calculated. The protein nitrogen and nucleic acids of the homogenate were also determined[2,3], and the analytical results were expressed in terms of the average whole liver by multiplying the values obtained per gram by the fresh weight of the livers.

Fig. 1 shows the changes observed in the total number of liver cells. As we reported in our recent paper[1], the number of cells per average liver remained unchanged for several weeks after the administration of 2-acetylaminofluorene was started. Two of the experimental animals died during the fifth week of the experiment, in agreement with our previous findings[1]. The early period of cell constancy was followed by a rapid increase in the number of liver cells, with the result that by 12 weeks in this experiment the number of liver cells had increased about three-fold. The cell proliferation of this second period was essentially linear; the points fit well the straight line drawn through them by the method of least squares. The slope of the line is 0·268; this means that on the average 268 × 10^6 new cells were produced every week. This linear growth has been maintained in other experiments through the twenty-third week, or up to the time at which tumours were beginning to appear, and hence is characteristic of the entire pre-cancerous period.

Figs. 2 and 3 show the corresponding changes in the protein nitrogen and ribonucleic acid in the same livers. After an early period in which some loss of these biochemical constituents occurred, they also increased in a straight line. The protein nitrogen increased at a constant rate of about 28 mgm. per week, and the ribonucleic acid at a constant rate of about 9 mgm. per week.

It was an unexpected finding that the number of liver cells increased at a constant rate. However, this linear growth has now been demonstrated in all of a current total of 8 different groups of experimental animals. Cell proliferation at a constant, and thus

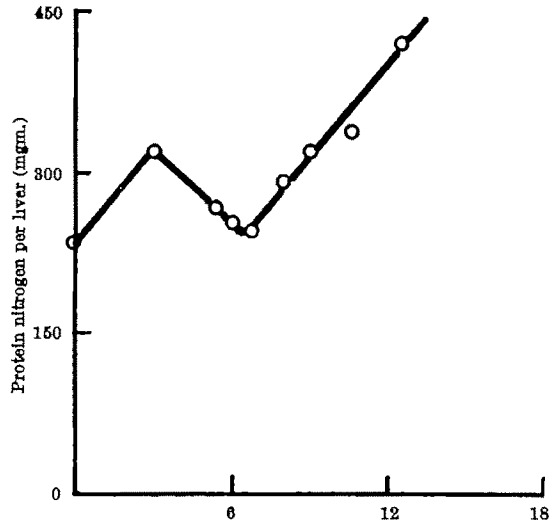

Fig. 2. Changes in the total quantity of protein nitrogen in the liver during the continuous administration of 2-acetylaminofluorene in the diet

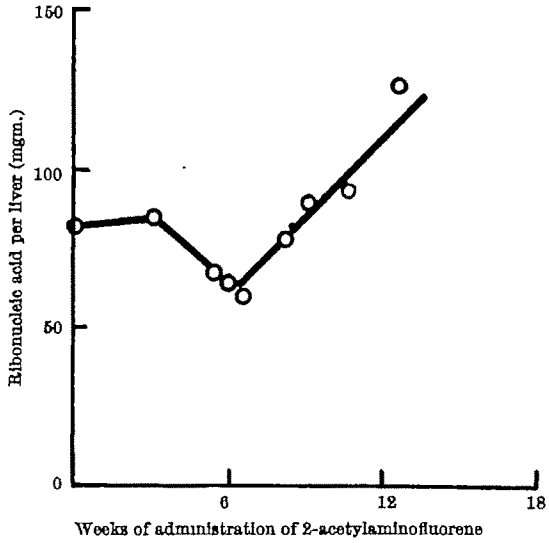

Fig 3. Changes in the total quantity of ribonucleic acid in the liver during the continuous administration of 2-acetylaminofluorene in the diet

statistically linear-rate can be assumed to occur normally in such tissues as intestinal epithelium and the blood-forming organs, where the total population remains essentially constant over long periods of time. In these tissues cell proliferation is not autonomous, but is under the control of regulatory mechanisms in the animal that assure the delicate compensatory adjustment of the production of new cells to the constant loss of mature cells from the system. The linear cell proliferation produced in the liver by 2-acetylaminofluorene is probably a compensatory phenomenon also. However, it cannot be compensatory to a loss of cells since the number of cells is actually increasing, and there is no evidence at any time of extensive necrosis in these livers[4,5]. This proliferation of liver cells might, however, be compensating a loss of some functional capacity of the liver that is inactivated or destroyed by 2-acetylaminofluorene and that is essential to the survival of the animal (usually a few of the animals die at the time the cell proliferation starts in the survivors[1]). The latent period preceding the onset of cell proliferation is to be expected if the functional capacity involved is normally present in an amount greater than the minimum necessary for survival. Although the exact mechanism is not understood at present, it is evident that the administration of 2-acetylaminofluorene in the diet at a constant rate produces a proliferation of liver cells at a constant rate, and it appears therefore that this cell proliferation represents a quantitative response to the amount of 2-acetylaminofluorene actually being consumed.

The relation of the large-scale proliferation of liver cells to the production of the few successful malignant cells which ultimately become tumours remains to be explained.

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Acetate Tolerance in the Young Lamb

RECENT work has shown that alterations can be produced in the tolerance to acetate and glucose in adult sheep by varying the nature of the diet[1,2]. With the inclusion of maize in a diet of lucerne and wheaten chaff the response of an adult sheep to an intravenous injection of glucose or acetate simulates much more closely the rapid rate of removal of these substances from the vascular system characteristic of a monogastric animal[1].

There are now many observations on the glucose tolerance[3,4], insulin sensitivity[5], hexokinase activity[6], and blood volatile fatty acids[7] in sheep and lambs which indicate that many aspects of the metabolism of carbohydrate in young lambs differ from those of adult sheep.

In view of these observations, the response to injected acetate in the very young lamb was determined and followed at intervals for a period of four months after birth. Five Merino wether lambs running with their dams on a mixed pasture were used. At intervals of a few days an injection of acetic acid neutralized to *p*H 7·0 with sodium hydroxide (5 m.moles acetic/kgm. body-weight) was given into the jugular vein and samples of blood obtained at 2, 15, 30 and 60 min. after the injection. The concentration of total volatile fatty acid was determined in each sample and also in urine collected over several hours by attaching a small rubber bag to the abdomen of the animal.

The results from two of the lambs, typical of the whole series, are presented in Table 1 and clearly indicate that the new-born lamb can very rapidly remove injected acetate from the blood stream. Analyses made on blood taken before the acetate injection showed a concentration of volatile fatty acid within the range 0·2–0·6 m.mole/l. for lambs of all ages; this range has also been observed for adult sheep feeding on green pasture.

Table 1. CONCENTRATION OF VOLATILE FATTY ACIDS IN BLOOD (m.moles/l.) AFTER THE INJECTION OF ACETATE (5 m.moles/kgm.)

Age	Lamb No. 18			Lamb No. 21		
	Min. after acetate injection			Min. after acetate injection		
	2	15	30	2	15	30
1–2 days	8·26	3·32	0·08	8·05	3·24	0·48
6–7 days	8·46	2·32	0·06	9·14	3·31	0·20
2–3 weeks	11·16	2·45	0·37	9·00	2·09	0·44
4–6 weeks	10·58	4·43	0·66	10·06	4·42	0·39
10–12 weeks	11·16	4·57	1·08	11·44	6·51	2·03
14–16 weeks	13·66	6·48	3·97	12·95	5·91	3·60
Adult	21·63	10·13	4·36	20·43	7·00	3·97

During the first four weeks of life all injected acetate was removed from the blood by the end of 30 min. whereas with older lambs and adult sheep a period of up to 60 min. was observed before the pre-injection level was reached. That this rapid rate of removal in the young lamb was not associated with a low renal threshold was indicated by the very small excretion of acetate during a 6-hr. period following the acetate injection (1–2 m.moles or less than 4 per cent of the injected dose).

It is thus apparent that as the lamb becomes older its tolerance to acetate alters until at approximately four months of age the rate of disappearance of injected acetate is similar to that of the adult sheep. This gradual change is comparable with the change which takes place in glucose tolerance and insulin sensitivity. Some other parameters, however, such as alterations in hexokinase activity[6] and liver coenzyme *A*-levels[8], change much more rapidly and at an earlier age.

These observations are of interest in that they add further support to the hypothesis that the young lamb behaves in many respects like a non-ruminant, and only gradually develops some of the metabolic characteristics of the adult sheep.

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Hydrothermal Denaturation of Collagen

IN a recent communication by Rigby and Spikes[1], structural breakdown of collagen is considered to be possible on its prolonged contact with water at a temperature as low as 40° C. Such alterations of human collagen are believed to be involved in the manifestation of rheumatic symptoms. Evidently, the authors are not aware of the fact that experimental evidence for the occurrence of gradual shrinkage and labilization of mammalian collagen in water at a temperature of 40–45° C. is on record. In the monograph[2] to which the authors refer in connexion with the correlation of hydroxyproline content of various collagens and their temperature of instantaneous shrinkage, T_S, work is cited[3] proving the rupture of intermolecular hydrogen bridges of collagen in the temperature-range mentioned (denaturation). Table 16 in the accompanying monograph[4] supplies substantiation. Hence, the speculative feature of their premise is removed.

By immersion of pieces of calf-skin (middle layer of corium) in water, covered with toluene, at 45° C. for one week, some 8 per cent of the protein was solubilized. The T_S of the corium was lowered from 67° C. to 56° C. The trypsin treatment (for method, see ref. 5) of the original corium resulted in 0·2 per cent degradation, whereas the corresponding figure for the corium treated with warm water was about 10 per cent. These findings indicate a marked labilization of the collagen on prolonged action of water at 45° C.

The main evidence referred to[2–4] was obtained by a method which was devised by me and applied in an extensive series of investigations of the effect of denaturation of collagen, by hydrogen-bond breakers and hydrothermal forces, on its reactivity and properties[6]. It relies on the fact that, by denaturation of the skin protein, its hydrogen-bonding capacity is drastically increased. However, its affinity for agents which react with the protein by electrovalent forces exclusively is not altered. Such agents are 0·1 *N* hydrochloric acid and cationic chromium complexes[6], indicating the non-participation of ionic protein groups in this denaturation. For chromium complexes of high degree of aggregation, partly in the non-ionic state (extremely basic chlorides and perchlorates, as well as sulphito-chromium-sulphates), the keto-imide groups serve as the chief binding sites. By breaking or rupture of the hydrogen bridges between adjacent keto-imide groups, resulting from steric effects induced by the shrinkage of the collagen, new binding sites on these uncompensated groups, and possibly on some hydroxy groups, are made available for reaction. Thus, corium which had undergone pretreatment in water at 45° C. fixed 7·4 m.equivalents of chromium per gm. of collagen irreversibly from a solution of 33 per cent acid chromium perchlorate[7], while original collagen combined with 5·1 m.equivalents of chromium only. For the sulphito-chromium sulphate[8], the corresponding figures were 11·7 and 8·0.

Supporting evidence for the breaking of hydrogen bridges, by the unfavourable steric condition produced by the shrinkage of collagen, supplies data on the fixation of polyphenols (vegetable tannins), which for their main fixation by collagen depend on the function of the keto-imide groups as acceptors for hydrogen bonds donated by the phenolic groups[6,9]; one of the main pieces of evidence being their binding by polyamides[9]. In the present instance, with mimosa bark tannins at a final *p*H of 5·0, the collagen treated with warm water fixed 87 per cent of its weight of these tannins irreversibly, while the original collagen combined with 66 per cent of tannins.

These results prove the occurrence of marked disorganization and impaired stability of the skin protein by water at 45° C., or at a temperature some 25° C. below the normal T_S of mammalian corium. This gradual shrinkage differs only in degree from the instantaneous shrinkage; for example, in alterations in stability and reactivity of the collagen. In

the present example, about 40 per cent of the maximum effect of the augmentation of the co-ordination potency due to complete shrinkage of collagen resulted.

These investigations were carried out at a time when the present, simple but powerful, techniques in protein chemistry were not available. Then, the nature of the degradation products could not be investigated. In the light of recent findings, polypeptides containing a disproportionately large amount of hydroxyproline residues are released on the shrinkage of *young* collagen[11]. The content of this important amino-acid should then be lowered by denaturation, conforming to the view of Rigby and Spikes[1]—a fact apparently of importance for their main problem. References given in footnote 11 should be noted in this context.

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We are pleased to find that Prof. Gustavson has further chemical evidence which supports our speculations. We were aware of the references[1,2] listed by Prof. Gustavson when referring to the gradual shrinkage of collagen at temperatures below the instantaneous shrinkage temperature. However, we took these observations to be complementary to the physical experiments of Weir[3], which show the 'rate process' nature of the shrinkage phenomenon and to which we did refer.

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PATHOLOGY

Carcinogenic Action of Diazomethane and of Nitroso-N-methyl Urethane

THE transformation of inactive or slightly active compounds into effective carcinogens by O-methylation has been discussed previously[1], and it was suggested that endogenous carcinogens may possibly be formed by alkylation of normal cell constituents in the body. Such a mechanism could account also for the carcinogenic effects of radiation and of remotely acting agents, such as the azo-dyes, ethionine, etc., which may give rise to alkyl radicals in the body.

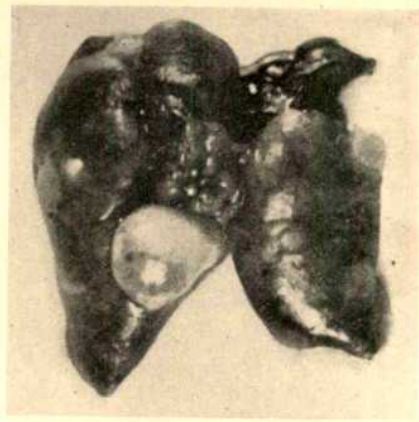

Fig. 1. Lung of an $A/2G$ male mouse that died after 11·5 months of application of etheral diazomethane to the skin, showing one large and one small adenomata. (× 3)

To test this hypothesis, diazomethane was chosen as a suitable alkylating agent. It is able to effect methylation under physiological conditions of *p*H and temperature, evolving nitrogen as the only other product. Diazomethane is a gas and is usually obtained in etheral solutions by the decomposition with alkali of some nitroso-N-methyl compounds[2]. Such compounds may possibly give rise to diazomethane or methylene radicals enzymatically in the animal body, without the need of alkali and drastic conditions. The commercially available nitroso-N-methyl-urethane was used for the preparation of diazomethane, and was itself tested for carcinogenic activity.

The results of the exploratory experiments proved sufficiently encouraging to warrant reporting at the present stage.

Male mice and rats, 1–3 months old, were used. Mice of the $A/2G$ strain were obtained from the Laboratory Animals Centre, Carshalton; Swiss albino mice were obtained from the National Institute for Medical Research, Mill Hill; rats were Wistar, bred locally from the Porton strain. All the animals were housed in metal cages and given the Medical Research Council diet 41*B* and water *ad libitum*.

Diazomethane was prepared according to Bachmann *et al.*[3]. Its etheral solutions were kept at − 5° C. for periods up to three months, and the concentration, estimated by the benzoic acid method, varied between 3·3 and 0·1 mgm./ml. The etheral solution was applied from a dropping pipette to the shaved skin of the interscapular region of twelve $A/2G$ mice, five times weekly. Eight mice survived more than five months of such treatment, but all these died within twelve months with lung adenomata, often multiple and of considerable size (Fig. 1). No abnormalities were present on the skin at the site of application, possibly because of the protective action of keratin.

The effect of inhalation of diazomethane was then examined using twelve $A/2G$ and six Swiss mice, and six Wistar rats. For this purpose the animals were placed in a desiccator, 6,250 ml. capacity (in groups comprising six mice or two to three rats at a time) and 1 ml. of etheral diazomethane solution was

introduced from a syringe through a plastic cover replacing the stopper in the lid. Control animals (twelve mice of the $A/2G$ strain and six Swiss mice, and two Wistar rats) were similarly exposed to ether only. The times of exposure were 1 or 2 min., twice weekly, for six months. When an animal appeared in poor condition, its treatment was terminated earlier. All the animals exposed to diazomethane by inhalation developed lung lesions, some dying acutely of lung œdema. Those dying later all had lungs grossly deformed, nodular and brownish.

All the mice of $A/2G$ strain died within seven and a half months, and the majority had lung adenomata. Mice of the $A/2G$ strain develop spontaneous lung adenomata in old age. However, in $A/2G$ mice treated with diazomethane the incidence of these tumours was greatly accelerated. Only one or two small adenomata were found in the control $A/2G$ mice killed at comparable age. Shimkin and Lorenz[4] observed similar acceleration of the development of adenomata in mice of the A strain injected intravenously with carcinogenic polycyclic hydrocarbons, and considered this as evidence of carcinogenic activity for the lung.

The lesions in the Wistar rats and in the Swiss mice affected mainly the bronchii. These became more prominent with time. Animals were killed at intervals even when still in good condition, in order to observe the evolution of the lesions. The last mouse and the last rat were killed eleven months after the beginning of treatment and about 5 months after its termination. The rat had a whitish big cellular tumour 2–3 cm. diameter in the right lobe of the lung, adhering to the chest wall. All the other lobes of the lung were studded with smaller whitish nodules, 1–5 mm. in diameter. Similar whitish nodules covered, and adhered to, the inner surface of the chest; they were particularly numerous at the upper right side and on the diaphragm. The organs in the peritoneal cavity did not appear grossly infiltrated by the tumour. Microscopically, the tumour and the disseminated nodules proved to be a carcinoma of the bronchial epithelium containing many mitotic figures. The control Swiss mice and Wistar rats, which were exposed to ether only, did not show any significant abnormalities when killed at the time of death of the last experimental animals.

Nitroso-N-methyl urethane was administered orally to Wistar rats. A single dose of 0·1–0·2 ml. of a 20 per cent or 2·5 per cent solution in 50 per cent or 5 per cent aqueous alcohol, respectively, was given by stomach tube to two groups of 10 and 6 rats respectively. The animals were then left without further treatment. The rats which received the 20 per cent solution all died within two to three days. Their lungs were dark red, some showed subcutaneous œdema, they had enlarged pale livers, and all had stomachs distended with fluid content, often containing blood, and hæmorrhagic petechiæ were present on the stomach walls. Microscopically, the livers showed necrosis confined to the portal areas, and the lungs, perivascular and peribronchial œdema and hæmorrhage into the alveoli.

Rats which were given the lower dosage survived from 10 days to 20 months. Their livers appeared normal, and lesions, if any, were confined to their stomachs and lungs. One of the rats which died 19 months after a single dose of the compound had a large, irregular, whitish mass in the abdominal cavity, involving the stomach, small intestines and spleen. There were also numerous nodules spread throughout the peritoneal cavity. Unfortunately, there was severe postmortem change, but microscopic examination indicated squamous carcinoma of the stomach with peritoneal spread (Figs. 2 and 3).

Fig. 2. Stomach of a male rat that died 19 months after a single oral dose (50 mgm./kgm. body-weight) of nitroso-N-methyl-urethane. (× 1·5)

Fig. 3. The same rat as Fig. 2, section showing squamous carcinoma of the fore-stomach. Hæmatoxylin and eosin. (×37·5)

In our colony no stomach tumours have been seen at autopsy of several thousand treated and untreated rats. There was also no reason to suspect vitamin A deficiency, therefore the stomach tumour was probably caused by nitroso-N-methyl-urethane.

I am grateful to Dr. P. N. Magee for the microscopic evaluation of the various lesions, which will be described in detail elsewhere, and to Dr. J. M. Barnes for his interest. I also thank Mr. M. R. Greenwood for valuable technical assistance, and Mr. R. F. Legg for the photographs.

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Serum Protein Abnormalities in 'Runted' Albino Rats

IN the course of previous investigations, we have observed that when either normal or neoplastic tissues of mouse origin are injected into new-born albino *CFN* rats (Carworth–Wistar origin) occasional animals will develop a wasting disease characterized by roughened scaly skin, sparse hair growth, failure to gain weight normally, and sometimes actual loss of weight[1,2]. This condition usually appears during the first 7–14 days of life and many of the animals so afflicted succumb within a few days. Others survive this crisis and live for at least 35 days. Apart from the sparse hair and stunted growth, these survivors are apparently normal.

The same phenomenon is occasionally observed following intraperitoneal inoculation of normal adult *DBA*/2 mouse spleen cells into new-born albino

rats[1]; but it occurs much more frequently after subcutaneous, intraperitoneal[2] or intracerebral injection of one of several transplantable mouse tumours into this host. The transplantable mouse tumours so far associated with this subsequent wasting disease are the Ehrlich ascites tumour, the lymphoma *L*4946, the lymphoma *P*1534, the lymphosarcoma 6*C*3*HED*, the mammary carcinoma *BW*10232, the melanoma *S*91 and the neuroblastoma *C*1300. Many of the young rats appeared to expire as a direct result of the growth of the Ehrlich ascites tumour, the lymphoma *P*1534, the lymphoma *L*4946 and the lymphosarcoma 6C3*HED*; but there were individuals in which the wasting condition became evident during or after tumour regression. Furthermore, this disorder occurred rather frequently after inoculation of the mammary carcinoma and the melanoma, neither of which ever demonstrated palpable growth.

This 'runted' rat is interesting because it is grossly similar to the runts described in homologous transplantation studies[3-5]. Autopsied rats dying with this disorder reveal some of the general characteristics noted by Billingham and Brent[3]; the spleen is small, the thymus absent or quite small, the mesenteric lymph node usually absent and lymphogenous tissue generally reduced. When we exclude from consideration those rats appearing under-developed at birth or those which were survivors of litters having a high mortality during the first few days of life, only 6 animals which might be grossly classified as runts have been encountered in 251 rats injected with control Tyrode solution or not injected at all. Unfortunately, these animals were not autopsied, since the significance of this condition had not then been realized. In contrast, 15 of 23 rats inoculated at birth with the mammary carcinoma *BW*10232 developed the runting disease.

Since it is probable that other abnormalities of the reticulo-endothelial system are present in the runted animals, we have begun an intensive investigation of the serum proteins. So far this investigation is limited to those animals surviving the first 5 weeks of life. At this age, normal litter mates raised under identical conditions weigh 75–100 gm., whereas the runts weigh 35–55 gm. This communication constitutes a preliminary report on the serum protein fractions in these animals.

Tissue suspensions of mouse melanoma *S*91, mammary carcinoma *BW*10232, and normal *DBA*/2 spleens were prepared by mincing with fine dissecting scissors followed by gentle manipulation in a glass homogenizer to which Tyrode solution had been added. New-born *CFN* rats were injected with approximately 20×10^6 cells from one of these suspensions. The normal spleen cells were administered intraperitoneally, whereas the tumour cells were injected subcutaneously. Control groups of rats having received either 0·1 ml. of Tyrode solution or no injection at all were included. The animals were inspected at intervals of 2–4 days and were weighed each week.

Following the weighing at 5 weeks of age, blood was drawn by cardiac puncture, the serum collected and paper electrophoresis of the serum proteins carried out with a Spinco model *RB* electrophoresis apparatus. Serum aliquots of 0·008 ml. were subjected to electrophoresis at 4·0 m.amp./cell for 18 hr. at room temperature. The strips were dried, stained, and analysed with a Model *RB* analytrol.

Table 1. SERUM PROTEIN FRACTIONS IN 5-WEEK-OLD NORMAL AND 'RUNTED' ALBINO RATS INJECTED AT BIRTH WITH MOUSE TISSUES

Material injected at birth	No. tested	Mean weight (gm.)	Serum protein fraction			
			Albumin (per cent)	α_1- and α_2- (per cent)	β- (per cent)	γ- (per cent)
None	15	88	60·6	20·8	14·7	3·9
Tyrode solution*	9	90	60·2	20·9	14·6	4·3
Adult mouse spleen†	6	84	58·2	21·7	15·8	4·3
Mammary carcinoma‡	3	89	60·5	20·0	14·8	4·7
Melanoma§	4	88	61·9	20·8	14·0	3·3
Adult mouse spleen†	7	45	45·0	20·3	21·0	13·7
Mammary carcinoma‡	3	31	48·1	20·6	18·6	12·7
Melanoma§	3	42	48·7	21·4	16·9	13·0

* Tyrode solution is utilized in preparation of the cell suspensions.
† Obtained from 12- to 16-week-old *DBA*/2 female mice.
‡ Mammary carcinoma, *BW*10232 indigenous to the *C*57*BL*/6 strain of mice.
§ Melanoma *S*91 indigenous to the *DBA*/2 strain of mice.

The serum protein fractions are indicated in Table 1. It can be seen that the β- and particularly the γ-globulins are elevated in those rats with subnormal weight. As Figs. 1 and 2 further indicate, the correlation is not with the kind of tissue injected at birth, but rather with the fact that a runt was produced by 5 weeks of age. For example, approximately 20×10^6 normal adult *DBA*/2 mouse spleen cells were injected intraperitoneally at birth into two rats, yet, as shown in Fig. 1, only the runt had an increased percentage of β- and γ-globulins. Furthermore, when melanoma *S*91 cells were inoculated subcutaneously into another pair as illustrated in Fig. 2, the increased globulin percentages were produced in the runt, but not in the normal animals.

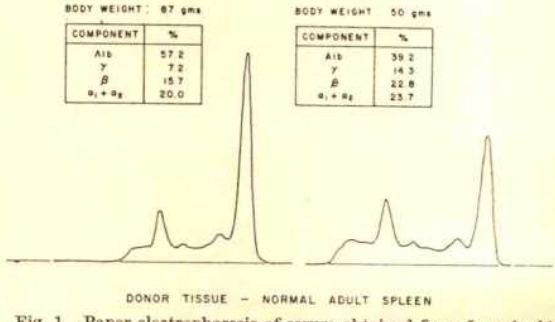

Fig. 1. Paper electrophoresis of serum obtained from 5-week-old albino rats inoculated at birth with normal adult mouse spleen cells. Note the decreased albumin and increased β- and γ-globulin percentages in the animal with subnormal weight

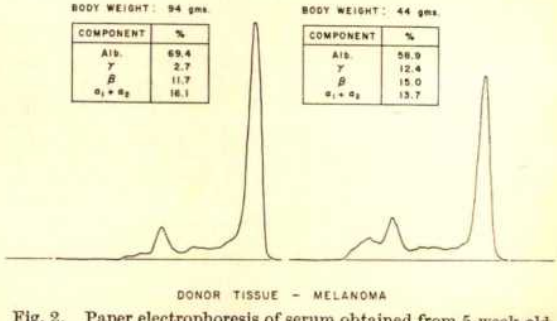

Fig. 2. Paper electrophoresis of serum obtained from 5-week-old albino rats inoculated at birth with melanoma *S*91 cells. Note the decreased albumin and increased β- and γ-globulin percentages in the animal with subnormal weight

The 6 untreated animals that died with the gross characteristics of wasting prevent us from concluding with certainty that the wasting disease in the young albino rat is directly attributable to the injection of normal or neoplastic mouse cells. We share with Billingham and Silvers[4] the opinion that in some instances the effect of this inoculation may rather be to aggravate or enhance another, as yet unrecognized, factor. These authors, moreover, have described a runted rat which follows the injection of homologous adult rat spleen or bone marrow cells. The most obvious feature of the homologous disease so produced was a severe dermatitis. Anderson *et al.*[5], however, have described runt disease produced by the intravenous injection of homologous thoracic duct lymphocytes into albino rats without reporting any skin involvement. We have not observed severe dermatitis in the runt disease of our albino rats following the inoculation of heterologous mouse tissues. Although the explanation of these discrepancies may lie in the fact that different strains of rats are utilized by each group, we must consider the possibility that different etiological mechanisms are operating in the three experimental systems. Nevertheless, our results indicate that whatever the etiology of the runt encountered in our work, the production of an unusually high percentage of γ- and β-globulins results.

Of particular interest is the recent work of Gengozian[6], who reports a consistent elevation in the lipoproteins (γ- and β-globulins) in the radiation-induced rat-to-mouse chimera. This abnormally high fraction seems to be produced by the mouse host and not by the donor rat tissues. Using similar techniques, we intend to measure quantitative changes in proteins with the view of determining directly whether the higher percentages of β- and γ-globulins observed by us are of host rat or donor mouse origin.

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BIOLOGY

Occurrence and Distribution of Cytochrome $a + a_3$ in Plant Cells

CYTOCHROME *a* occurs in plant materials only in very low concentrations and its activity is rapidly lost in homogenates kept at room temperature. Numerous visual observations of its presumed α-band have nevertheless been recorded for a variety of plant materials[1–5]. The reported values have a rather wide scatter lying between $\lambda = 600$ and 605 mμ. Recently, cytochrome *a* has also been recorded spectrophotometrically, but still with an equally wide scatter of the position of the α-band[6–10]. Observations tending to show the presence of the a_3 compound in plant materials have so far been very few.

Embryos of wheat appear to contain relatively large amounts of cytochrome *a* and its α-band appears stronger in comparison with the α-bands of cytochromes *b* and *c* than is usual in visual low-dispersion spectra. The spectrum is best observed in a mitochondrial pellet of the consistency of a thick paste.

Mitochondria were extracted by conventional methods from viable wheat germ freed from endosperm particles by flotation on a mixture of cyclohexane and carbon tetrachloride (10 : 25 v/v). The mitochondrial pellet was finally centrifuged down at 10,000*g* from a medium containing 0·2 *M* sucrose, 0·05 *M* phosphate *p*H 7·2 and 0·001 *M* magnesium sulphate, and examined in a layer about 10 mm. deep with a Beck microspectroscope. After reduction with sodium ascorbate a well-defined absorption band was visible at $\lambda = 600$ mμ and another at 552 mμ. They were still visible after 24 hr. in a deep freeze when again reduced with dithionite. After each reduction the cuvette containing the pellet was flushed out with carbon monoxide and the spectrum re-examined shortly after. The band at 600 mμ moved to 590–592 mμ, while that at 552 mμ remained unaltered.

Attempts to confirm these observations with a spectrophotometer were at first frustrated by the very high degree of light scatter caused by the mitochondria in suspension. Even after addition of 0·025 gm. cytochrome *c* to 3·0 ml. of mitochondrial suspension no definite absorption band was recorded. Effective observation was achieved by the following method using a Unicam *SP* 500 spectrophotometer with a *SZG* 500 photomultiplier attachment. The mitochondria were re-suspended in the sucrose-phosphate medium and subjected to ultrasonic vibration (5,000 cycles per min.) for 20 min. and then centrifuged down at 100,000*g* for 30 min. The pellet was re-suspended in 2 ml. of 60 per cent glycerol + 40 per cent sucrose-phosphate medium. The cuvette containing the suspension was placed as close to the photomultiplier unit as the construction of the apparatus would allow (about 1 cm. distance) instead of in its normal position by the light slit. With these precautions absorption curves could be recorded between wave-lengths 580 mμ and 610 mμ. The continuous curve in Fig. 1 shows the difference in absorption by the mitochondrial suspension before and after reduction with a trace of dithionite. The usual α-peak is shown at 602 mμ and a secondary peak at 594 mμ due to reduced peroxidase[11]. After treatment with carbon monoxide the absorption-difference curve was changed to that shown by the broken line.

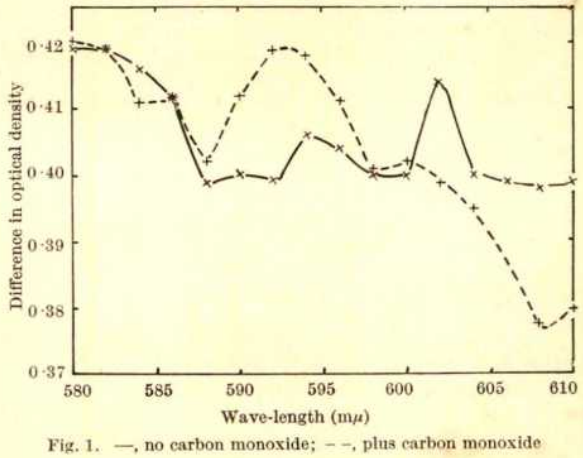

Fig. 1. —, no carbon monoxide; – –, plus carbon monoxide

revealing the formation of the cytochrome a_3–carbon monoxide compound with an absorption maximum at about 592 mμ. At the same time a corresponding change occurred in the deep blue region of the spectrum, a small peak appearing at 424–426 mμ, attributable to the γ-band of the cytochrome a_3–carbon monoxide compound.

Electronmicrographs of thin sections of the mitochondrial pellets treated with osmium tetroxide have been prepared for us by Dr. M. S. C. Birbeck. The mitochondria show the normal type of structure as seen in thin sections of tissue. Broken mitochondria and other detritus are rare. After vibration the walls and lamellæ were entirely broken down into a fairly uniform mass of particles with a mean diameter of about 30 mμ. Any soluble contents of the mitochondria would, of course, have been removed by the final centrifugation.

The above observations seem to make it clear that both components of the cytochrome $a + a_3$ complex are present in the cells of wheat embryos. Their spectra can only be clearly observed after the cell components other than mitochondria have been discarded, and no bands have been observed in the supernatant after the mitochondria have been removed. Disintegration of the mitochondria shows that the two components are both attached to the mitochondrial membranes and are not discarded with the internal fluids.

Repeated spectroscopic investigation of preparations of isolated nuclei from the same tissues have failed to reveal any bands attributable to any of the respiratory cytochromes. None was detectable in nuclear suspensions having twenty times as much total nitrogen as that required to give visible bands with mitochondria. The embryonic cells investigated did not contain chloroplasts; but it has already been shown that the chloroplasts of green cells do not contain any detectable cytochromes other than b_6 and f (refs. 12, 13). It appears probable that the cytochrome $a + a_3$ complex occurs in higher plant cells, as previously shown for others, only on the membranes of the mitochondria.

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A New Type of Citrus Fruit Rot caused by *P. italicum* Wehmer

During the past five years, while engaged on the examination of arrivals of Israeli citrus fruit in Britain and on the Continent, an unfamiliar type of dark red varying to bronze-red mould rot on oranges and grapefruit was occasionally found. So far as I am aware this rot has not been previously recorded.

Microscopic examination of the affected rind tissue revealed fungal penetration, and that many of the fungal cells within the tissue and on the rind surface had reddish pigmented contents. Sub-plants on common nutrient agar media invariably produced the blue mould fungus *Penicillium italicum*, yet it seemed inconceivable that the citrus blue mould rot fungus could be the causal organism of this new type of fruit rot.

The new fruit rot is of minor economic significance, as demonstrated in Table 1, which records the incidence of the rot as compared with the total fungal waste found in personally examined orange and grapefruit consignments in the four years 1957–60.

Table 1. Comparison of the Incidence of the Red Fruit Rot with the Total Fungal Waste seen in Fruit Consignments in the Years 1957–60

	1957	1958	1959	1960
No. of citrus fruits examined	128,228	226,270	218,030	100,553
Total number of rots	7,304	5,997	4,420	601
No. of red rots	36	34	93	18
Percentage of red rots to total rots	0·5	0·6	2·1	3·0

In a single instance a reddish-brown fungus was isolated in culture as well as *P. italicum*. The former organism was identified by Mr. E. W. Mason of the Commonwealth Institute of Mycology, Kew, as *Ascocybe grovesii* Wells, an unusual type of Ascomycete which was diagnosed, classified and recognized as a new organism by Doreen E. Wells, and given its nomenclature as recently as 1954. The organism is of common occurrence on lumber wood, causing a brown surface stain.

Oranges inoculated with the *Ascocybe* fungus developed a very slow rot, in initial stages reddish-brown in colour but turning dark brown with age, and the fungus was readily isolated from the induced rot.

Uncertain as to whether the single isolate of the *Ascocybe* fungus was of chance occurrence or indeed primarily responsible for the dark red citrus fruit rot and later retarded by the development of the common blue mould fungus, the influence of diphenyl on the growth of both organisms on common nutrient agar media at different *p*H levels was studied, with the view of applying the knowledge gained to further attempts on the isolation of the causal organism of the new fruit rot.

Diphenyl, a fungistat much used in the citrus industry, proved to have little influence on the *Ascocybe* fungus. The rate of growth of the fungus was in some instances somewhat reduced, but the fungal fructifications—the hyaline conidia, the erect brown ascophores and hyaline ascospores—and the production of a characteristic reddish-brown diffusible pigment, remained unaffected by the diphenyl.

The response of the blue mould fungus *P. italicum* to diphenyl was most extraordinary. Instead of the normal fasicular development of a blue conidial mat on the culture media plates, growth was strikingly arrested, and very small atypical, well-raised, furrowed colonies developed changing in colour from whitish to yellow-bronze to reddish-bronze, often with a relatively wide dark red peripheral zone.

Conidia formation was generally inhibited, at times atypical with coarse stunted conidiophores bearing very few sterigmata and very few conidia. Most of the hyphal cells in the pigmented zone had reddish pigmented contents.

Oranges wounded and inoculated with *P. italicum* and placed with diphenyl under a bell-jar under dry and moist conditions developed the common blue mould rot, but with diphenyl in closed screw-capped jars the rot developed slowly and instead of the typical blue mould rot, irregularly scattered fascicular growths appeared, changing in colour in irregular patterns from dirty white to yellow-bronze to reddish-bronze, and blood red patches were also formed. Inoculated oranges without diphenyl in closed jars developed normal blue mould rot. In short, inoculated oranges with diphenyl in closed jars had produced, under the conditions of the experiment, a rot similar to some of the rot samples which showed visible reddish fungal growth on the fruit rind found in fruit consignments from Israel.

Whether the lack of oxygen or the increased ratio of carbon dioxide in the air mixture, and other substances as ammonia gas can induce the same type of rot is under investigation. It should be noted that two oranges in ammonia-treated experimental fruit consignments from Israel in 1958 actually showed the new type of red rot.

Fuller details will be published elsewhere.

I wish to express my gratitude to Mr. Marcus J. Sieff, director of Marks and Spencer, Ltd., and also to Mr. Nathan Goldenberg, chief of Marks and Spencer's Food Development Department, for generously placing at my disposal all laboratory facilities at Marks and Spencer's Analytical Laboratory.

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Growth Requirements of Pome-Fruit Tissues

CORTICAL and pith tissue from apple fruitlets undergoing cell division and vascular tissue from more mature fruits have been grown in sterile culture[1]. In this communication further definition of the growth requirements of apple and other pome-fruit tissues is made.

Growth of pear and quince fruit tissues in sterile culture was obtained on media similar to those used for apple tissue culture. Disks of tissue (thickness × diameter, 1 mm. × 3·8 mm.) excised from the mid-cortex of immature pear (Packham's Late, 45 days from fertilization, weight 20 gm.) and quince (Van Deman, 66 days from fertilization, weight 20 gm.) fruits showed no growth on a modified White's medium (agar content 0·55 per cent). Addition of coconut milk was without effect but addition of 2,4-dichlorophenoxyacetic acid (2 p.p.m., resulting medium termed *A*) induced active growth involving cell division. Addition of coconut milk to *A* (final concentration 10 per cent by volume) further stimulated growth. These responses to coconut milk and 2,4-dichlorophenoxyacetic acid resemble those obtained with apple fruitlet tissue excised during the period of cell division.

The effect of kinetin on the growth of these tissues has also been studied. Kinetin and *l*-asparagine, when both added to medium *A*, stimulated markedly the growth of pear cortical tissue, the stimulation exceeding that of coconut milk. With quince cortex this stimulation was less marked, the response being less than that obtained with coconut milk. The influence of *l*-asparagine, kinetin and 2,4-dichlorophenoxyacetic acid on the growth of immature pear cortex is indicated in Table 1.

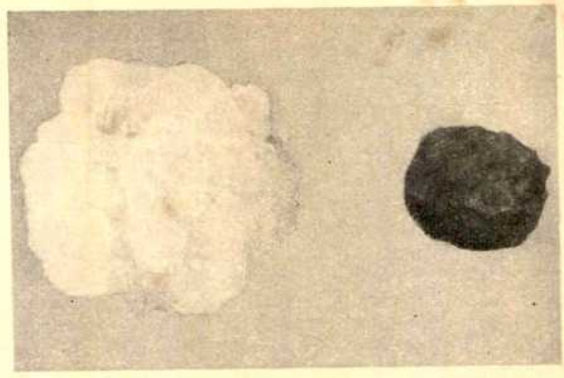

Fig. 1. Pear explants excised 45 days from fertilization after 34 days in culture. Right, explant which has shown negligible growth was cultured on medium *F*; left, on medium *E*

Table 1

Medium	Mean weight (mgm.) of explants after growth for 34 days
A (modified White's medium + 2,4-D 2 p.p.m.)	36
B (*A* + *l*-asparagine 180 p.p.m.)	67
C (*A* + *l*-asparagine − 2,4-D)	17
D (*A* + kinetin 0·1 p.p.m.)	46
E (*A* + *l*-asparagine + kinetin)	120
F (*A* + *l*-asparagine + kinetin − 2,4-D)	17

(*LSD* at 5 per cent level = 9, at 1 per cent = 12)

2,4-D = 2,4-dichlorophenoxyacetic acid.

Kinetin does not influence growth in the absence of 2,4-dichlorophenoxyacetic acid, stimulates only slightly in its presence, but stimulates appreciably in the presence of 2,4-dichlorophenoxyacetic acid + *l*-asparagine. Apple vascular tissue also responds to kinetin in the presence of 2,4-dichlorophenoxyacetic acid[1]. The growth effects of kinetin on other cultured tissues have all been observed in the presence of indole-3-acetic acid[2].

The rates of growth of pear cortical tissue on medium *E* and of quince on medium *A* + coconut milk were several times greater than those of apple vascular and fruitlet tissue on either of these media. Cultured pear and quince tissue is composed of very small cells, and percentage growth increment expressed on a cell-number basis is usually greater than that expressed on a fresh-weight basis.

Attempts have also been made to culture tissue from relatively mature pear and quince fruits. Only slight proliferation was obtained from pear cortical explants excised 113 days after fertilization and cultured on medium *A* supplemented with coconut milk, but more active growth was obtained from quince (variety Missouri Mammoth) cortical tissue excised 90–154 days from fertilization. Both 2,4-dichlorophenoxyacetic acid and coconut milk were needed to induce this proliferation. No information is available about the length of the period of cell division in pear and quince fruits, but it might be expected to be of short duration as in the apple. Since picking time for quince is about 170 days from fertilization, it is likely that with this fruit growth has been obtained from cortical tissue after the cessation of

cell division. Explants from mid-cortex and pith of apple fruits of similar maturity showed negligible growth. Disks of tissue from relatively mature pear fruits excised so that a vascular bundle ran centrally through each explant showed more active growth than tissue from the cortex, medium *E* giving more rapid growth than medium *A* + coconut milk. Apple vascular tissue (variety Sturmer) requires both 2,4-dichlorophenoxyacetic acid or an equivalent and a cell-division stimulant (coconut milk or kinetin) for active growth in culture[1]. 2,4-Dichlorophenoxyacetic acid or an equivalent is also essential for growth of pear vascular tissue, but this tissue is apparently much less dependent on a cell-division stimulant.

The possibility of replacing 2,4-dichlorophenoxyacetic acid by other compounds has been investigated. Apple and pear vascular tissue did not grow when 2,4-dichlorophenoxyacetic acid (1–5 p.p.m.) was replaced by indole-3-acetic acid (0·3–5 p.p.m.). Higher concentrations (30 p.p.m.) of indole-3-acetic acid produced some growth, but still considerably less than 2,4-dichlorophenoxyacetic acid. Potato-tuber tissue in the presence of coconut milk also shows this unusual dependence on 2,4-dichlorophenoxyacetic acid[3]. Quince cortex was more responsive to indole-3-acetic acid which, although relatively ineffective at 5 p.p.m. with this tissue, at 30 p.p.m. was nearly as effective as 2,4-dichlorophenoxyacetic acid (5 p.p.m.). For the growth of apple and pear vascular and quince cortical tissue, 2,4-dichlorophenoxyacetic acid can be replaced by some related phenoxy acids (for example, 2,4,5-trichlorophenoxypropionic acid).

Tissue has also been cultured from other pome fruits, namely, medlar (*Mespilus germanica* L.), Japanese quince (*Chaenomeles superba* Rehd.) and oriental pear (*Pyrus calleryana* Decne.).

The work reported has been assisted by grants from the Rockefeller Foundation and from the New Zealand Apple and Pear Marketing Board. Thanks are expressed to Mrs. G. E. Mark and Miss D. A. Bridson for skilled assistance and to Dr. H. R. Thompson for statistical analyses.

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Protoplasts from *Penicillium glaucum*

Bachmann and Bonner[1] were able to obtain free protoplasts from *Neurospora crassa*, if this fungus was cultivated in thick liquid media, such as 20 per cent sucrose and 10 per cent enzyme preparations. Protoplasts emerge through pores in the hyphal walls. The authors showed, by means of a microscopical photo-series, that the protoplasts regenerate to form a complete new fungus mycelium.

If *Penicillium glaucum* was cultivated on thickened serum it was also possible to form protoplasts. Cells of the fungus were inoculated in thickened guinea pig serum between two sterilized glass plates and the upper glass bordered and fastened with paraffin. After some time (7–14 days) those upper plates were loosened, dried and stained with a May-Grünwald-Giemsa solution. (This simple method is very suitable for staining the internal structures of hyphæ in microscopical preparations.) Fig. 1 shows the connexion of the protoplasts with the 'vacuoles' of the interior structures of the hyphæ.

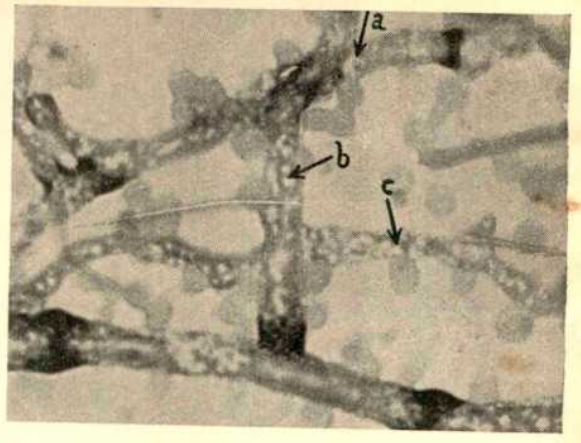

Fig. 1. Formation of protoplasts from *Penicillium glaucum* in a medium of thickened cell-free guinea pig serum. (× *c.* 1,500)

The photomicrograph shows reddish-grey, very tender forms between and on the blue hyphæ. Some of these forms are in direct connexion with the pores and 'vacuoles' of the hyphæ (*a*). Arrows *b* and *c* show these forms flowing out of the vacuoles.

In similar experiments with thick liquid media, such as sera and cell liquids, a wide extension of the hyphæ was observed. Here the typical internal structures of broad hyphæ found continues outside the hyphæ. They are embedded in complexes, the finest structures of which seem to move slowly into the surrounding medium without producing definite contours. The same effect could be seen if *Penicillium glaucum* was embedded into living plants. This, together with some photomicrographs, is published elsewhere[2].

Other experiments have been carried out on soft forms of protoplasts[3]. These results concerning the extension of internal structures may help towards understanding the above phenomenon[4].

In spite of the fact that these observations are different from the growth of fungi in normally used media, which regularly produce a quick and unrestricted growth, the present observed forms are unnatural. Under natural conditions there are many opportunities for fungi to move into living tissues or thick cell liquids and cause fermentation. Therefore it is necessary to pay attention to those alterations in the fungal elements, in order to prevent mistakes of diagnosis. Also for the sake of common biological examinations the study of changes of the cell elements, caused by alterations of the surroundings, is most important[4,5].

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ENTOMOLOGY

Food of Housefly Larvæ

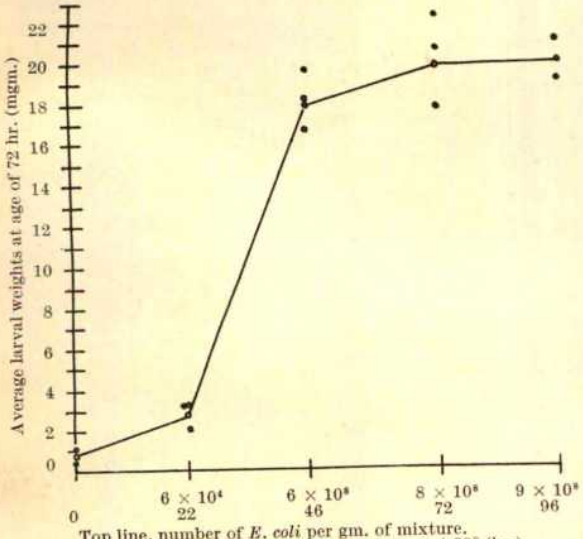
ALTHOUGH considerable information has been published on the nutritional requirements of fly larvæ (refs. 1–5 and Mer, G. G., personal communication) the actual natural food of these insects has never been unequivocally described. The biotopes of housefly larvæ consist of a variety of materials which by themselves appear nutritionally inadequate, but which have dense microbial floras (for example, animal excrements).

Culture methods for fly larvæ commonly used in laboratories require the addition of yeast to aqueous suspensions of either wheat bran, grass meal, oats or other similar materials[2]. Silverman and Silverman[3] replaced yeast by a controlled bacterial flora and achieved a more uniform growth of larvæ. In larvæ reared on this medium Mer (Mer, G. G., personal communication) found mainly bacterial cells in their foreguts. That living micro-organisms are not necessary for larval growth was shown by Greenberg[4]. He found that '*CSMA*' medium containing an uncontrolled microbial flora could be used, after being autoclaved, for culturing *M. domestica* under sterile conditions.

The aim of the present experiments was to clarify the larval relationship to *Escherichia coli*, which is the dominant micro-organism in breeding sites of housefly larvæ.

Newly hatched larvæ of *Musca vicina* Macq. were reared aseptically[5] for 3 days (to maximal body weight) at 35° C. at a density of one larva per gm. of experimental diets. These were mixtures of wheat bran (40 per cent), milk powder (2·5 per cent), and water (57·5 per cent) incubated for varied periods (Fig. 1) at 30° C. with approx. 4×10^4 *E. coli* (laboratory strain) per gram of medium, and autoclaved prior to use.

The results, which are summarized in Fig. 1, show that the wheat bran–milk suspension does not support larval growth when sterilized before substantial bacterial multiplication took place. This nutritional deficiency is, however, progressively compensated by the accumulation of *E. coli* cells in the initial mixture. Larval growth was optimal when the bacterial concentration had increased to 8×10^8 per gram of diet, which corresponds to an approximately 9·6 per cent weight increase over that of the deficient initial medium. On diets containing the above or higher concentrations of *E. coli*, rates of pupation and adult emergence were comparable to values obtained on stock culture or natural housefly media.



Top line, number of *E. coli* per gm. of mixture.
Bottom line, incubation period of mixture at 30° (hr.).

Fig. 1. Relationship between growth of *Musca* larvæ and concentration of *E. coli* in the wheat bran–milk mixture

Table 1. THE EFFECT OF FEEDING DRIED CELLS OF *E. coli* TO HOUSEFLY LARVÆ. 35 NEWLY HATCHED LARVÆ WERE USED PER EXPERIMENT

Amount of desiccated *E. coli* in diet (gm.)	(per cent)	No. of larvæ surviving at 72 hr.	Average larval weight at age of 72 hr. (mgm.)	No. of larvæ pupating	No. of flies hatching
0·3	1·2	0	—	—	—
0·6	2·3	13	1·4	0	—
1·25	4·8	33	10·8	18	11
2·50	9·1	32	20·6	31	28
3·40	12·0	35	21·0	33	32
Wheat bran–milk mixture containing 7×10^8 *E. coli*/gm.		32	18·9	31	29
Synthetic diet*		28	14·8	23	21

* This consists of vitamin-free casein 2·5 gm., cholesterol 0·025 gm., ribonucleic acid 0·025 gm., salt mixture No. 2 0·016 gm., 'Nipagin' *M* 0·07 gm., powdered filter paper 8·0 gm., water 17·5 gm.; and the following vitamins (μgm./gm. dry diet): thiamine 47, riboflavin 47, pyridoxine 38, pantothenic acid 95, nicotinic acid 238, folic acid 19, choline chloride 2,377, biotin 0·4, inositol 1,902, *p*-aminobenzoic acid 95, and vitamin B_{12} 0·2.

To determine whether the nutritional value of *E. coli* is due to its cellular constituents or products of its metabolic activity, Seitz filtrates of the *E. coli* diets, supplemented with cholesterol (0·1 per cent) and adjusted to the texture of the initial mixture by addition of powdered filter paper, were prepared. Since these diets failed to support larval growth, it is evident that *E. coli* cells contain essential nutrients.

Washed *E. coli* were desiccated to constant weight, and were afterwards mixed in graded amounts (see Table 1) with portions of 25·0 ml. of water and 8·0 gm. of powdered filter paper (particle size <10 mesh) which had been previously impregnated with 0·05 gm. of cholesterol[5]. The texture of the diets resulting after autoclaving was as loose as that of media incubated with living bacteria. Thirty-five newly hatched larvæ were grown aseptically for 3 days on each of these diets.

The results of a typical experiment are summarized in Table 1. The growth-rate of *Musca* larvæ is obviously proportional to the dietary level of the dried bacteria and becomes optimal at concentrations (9·1–12·0 per cent) which closely resemble the weight addition of *E. coli* cells required to 'complete' the wheat bran–milk mixture. This indicates that, apart from cholesterol and water, *E. coli* cells are the only food derived by the larvæ from the above media.

When compared with a synthetic diet, the nutritional superiority of *E. coli* diets is striking. It should be recalled that dried *E. coli* contain 75 per cent of a protein which has a notably higher nutritional value for rats, chicks[6] and housefly larvæ[1] than conventional animal proteins. However, since cholesterol addition to the *E. coli* diet was indispensable for larval growth, the bacteria used appear to lack this constituent of animal cells.

One may conclude that the diverse materials on which housefly larvæ seem to thrive in Nature[7] are

merely substrates for bacteria, and these are most likely to be the actual food of the larvæ. It might be worth considering the use of desiccated *E. coli* with the above-mentioned supplements as a medium for standardized housefly rearing.

This work was carried out at the Medical Research Laboratories of the Medical Corps, Israel Defence Forces, during 1957.

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BACTERIOLOGY

Comaprison of Strains of *Streptomyces griseus* which produce Streptomycin and those which do not

WE have examined a streptomycin-producing strain of *Streptomyces griseus*[1] and two mutants derived from it which did not produce streptomycin. The two mutants arose by treatment with mustard nitrogen[2]. They were isolated as a single colony by the method previously described[3]. Out of 1,387 *Streptomyces griseus* colonies grown from single spores after treatment with mustard nitrogen there appeared 33 non-producing colonies. Only two of them remained stable non-producers after being transferred several times. Their cultural and physiological characteristics differed from the parent strain.

After cultivation in media proposed by Waksman[4] they behaved as different species.

Comparing our strains on various sources of carbon, they proved to have different characteristics. They all grew on 1 per cent maltose, dextrose, pectin, amylum soluble, glycogen, *d*-ribose, xylose, *d*-fructose, mannose, *d*-galactose, dextrose, *l*-arabit, mannitol, glycerol, malate, succinate and fumarate, but did not grow, or very weakly so, on media containing 1 per cent saccharose, cellulose, inulin, rhamnose, sorbose, dulcit, inositol, acetate, tartarate, formate, pyruvate. Pronounced differences have been revealed on media containing arabinose and citrate (Table 1). One of the non-producing strains (No. 45) which was isolated first was not able to grow on citrate as the sole source of carbon. The inability to grow on citrate, however, was not connected with streptomycin production because the other non-producing strain (No. 20/52) was able to use this substrate in the same way as the parent strain did. The inability to make use of citrate was not connected with decreased permeability towards citrate. All three strains were able to decompose citrate. Citrate disappeared from the medium and oxygen consumption, measured in a Warburg apparatus, increased. (Citrate disappearance

Table 1. CARBOHYDRATE UTILIZATION BY *Streptomyces griseus*

Carbon source	Parent strain *Streptomyces griseus*	Mutant strain No. 45	Mutant strain No. 20/52
Arabinose	φ	++++	++++
Citrate	+++	φ	+++

Inoculations were made by spore suspension on agar slopes, and results read on the fourteenth day of incubation.

was measured by chemical[5] determination of citrate in the supernatant, and by measuring the carbon-14–citrate isotope activity in the supernatant.)

The parent strain and mutant 20/52 consumed citrate with a lag phase of about 1 hr.; the other mutant without any lag phase promptly oxidized citrate and increased its Qo_2.

No metabolic block could occur in the two mutant strains in connexion with their inability to produce streptomycin, because both of them could synthetize their protoplasm from simple carbon sources and inorganic nitrogen sources.

There was, however, one striking difference between producing and non-producing mutant strains. The mutants in shaken culture grew only for a very short period of time. The young hyphæ branched very early in their development in every direction and they soon were packed together into spherical clumps, characterized by an almost homogeneous centre and short hyphæ protruding from it into the medium. These clumps grew in size, and spores were produced in very great numbers during the first 24 hr. of the culture. This mode of growth could be observed both in synthetic and complex organic media. It was not possible to achieve normal growth by changing the carbon–nitrogen ratio.

These results indicate that there exists some difference between streptomycin-producing and non-producing strains which lies in some fundamental metabolic change. Although the mutants were able to go through all important metabolic processes, they were not able to develop normally.

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Metabolism of Small Bodies isolated from a Stable *Proteus L* Form

BACTERIAL *L* forms consist of morphological elements of various sizes and shapes[1]. Many investigators of the *L* forms have paid special attention to granular bodies of a diameter of about $0 \cdot 2\mu$, which are very often found in *L* cultures. According to Tulasne, these granules, or some of them, are viable and represent an important stage in the life-cycle of the *L* form[2]. This view has, however, been criticized by other workers[1,3].

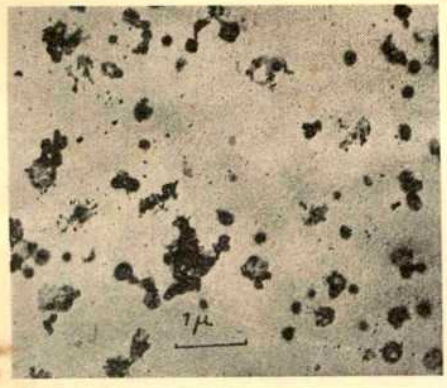

Fig. 1. Electron micrograph of small bodies isolated from a culture of *Proteus L9* by means of differential centrifugation

Separation of various morphological elements in an L culture by means of differential centrifugation has been described by Mandel *et al.*[4,5]. This technique has been applied in the present work. A stable L strain ($L9$) derived from *Proteus vulgaris*[6], was grown in a serum-free medium[7] and subjected to centrifugations at 5,500–78,000g. Thus fractions were obtained which essentially consisted of granules having a diameter of 0·1–0·3μ (Fig. 1).

The respiration of these granules, when suspended in the growth medium, was measured and compared with the respiration of the total culture. Table 1 gives the average values obtained from a number of experiments of this kind. It can be seen that the respiration of the small L granules is of the same order of magnitude as that of unfractionated L cultures. L bodies mechanically disintegrated for 5 min. in a Mickle disintegrator show at the most a very low respiration.

Table 1. AVERAGE VALUES OF RESPIRATION-RATES EXHIBITED BY L BODIES AS MEASURED BY THE WARBURG TECHNIQUE. THE L BODIES WERE SUSPENDED IN THE GROWTH MEDIUM

	Small granules	Total cultures	Total culture after mechanical disintegration
Qo_2	200	402	< 5

The change in the nucleic acid content of the granules and the incorporation of phosphorus-32 into these bodies during 2–4 hr. incubation in the growth medium were also studied. The nucleic acid content remained approximately constant or decreased somewhat. The incorporation of phosphorus-32 in the nucleic acid fraction of the granules (prepared by the Schneider procedure) corresponded to less than 0·2 per cent of the nucleic acid content of these bodies. Under similar conditions, the nucleic acid content of whole *Proteus L9* cultures increased 2–3 times. Therefore, the possibility that the small amount of phosphorus-32 incorporated into the granular fraction could be attributed to contaminating L bodies of larger sizes cannot be excluded. Similarly, no significant incorporation of phosphorus-32 into the protein and lipid fractions of the small L granules could be ascertained.

The ribonucleic acid-content of the granules was found to be about the same (about 4 per cent) as that of unfractionated L bodies. The deoxyribonucleic acid content varied considerably and was often remarkably low (cf. Mandel *et al.*[5]).

The specific activities of the enzymes, succinic dehydrogenase and catalase, in the granules were found to be comparable to those of L bodies present in unfractionated cultures.

The experiments which have been described indicate that, under the prevailing conditions, the biosynthetic capabilities of the L granules studied are at the most very low compared to unfractionated L cultures. The high respiratory power of the granules is, however, worth emphasizing. Mandel *et al.*[4] reported that the small L bodies isolated by them from *Proteus P18* cultures did not degrade glucose aerobically. In these experiments, however, the L granules were not suspended in the growth medium, but in a Krebs medium. We have found that neither fractionated nor unfractionated *Proteus L9* bodies respire in the latter fluid.

The view has been presented that the granular elements found in L cultures represent protoplasmic debris[3]. As shown in Table 1, however, mechanically disintegrated *Proteus L9* bodies exhibit at the most a very low respiration. Thus, the granular bodies described above seem to be characterized by a higher structural organization than the dispersed protoplasm. The presence in the granules of succinic dehydrogenase, catalase and ribonucleic acid, in roughly similar amounts per mgm. dry weight as in L bodies not subjected to differential centrifugation, is also worth mentioning in this connexion.

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GENETICS

Relation between X-Ray Sensitivity and Cell Stages in Males of *Drosophila melanogaster*

LÜNING[1] has shown that the rate of dominant lethals and gross rearrangements varies with the time from irradiation to insemination, with a peak around 7–10 days after the treatment. He suggests that the peak corresponds to irradiated spermatids which hence are supposed to be more sensitive than mature sperm. Auerbach[2] claims that the sensitive stage, although it may include late meiosis, consists mainly of spermatid stages. Khishin[3], comparing the mutation pattern from irradiation of larvæ, pre-pupæ and pupæ, agrees with Auerbach. Fritz-Niggli[4] adopted the same technique and deduced by analogy the following pattern of time-lapse between irradiated stages and insemination: mature sperm the 1st–4th day; spermatids the 4th–7th day; meiosis the 7th–10th day; and from the 10th day after irradiation spermatogonia.

The present investigation is an attempt to find the time of the appearance of the sperm irradiated in

meiosis by a direct method, and at the same time to correlate this with the sensitivity pattern. Mavor[5,6] showed that irradiation of females caused primary nondisjunction. The same ought to be true also in males if meiotic stages are irradiated. The appearance of individuals in which the paternal sex-chromosomes both have entered the sperm cell will indicate that the cell had been treated before anaphase I. In the present experiment the occurrence of *XO* males has been used as an indication of genetical damage. At the same time the induction of nondisjunction between the *X* and *Y* chromosomes in the males has served as a criterion of early meiosis (prior to anaphase I).

The following stocks were used: the females were taken from a *y w sn* ♀♀ × *y w sn*; sc^8Y ♂♂ stock and the males from a y^{16} ♀♀ × y^{16}; sc^8Y ♂♂ stock. The normal offspring would be *y* females and *w sn* males. Individuals which had lost the *X* and/or sc^8Y, and consequently were *XO*, would phenotypically be *y w sn*; and eggs fertilized by an *X*; sc^8Y carrying sperm (nondisjunction) would give wild-type females due to the presence of the y^+ locus in the *Y* chromosome (*y w sn*; y^{16}; sc^8Y). As these females also may arise through induced crossing-over between the *X* and the *Y* chromosome, each wild-type female was tested individually. The majority of these were due to nondisjunction. The males were picked out when 0–1 day old. They were either irradiated when they had woken up after treatment with ether or kept without females for 3 days prior to irradiation. The males were irradiated with a dose of 1,100 r. (2 min.). Immediately after irradiation the males were transferred to a mating box. The first mating period lasted 4 hr., but from the 4th day onwards each period consisted of 24 hr. Between the first mating period and the 4th day the males were kept with an excess of females.

Table 1. 0–1-DAY AND 3–4-DAY-OLD y^{16}; sc^8Y MALES WERE GIVEN 1,100 R. IN AIR AND WERE THEN MATED TO *y w sn* FEMALES. TOTAL NUMBER OF OFFSPRING AS WELL AS RATE OF *XO* MALES AND WILD-TYPE FEMALES ARE GIVEN

Mating period after irradiation	0–1-day-old males			3–4-day-old males		
	Percentage *XO* ♂♂	Percentage wild type ♀♀	Total offspring	Percentage *XO* ♂♂	Percentage wild type ♀♀	Total offspring
0–4 hr.	0·46	0·01	20,538	0·32	0·03	44,635
Fourth day	0·33	0·03	62,692	0·20	0·04	43,016
Fifth day	0·75	0·03	50,552	0·43	0·02	38,766
Sixth day	1·33	0·01	24,735	0·61	0·02	17,571
Seventh day	2·21	0·22	18,100	1·24	0·12	14,155
Eighth day	3·47	0·51	13,350	1·55	0·21	11,706
Ninth day	2·39	0·19	7,772	0·96	0·13	8,724
Tenth day	0·54	0·18	27,946	0·49	0·14	8,312
Eleventh day	0·46	0·14	30,044	0·19	0·05	7,807

From Table 1, which shows the results after irradiation of 0–1-day- and 3–4-day-old males, it can be seen that, independent of the age of the males at time of irradiation, the number of induced *XO* males rises steeply from the 4th day, reaching a peak on the 8th day after treatment and then decreasing towards the 11th day. As regards the frequency of induced wild-type females, the rate is practically unchanged from the first mating period until the 6th day after irradiation. On the 7th day after irradiation there is a sharp increase in the frequency of wild-type females. The frequency reaches a peak during the 8th day after irradiation, followed by a drop towards the 11th day.

It is of special interest to compare the frequency of induced *XO* males and the rate of induced nondisjunction females during the 4th–10th day after irradiation. It can be seen that the peak of *XO* males coincides with the peak of nondisjunction females. Since the occurrence of nondisjunction females is used as the criterion of early meiosis (prior to anaphase I) there is an agreement between the highest X-ray sensitivity and cells treated at early meiotic stages.

About the same sensitivity pattern is obtained after irradiation of 0–1 and 3–4 day old males respectively. There exists, however, a discrepancy in the amplitude of the sensitivity. The frequency of induced *XO* males, as well as the rate of induced nondisjunction females, is much lower in the experiments with 3–4 day old males. This difference is statistically significant except for the first mating period. There is a fairly good agreement between these findings and Lüning's[1] conclusions that 6–7-day-old males vary much less than 0–1-day-old males between different stages of spermiogenesis.

These experiments show that the treated meiotic cells become available for insemination during the 7th day after irradiation and onwards. From the present material it can be concluded that the peak of sensitivity presumably corresponds to cells treated during metaphase I or before anaphase I is completed. This conclusion is supported by sensitivity studies performed on different material[7–10].

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VIROLOGY

Virus Survival as a Seasonal Factor in Influenza and Poliomyelitis

THE pronounced seasonal fluctuations in the morbidity of influenza and poliomyelitis are largely unexplained. Both diseases can probably be transmitted by airborne infection and by many other ways which involve the survival of the causative virus in the dry state. For many organisms survival in air can be taken as indicator for survival in the dry state in general. Consequently it seemed worth while to study the influence of temperature and humidity on the survival of the viruses of influenza and poliomyelitis in air.

Earlier experiments with aerosols[1] of many organisms showed that—at least in the range of indoor temperature—the influence of temperature is small (Q_{10} = 2–3) compared with the influence of humidity. Furthermore it became evident that the relative humidity and not the absolute humidity is the determining factor.

Both viruses were aerosolized for 2 min. with an indirect spray (mean droplet diameter 6μ) into a

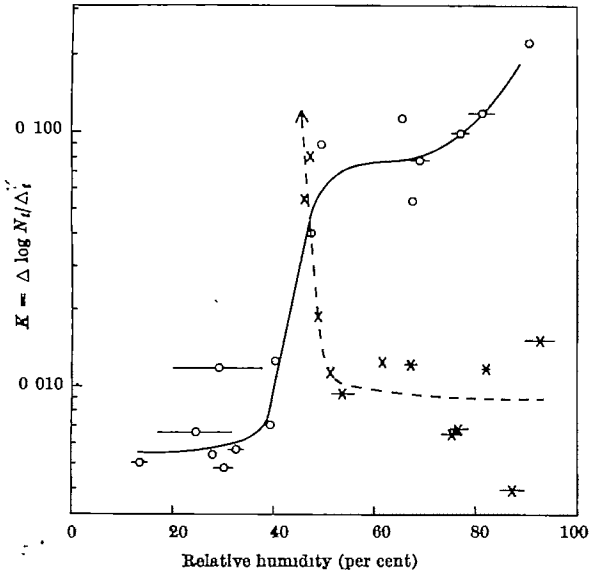

Fig. 1. Death-rates for influenza virus (○) and poliomyelitis virus (×) in air plotted against relative humidity

static system (4 M^1). Influenza virus (PR_8) was suspended in one part allantoic fluid and one part 2 per cent Difco peptone. Poliomyelitis virus (type 1 *CSL*) was suspended in one part Hanks salt solution with lactalbumin-hydrolysate and 5 per cent horse serum and one part peptone. At various times samples were taken for 2 min. with modified capillary impingers containing 1 per cent peptone or 1 per cent peptone with Dulbecco buffer.

Virus was titrated by amnion inoculation for influenza and by the plaque method on human amnion cells (strain *U*) for polio-virus.

From the logarithmic phase of the inactivation curves at various relative humidities, death-rate constants were calculated, using $K_2 = \Delta \log N_t/\Delta_t$ (t denoting time in minutes). K is plotted against relative humidity in Fig. 1. For influenza virus the death-rate is high (0·091 ± 0·024) at 50–90 per cent relative humidity and low (0·0073 ± 0·0031) in the range 15–40 per cent relative humidity. The transition is rather sharp. These results are mainly in accordance with the limited experiments published previously by other authors[2-6]. For poliomyelitis the inverse is true. Inactivation is slow (K = 0·0089 ± 0 0036) at high relative humidity and very fast at low relative humidity. In fact, below 45 per cent no virus could be detected 30 sec. after spraying, which means that less than 0·03 per cent of the virus was left. The transition is again sharp.

In temperate climates influenza generally is a winter disease, occurring during the period when the relative humidity indoors is low as a result of heating. In Fig. 2 the seasonal variation of indoor humidity is plotted. The period of increasing influenza morbidity coincides with the period during which the survival of the virus in air is optimal.

Increase of poliomyelitis morbidity occurs during summer, that is, during the period when the indoor relative humidity is optimal for the survival of the virus in air (and presumably in the dry state in general).

Consequently the relative humidity, indoors, is considered as an important environmental factor contributing to the seasonal fluctuations of the morbidity of these two virus diseases.

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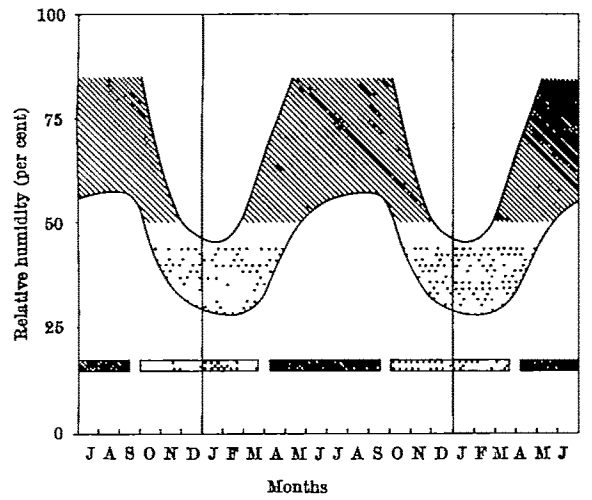

Fig. 2. Seasonal variation of relative humidity indoors in the Netherlands. The upper and lower curves represent mean maximal and minimal relative humidity as calculated from temperature and absolute humidity. The range for optimal virus-survival is stippled for influenza virus and hatched for polio virus. The period of increasing morbidity of influenza (data for England and Wales) and for poliomyelitis (Dutch data) are given at the bottom of the figure as stippled and hatched bars

Association of *Olpidium brassicae* and Tobacco Necrosis Virus

Tobacco necrosis virus infects the roots of many plants, usually without symptoms. The virus is soil-borne[1-3], but the conditions necessary for natural infection have not been determined. Attempts to obtain artificial infection of roots by adding virus suspensions to roots of plants grown in sterilized soil commonly fail.

The relationship of *Olpidium brassicae* to tobacco necrosis virus infection was investigated because of claims[4-7] of an association between tobacco necrosis virus and lettuce big vein disease, with which *O. brassicae* is invariably associated[8,9].

Further circumstantial evidence for the association of tobacco necrosis virus and *O. brassicae* was obtained in the present work by microscopic detection of *Olpidium* in the roots of *Cleome spinosa*, *Fragaria vesca*, *Chenopodium amaranticolor*, tobacco, and French bean infected with tobacco necrosis virus.

When suspensions of *Olpidium* zoospores from lettuce plants shown by root assay to be free of tobacco necrosis virus, and suspensions from macerated virus-infected cowpea leaves were simultaneously watered on to potted lettuce seedlings, much greater

Table 1. AVERAGE NUMBERS OF TOBACCO NECROSIS VIRUS LESIONS PER ASSAYED PLANT FROM INOCULATION OF LETTUCE ROOTS WITH *Olpidium brassicae* AND TOBACCO NECROSIS VIRUS

Treatment	Total number of plants assayed	Total number of plants infected with virus	Average number of virus lesions per plant assayed
Olpidium + virus	40	38	36 7
Virus only	31	17	0 7
Olpidium only	20	3	0 1*
Nil	14	1	0 1*

* Infection probably resulting from contamination.

root infection by tobacco necrosis virus occurred than when the virus alone was applied. Results in three experiments are summarized in Table 1.

Similar results were secured when cowpea, French bean, cabbage, cucumber, and tobacco were inoculated with *Olpidium* and tobacco necrosis virus. The results have been repeated in water culture in the laboratory with seedlings raised in Petri dishes.

The mode of action of *Olpidium* zoospore suspensions in thus increasing root infection with tobacco necrosis virus is not known. Conceivably, the fungus may act as a virus vector or it may predispose the roots to infection. Zoospore suspensions from lettuce roots infected with both *Olpidium* and tobacco necrosis virus have caused virus infection of roots even without added virus. As tobacco necrosis virus is released naturally by infected roots[10], however, this does not necessarily mean that *Olpidium* is acting as a virus vector.

It is possible, but unlikely, that some factor other than *Olpidium* obtained from lettuce roots is responsible for the increased virus infection; a final decision on this must wait until it becomes possible to grow *Olpidium* in pure culture.

The advice of C. E. Yarwood and R. G. Grogan is gratefully acknowledged. C. E. Yarwood, N. W. Frazier, and T. Bowman kindly furnished plants naturally infected with tobacco necrosis virus.

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AGRICULTURE

Contribution of Rainwater to the Nutrient Economy of Soil in Northern Nigeria

THE contribution of rainwater to the nutrient economy of soil in many regions of the world has been studied. At Samaru, Northern Nigeria, 80 litres of rainwater from eight rain gauges were collected in 1959. The water was concentrated by evaporation from dilute sulphuric acid and the concentrate analysed for all major nutrients except sulphur. Forty-two inches of rain fell during the 1959 season. The results are expressed in p.p.m. of each element

Table 1. NUTRIENT CONTRIBUTION OF RAINWATER IN 1959 AT SAMARU, NORTHERN NIGERIA

Nutrient	p.p.m.	lb./acre
Nitrogen		
Ammonium	5 000	47 6
Nitrate	0 230	1·2
Organic	0·125	2·0
Total	5 355	50·8
Phosphorus	0·555	2·3
Potassium	3 500	32·8
Calcium	0 100	0·9
Magnesium	0 110	2 60
Sodium	5 750	53·8

in the total composite sample, and have been converted to pounds per acre (Table 1). Sampling procedure excluded any measure of seasonal distribution.

So far as I am aware, the nitrogen, potassium and sodium figures are the highest recorded. Despite the high values, the sodium/potassium ratio is of the order found in New Zealand by Wilson[1]. He has shown that the nutrients present in snow originate from the surface of the ocean where a large number of plankton, etc., in various stages of growth and decomposition are concentrated. These organisms narrow down the potassium/sodium ratio of the underlying sea. The potassium/sodium ratio of sea-water is 1 : 27, snow-water in New Zealand showed a ratio of 1 : 2·7 and at Samaru a ratio of 1 : 1·6 was found. The narrower ratio at Samaru may be due to a higher or different biological activity in the warm ocean around West Africa compared with New Zealand conditions. The low nitrate figure eliminates the possibility of large contributions from dust and electric storms. The lack of seasonal distribution figures makes the evaluation of the various factors impossible. Generally, the figures to date point to the ocean as the main source of rainwater nutrients, but do not exclude contributions from other factors.

The presence of such large and varied quantities of nutrients in the rainwater helps to explain several aspects of soil fertility in Northern Nigeria.

(1) Potassium fertilizers have never shown a positive response on annual crops of the region. Potassium from rainwater is probably adequate for crop growth, and the fertilizer potash aggravates what must be already an imbalance of potassium to other nutrients.

(2) Despite the lack of leguminous plants in bush fallows, build up of organic nitrogen is appreciable. From unpublished soil analysis data at Samaru, it has been calculated that an increase of 0·025–0·03 per cent total nitrogen can be expected over a period of five years. Rainwater, if not lost by run-off, would contribute 0·013 per cent nitrogen.

(3) Light sandy soils in the extreme north of the region show very low levels of total nutrients, and crop growth would seem to be impossible. The contribution of rainwater helps to explain the growth of crops on these soils.

These results indicate the importance of rainwater as a source of nutrients in the soil of Northern Nigeria. More detailed studies are in progress.

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FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, October 31

BRITISH SOCIETY FOR THE HISTORY OF SCIENCE (in the Council Room (second floor) of the Science Museum, Exhibition Road, London, S.W.7), at 5.30 p m —Prof. Benjamin Farrington: "Francis Bacon at the Crossroads".

INSTITUTION OF MECHANICAL ENGINEERS, APPLIED MECHANICS and LUBRICATION GROUPS (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Discussion on "Rolling Bearing Problems—Is There a Need for Fundamental Research ?".

INSTITUTION OF THE RUBBER INDUSTRY (at the Café Royal, 68 Regent Street, London, W.1), at 6 p.m.—Mr. E. B. Storey: "Estimation of Wear Resistance of Tread Vulcanizates".

Tuesday, November 1

UNIVERSITY OF LONDON (at the Middlesex Hospital Medical School, Mortimer Street, London, W.1), at 5.15 p.m.—Prof. Hans Schaefer (University of Heidelberg). "Principles of Circulatory Regulation" *

INSTITUTION OF ELECTRICAL ENGINEERS, MEASUREMENT AND CONTROL SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. G. G. Haigh: "Transistor Instrumentation in Rockets".

UNIVERSITY OF LONDON (at the Imperial College of Science and Technology, London, S.W.7), at 5.30 p.m.—Prof. K. G. Denbigh: "The Science of Continuously Operating Systems" (Inaugural Lecture).

Wednesday, November 2

SOCIETY FOR ANALYTICAL CHEMISTRY (at the Wellcome Building, Euston Road, London, N.W.1), at 2 p m.—Meeting on "Analysis of Semi-Conductors".

UNIVERSITY OF LONDON (at the Postgraduate Medical School of London, Ducane Road, London, W.12), at 2 p.m.—Prof. R. H. S. Thompson: "Biochemistry of Multiple Sclerosis".*

GEOLOGICAL SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p m.—Dr. M. J. Rickard. "The Stratigraphy and Structure of the Errigal Area, Co. Donegal"; Dr. B. A. Sturt. "The Geological Structure of the Area South of Loch Tummel".

INSTITUTE OF PETROLEUM (at 61 New Cavendish Street, London, W.1), at 5 30 p m.—Mr J. Tubman and Mr. J. F. Manger. "Applied Petroleum Research on a Vehicle Dynamometer".

INSTITUTION OF ELECTRICAL ENGINEERS, ELECTRONICS AND COMMUNICATIONS SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Prof. W. J. G. Beynon: "The Ionosphere—a Review of Recent Progress".

ROYAL METEOROLOGICAL SOCIETY (at 49 Cromwell Road, London, S.W.7), at 5 30 p m.—Dr. A. W. Brewer. "The Stratosphere".

INSTITUTION OF MECHANICAL ENGINEERS, INTERNAL COMBUSTION ENGINE GROUP (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m —Discussion on "The Days of the Diesel Engine are Numbered".

BRITISH INSTITUTION OF RADIO ENGINEERS, RADAR GROUP (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C 1), at 6.30 p.m —"Radar—Pulse or C.W.?" (a Discussion on Relative Merits).

SOCIETY FOR VISITING SCIENTISTS (at 5 Old Burlington Street, London, W.1), at 7 30 p m.—Discussion Meeting on "Noise". Chairman: Sir Gordon Sutherland, F.R.S. Speakers: Mr. D. W. Robinson, Prof. W. Burns and Dr. A. Carpenter.

Thursday, November 3

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Dr. A. M. Lwoff, For.Mem R.S: "Viral Functions" (The Leeuwenhoek Lecture).

MINERALOGICAL SOCIETY (at the Geological Society of London, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Scientific Papers (Anniversary Meeting).

UNIVERSITY OF LONDON (at Wye College, Wye, Ashford, Kent), at 5 p.m.—Dr J. T. Martin: "The Plant Cuticle. Its Structure and Relation to Spraying Problems".*

UNIVERSITY OF LONDON (at the Middlesex Hospital Medical School, Mortimer Street, London, W 1), at 5.15 p.m.—Prof. Hans Schaefer (University of Heidelberg): "The Theory and Interpretation of the Electrocardiogram".*

INSTITUTION OF ELECTRICAL ENGINEERS (joint meeting with the INSTITUTIONS OF CIVIL and of MECHANICAL ENGINEERS, at Savoy Place, London, W.C 2), at 5 30 p.m.—Dr. W. Abbott "The Training of Oversea Graduate Engineers, with particular reference to the F.B.I. Scholarships Scheme".

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p m.—Dr. Charles Wilcocks: "Aspects of Medical Investigation in Africa—Schistosomiasis".* (Second of four Heath Clark Lectures Further lectures on November 9 and 10.)

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. K. M. Rudall: "Regular Folds in Protein and Polysaccharide Chains".* (Fifth of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

ARTHUR STANLEY EDDINGTON MEMORIAL TRUST (at Friends House, Euston Road, London, N.W.1), at 6 p.m.—Dr. William H. Thorpe, F.R.S.: "Biology, Psychology and Belief" (Fourteenth Eddington Memorial Lecture).

INSTITUTE OF METALS, LONDON LOCAL SECTION (at the Royal School of Mines, Prince Consort Road, London, S.W.7), at 7 p m.—Dr. N. P. Allen, F.R.S.: "Long Term Creep Tests. a Discussion of Recently Expressed Views".

ROYAL INSTITUTE OF CHEMISTRY, LONDON SECTION (joint meeting with the BRUNEL COLLEGE OF TECHNOLOGY CHEMICAL SOCIETY, at the Brunel College of Technology, Woodlands Road, London, W.3), at 7 p.m.—Dr. C. C. Addison: "Non-aqueous Solvent Systems".

CHEMICAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 7.30 p.m.—Scientific Papers.

Friday, November 4

MINERALOGICAL SOCIETY, CLAY MINERALS GROUP (at the Geological Society of London, Burlington House, Piccadilly, London, W.1), at 10.45 a.m.—Autumn Meeting.

UNIVERSITY OF LONDON (at the Institute of Obstetrics and Gynaecology, Chelsea Hospital for Women, Dovehouse Street, London, S W.3), at 3 p.m.—Prof E. C. Amoroso: "The Endocrinology of Pregnancy".*

CIBA FOUNDATION FOR THE PROMOTION OF INTERNATIONAL COOPERATION IN MEDICAL AND CHEMICAL RESEARCH (at the Royal Institute of British Architects, 66 Portland Place, London, W.1), at 5 p.m.—Prof. J. Konorski (Warsaw): "Changing Concepts Concerning Physiological Mechanisms of Animal Motor Behaviour" (Twelfth (Annual) Ciba Foundation Lecture).

INSTITUTION OF ELECTRICAL ENGINEERS, MEDICAL ELECTRONICS DISCUSSION GROUP (at Savoy Place, London, W.C.2), at 6 p.m.—Discussion on "Electro-Convulsive Therapy" opened by Dr. A. Spencer-Patterson and Mr. W. H. Stanton.

SOCIETY OF DYERS AND COLOURISTS, LONDON SECTION (at the Royal Society, Burlington House, Piccadilly, London, W.1), at 6 p.m.—Mr. A. J. Lenz: "Fastness of Dyes and Finishes".

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 9 p m.—Prof. G. Porter: "Very Fast Chemical Reactions".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

EXPERIMENTAL OFFICER (at least 26, with a pass degree or equivalent, experience in radiochemistry and the use of normal beta counting equipment, and preferably a working knowledge of alpha and gamma counters), for work involving the measurement of radioactivity in biological materials—The Director, Agricultural Research Council, Biological Laboratory, Letcombe Regis, Wantage, Berks (November 2).

BIOCHEMIST (non-medical), for research on problems connected with tropical diseases—The Secretary, Hospital for Tropical Diseases, 4 St. Pancras Way, London, N.W.1 (November 5).

LABORATORY TECHNICIAN (qualified, with experience of laboratory work) at Brentwood Teacher Training College—Chief Education Officer (Ref. F.5.k), County Offices, Chelmsford (November 5).

RESEARCH ASSISTANT IN THE DEPARTMENT OF BOTANY, to carry out research with Dr. L. Fowden on nitrogen metabolism—The Secretary, University College, Gower Street, London, W.C.1 (November 7).

HEAD (with high qualifications and experience) OF THE DEPARTMENT OF PHYSICS—The Bursar, College of Advanced Technology, Gosta Green, Birmingham 4 (November 8).

LECTURER (with medical qualifications registrable in this country) IN PSYCHIATRY—The Registrar, The University, Manchester 13 (November 12).

CHAIR OF PHYSICS in the University of Khartoum—The Registrar, University of Khartoum, c/o Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (November 15).

LECTURER or ASSISTANT LECTURER (with special qualifications in applied mathematics) IN THE DEPARTMENT OF MATHEMATICS of the Faculty of Science—The Registrar, The University, Manchester 13 (November 16).

EXPERIMENTAL AND THEORETICAL PHYSICISTS (with a first- or second-class honours degree in physics or mathematics), for research work in the Reactor Development Division—Personnel Branch (W.348/34), U.K.A.E.A., Atomic Energy Establishment, Winfrith, Dorchester, Dorset (November 17).

LECTURER (with a science degree with zoology as a major subject, followed by postgraduate experience leading to a higher degree and/or to published work) IN ZOOLOGY in the University College of Townsville, University of Queensland, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W C.1 (Australia and London, November 19).

LECTURER (with a degree in science with honours in physics, some experience in the use of ionizing radiation, and preferably experience in using radioactive substances and in the principles of hospital or health physics) IN RADIATION PHYSICS AND RADIATION SAFETY OFFICER at the University of Queensland, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W C.1 (Australia and London, November 19).

LECTURER or ASSISTANT LECTURER (with a special interest in plant physiology) IN BOTANY at the University College of Rhodesia and Nyasaland—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (November 30).

SENIOR LECTURER or LECTURER (with an honours degree or equivalent qualifications, and industrial and/or research experience) IN STRUCTURAL ENGINEERING—The Registrar, Bristol College of Science and Technology, Ashley Down, Bristol 7 (December 3).

LECTURER IN BIOCHEMISTRY at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, December 5).

PLANT PHYSIOLOGIST (with a good honours degree in botany and research experience), for investigation of effects of temperature, oxygen and carbon dioxide on the respiration of apples—The Director, Ditton Laboratory, Agricultural Research Council, Larkfield, Maidstone, Kent (December 10).

SENIOR LECTURER IN PHILOSOPHY at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, December 10).

EMPIRE RHEUMATISM COUNCIL FELLOW (with medical or scientific qualifications), to prosecute research in the field of rheumatism—The General Secretary, Empire Rheumatism Council, Faraday House, 8/10 Charing Cross Road, London, W.C.2 (December 15).

AGRICULTURAL OFFICER (TOBACCO RESEARCH) (with a good honours degree in natural science (botany), or a degree in horticulture, with suitable postgraduate training or experience) in Nyasaland, for experimental work on tobacco including agronomy trials and plant breeding—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/4/04.

ASSISTANT, Grade B (with a university degree and preferably some teaching experience), TO TEACH BOTANY AND ZOOLOGY to Advanced Level students—The Clerk to the Governors, South-West Essex Technical College and School of Art, Forest Road, Walthamstow, London, E.17.

ASSISTANT PROFESSORS, INSTRUCTORS or LECTURERS (2) (with the degree of Ph.D.) IN PHYSICS, to direct experimental research in low temperature or solid state physics—The Chairman, Department of Physics, Western Reserve University, Cleveland 6, Ohio, U.S.A.

CLAY MINERALOGIST (with an appropriate academic background and experience) IN THE DEPARTMENT OF MINES AND TECHNICAL SURVEYS, Canada, for research aimed at the development of useful properties in Canadian clays and shales—Dept. MTS 1518, National Employment Service of Canada, 61 Green Street, London, W.1

GRADUATE RESEARCH ASSISTANT IN THE DEPARTMENT OF PHYSICS, for a study of crystal structure and texture of materials by the techniques of electron diffraction and microscopy leading if desired to a higher degree—The Secretary, Birkbeck College (University of London), Malet Street, London, W.C.1

LECTURER IN THE DEPARTMENT OF PHYSICS—The Principal, Huddersfield College of Technology, Huddersfield

LECTURER (with marked ability at conducting and supervising research) IN THE CHEMICAL PHYSICS OF SOLIDS—Prof. A. R. Ubbelohde, F.R.S., Department of Chemical Engineering and Chemical Technology, Imperial College of Science and Technology, London, S.W.7.

MASTER TO TEACH PHYSICS (the post involves some Sixth Form work)—The Headmaster, King's College School, Wimbledon, London, S.W.19.

RESEARCH ASSOCIATE IN ORGANIC CHEMISTRY, for work involving the isolation and identification of products formed by action of gamma radiation or organic compounds (mainly amines)—The Professor of Organic Chemistry, King's College (University of Durham), Newcastle upon Tyne 1.

RESEARCH FELLOWS and RESEARCH ASSISTANTS (4) IN THE DEPARTMENT OF PHARMACY—The Registrar, Bradford Institute of Technology, Bradford 7.

SENIOR LECTURER or LECTURER (with a first- or second-class honours degree and a thorough grounding in electronics, and preferably experience in radar, telecommunications or radio guidance of missiles) IN ELECTRONICS at the Royal Military College of Science, Shrivenham, Berkshire—The Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting D.690/0A.

TECHNICAL OFFICER (preferably with workshop and electronics experience), for research in muscle biophysics, using the electron microscope, X-ray diffraction, etc.—The Director, Medical Research Council Biophysics Research Unit, King's College, Strand, London, W.C.2.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Colour Filmstrips on Soil. No. 1: Rocks and Erosion. 38 frames. Notes. Pp. 14. No. 2 Plants and Decay. 35 frames. Notes. Pp. 16. No. 3. Soil Profiles and Their Information. 37 frames. Notes. Pp. 12. No. 4: Composition of Soil. 35 frames. Notes. Pp. 17. No. 5: Soil and Farming. 37 frames Notes. Pp. 26. (Surbiton: Marian Ray, 36 Villiers Avenue, 1960.)

The Morgan Crucible Company Limited. The Chairman's speech at the 26th Annual General Meeting held at Battersea Works on Thursday, 28th July, 1960. Pp. 4. (London: The Morgan Crucible Company, 1960.) [28

Ministry of Agriculture, Fisheries and Food. At the Farmers' Service: a Handy Reference to various services available to Farmers in England and Wales. Pp. 81. (Kew, Surrey: Ministry of Agriculture, Fisheries and Food (Publications), 1960.) [28

Freshwater Biological Association. Twenty-eighth Annual Report for the year ended 31 March 1960, including Reports of the Council and of the Director, and Accounts for 1959–60, with Lists of Officers, Council, Staff and Members. Pp. 93. (Ambleside. Freshwater Biological Association, 1960.) [28

Beecham Group Journal, Vol. 1, No. 1 (Summer, 1960). Pp. 22. (Brentford, Middx. Beecham Group Ltd., 1960.) [28

Department of Scientific and Industrial Research. Report of the Tropical Products Institute 1959: The Report of the Tropical Products Institute Committee, with the Report of the Director of the Tropical Products Institute. Pp. iv+40. (London: H.M. Stationery Office, 1960.) 2s. 6d. net. [38

Philosophical Transactions of the Royal Society of London. Series A: Mathematical and Physical Sciences. No. 1020, Vol. 253 (28 July 1960): Stability of Flow in a Rotating Viscous Incompressible Fluid Subjected to Differential Heating. Pp. 1–25. 8s. No. 1021, Vol. 253 (28 July 1960). Hassitt-Type Young Operator Expansions. 1: An Orthogonal Transformation between (a) the Young Operators of the Symmetric Group S_{A+1} and (b) The Two-Sided Products of the Young Operators of S_A with the Transposition $P_{A,A+1}$. By H. A. Jahn. Pp. 27–53. 8s. 6d. (London: The Royal Society, 1960.) [38

Other Countries

Parapsychology Foundation, Inc., New York. Parapsychological Monographs No. 2 ESP in Relation to Rorschach Test Evaluation. By Gertrude Schmeidler. Pp. iii+89. (New York. Parapsychology Foundation, Inc., 1960.) [28

Louisiana Agricultural Experiment Station. Southern Co-operative Series. Bulletin No. 63. Summer Climate and Its Effects on Dairy Cattle in the Southern Region. Pp. 63. (Baton Rouge, Louisiana: Louisiana Agricultural Experiment Station, 1959.) [28

Chicago Natural History Museum. Fieldiana. Geology. Vol. 11, No. 10: Fishes of the Devonian Holland Quarry Shale of Ohio. By Robert H. Denison. Pp. ii+555–613. 1.50 dollars. Vol. 14, No. 1: The Stratigraphy of the Devonian Holland Quarry Shale of Ohio. By J. Ernest Carman. Pp. 5. 15 cents. Fieldiana: Zoology. Vol. 39, No. 35: Two Eels of the Genus *Synaphobranchus* from the Gulf of Mexico. By P. H. J. Castle. Pp. 387–398. 30 cents. Vol. 39, No. 36: A New Genus of Blind Beetles from a Cave in South Africa. By Henry S. Dybas. Pp. 399–405. 20 cents. (Chicago Natural History Museum, 1960.) [28

United States Department of the Interior: Fish and Wildlife Service. Fishery Bulletin No. 172: Seasonal Abundance and Vertical Movements of Planktonic Crustacea in Lake Michigan. By LaRue Wells. Pp. iv+343–369. (Washington, D.C.: Government Printing Office, 1960.) 25 cents. [28

Smithsonian Institution. Proceedings of the United States National Museum. Vol. 112, No. 3431: Lace-Bug Genera of the World (Hemiptera: Tingidae). By Carl J. Drake and Florence A. Ruhoff. Pp. 1–105. Vol. 112, No. 3432. Flies of the Family Conopodae from Eastern Asia. By Sidney Camras Pp. 107–131. Vol. 112, No. 3433: Fireflies of the Genus *Pyractonema* (Coleoptera. Lampyridae). By Frank A. McDermott. Pp. 133–157. Vol. 112, No. 3434: North and South American Copepods of the Genus *Hemicyclops* (Cyclopoida: Clausidiidae). By Richard U. Gooding. Pp. 159–195. Vol. 112, No 3435: Chironomid Midges of California. 1: Chironominae, exclusive of Tanytarsini (=Calopsectrini). By James E. Sublette. Pp. 197–226. (Washington, D.C.: Government Printing Office, 1960.) [28

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United States Department of Commerce: Coast and Geodetic Survey Technical Bulletin No. 11: Use of Near-Earth Satellite Orbits for Geodetic Information By Paul D. Thomas. Pp. ii+36. (Washington, D.C.: Government Printing Office, 1960.) 45 cents. [28

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World Meteorological Organization: The First Ten Years. Pp. 32. (Geneva World Meteorological Organization, 1960.) [28

A Study of Air Pollution: Diffusion and Sampling. By Dr. L. A. Clarenburg. (Doctoral Thesis.) Pp. xi+89. (Utrecht. Drukkerij Schotanus and Jens, 1960.) [28

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THE BALANCE OF BRITISH SCIENTIFIC EFFORT

THE thirteenth annual report of the Advisory Council on Scientific Policy, covering the year from July 1, 1959, to June 30, 1960, and the first to be submitted to Lord Hailsham as Minister for Science, is concerned with one main topic: the balance of scientific effort. There is also a brief but important discussion of the implications for scientific education of the Crowther Report; and a paragraph on space research states that, after reconsidering the subject, the Advisory Council reaffirms its previous advice that a programme of scientific research in space using satellites on a purely national basis would not, in itself, justify the very large expenditure necessary for a full-scale programme, including the development of a launching vehicle. This in itself is a particular aspect of the balance of our scientific effort, and that comment applies equally to the section of the report which contains the Council's observations on two particular fields of pure science, optical astronomy and seismology, which have become, for various reasons, neglected. In addition to the detailed results of the review of the Statistics Committee on Expenditure on research and development in the United Kingdom, 1958–59, there are appended, as usual, details of the numbers of graduate teachers of science and mathematics in schools and technical colleges, degrees and diplomas in science and technology, and estimated Government expenditure on civil research.

The review of the balance of our scientific effort follows the two earlier general surveys undertaken by the Council described in its reports for 1953–54 and 1956–57. In the first of these, the Council expressed the view that "a country's wealth and power are to-day largely determined by the extent of its scientific knowledge and its capacity to use that knowledge". In the second the Council found that the resources devoted to research and development for civil purposes were still far too small for Britain's needs. Government expenditure on civil research was then estimated at some £26·6 million. Excluding Treasury grants-in-aid to the universities and expenditure on civil research by the Ministry of Aviation and the Atomic Energy Authority, expenditure has since risen from an estimated £30·45 million in 1958–59 to £38·868 million in 1960–61, and these figures should be compared with the estimate of £300 million for the expenditure by British manufacturing industry on research and development given in the Department of Scientific and Industrial Research's report, "Industrial Research and Development Expenditure, 1958", published last April (see *Nature*, 186, 997; 1960).

The present review was undertaken at the request of the Minister for Science, who asked the Council for an authoritative review of the balance of scientific effort in resources and man-power in the civil field, and in accepting this responsibility the Council has rightly attempted to define clearly both the aim and the limitations of any such review. It disclaims any attempt to seek a formal structure, but emphasizes rather the prime importance of devising criteria by which the points can be identified at which additional effort and resources will pay the greatest dividends. It is not concerned with administrative matters but with the strategy of scientific affairs, and suggests that it should be possible, on the basis of a comprehensive review, to indicate broad fields where further work is required, or where a new assessment or reorientation of effort seems desirable. It believes that the Research Councils and other government agencies operating in scientific and technological matters are the appropriate bodies to interpret its recommendations in terms of programes of work.

In its reference to strategy it does not mean to imply that the advance of scientific knowledge can be directed: it uses the term in the sense in which it has been used by Sir Henry Tizard and Sir Hugh Beaver, for example, and again in the Barlow Report on scientific staff. Basic advances in science depend on the creative individual, or perhaps also on the creative minority, but from time to time obstacles can be removed, encouragement and resources provided for people who have ideas and the best use made of our limited resources. In other words, the Advisory Council is seeking to act on the policy that has long influenced and guided such bodies as the Nuffield Foundation and Rockefeller Foundation, and identify the growing points and ensure that they are adequately supported.

Clearly an official body, even if its functions are purely advisory, cannot commit public support with the freedom with which the private foundation can allocate resources, but there is no more encouraging feature of the present report than the way in which the Minister for Science and the Advisory Council itself take such a wide view of the Council's advisory function. If this is sustained, Britain will have at last one body responsible for considering how new scientific developments may interact among themselves and with the functions of existing institutions. There is a welcome note both of confidence and of authority about the present report which promises well for the future, and suggests that the Minister intends to use the Advisory Council as it could and should be used.

In the present survey the Advisory Council had some general problems much in mind. If advance is to be made with economy of effort, the growing points of knowledge require review from time to time to ensure that there is maximum contact and inter-

action between different fields of activity, and that the greatest range of professional skill is brought to bear on them. Paying particular attention to the frontiers of traditional disciplines, the Council notes the need to organize studies which cut across customary educational patterns or organizations, in order to attack a central or particularly resistant problem. The growing points in science are most frequently found in areas lying between the traditional disciplines and often involve the participation of several of them. The rigid separation of these disciplines can be awkward; but the solution of such problems is not necessarily to be found in the creation of new university departments and new disciplines. The research institute offers one solution, though the Advisory Council believes that universities should consider carefully the patterns which are emerging and encourage the effective interaction of the traditional skills.

Undoubtedly the expansion of universities and perhaps especially the establishment of new universities offer opportunities for flexibility and experiment, not so much in the new universities, which have first to prove themselves, as in the older universities. The colleges of technology, too, could play an important part, and the Council thinks that current schemes for training increasing numbers of scientists and technologists should not be planned without due regard to the changes which are taking place and to the fields where further effort is required. It had repeated evidence that it is very necessary for educational and professional structure to keep in step with the rapid evolution of science and technology.

The Council appreciates that its survey has important implications for economic and financial policy which strictly fall outside its purview. Its recommendations concern both subjects selected for their intrinsic scientific value or potentialities, and others chosen because of their importance for the British economy, or the conservation of its natural resources. No survey in the field of technology can ignore economic factors, and the review demonstrates once again how scientific and technical factors penetrate into every field of public policy and require evaluation along with other factors if sound decisions are to be made.

The review is based on a number of separate inquiries designed to present the widest body of evidence and of informed opinion about current scientific effort. The statistical basis is provided by a comprehensive survey carried out by the Council's Statistical Committee and already noted as appended to the report. Information and advice were also sought from the four Research Councils as well as the Royal Society, the principal professional institutions and Government departments mainly concerned with important aspects of applied science or technology. A list of such departments, public corporations, learned societies and institutions which is appended, however, shows some curious gaps among professional institutions, the names of the Royal Institute of Chemistry, the Royal College of Surgeons and the Institute of Physics, for example, being absent, while it is also surprising that on the industrial side such bodies as the Federation of British Industries, the Association of British Chemical Manufacturers and the Society of Chemical Industry do not appear to have been consulted.

The result, nevertheless, appears to be a more comprehensive picture than was given in the Council's report for 1956–57, and the total expenditure of £480 million represents an increase in constant-value terms of about 40 per cent, or about 2·3 per cent of gross national product against 1·7 per cent in 1955–56. The pattern of cost of research in each sector, and to a lesser extent of sources of finance, remains broadly similar; but private industry is now financing 29 per cent of the total compared with 23 per cent previously, and the Government two-thirds instead of three-quarters. Non-defence expenditure has risen from £122 million to £243 million, and this expansion appears to be continuing. Estimates for the four Research Councils aggregate 37 per cent higher for 1960–61 than for 1958–59, but the table appended to the report shows a reduction in grants to learned and other scientific societies from £207,000 to £166,000 in 1960–61. Grants for overseas research increased from £1,735,000 in 1958–59 to £2,265,000 in 1960–61, and it should be noted that of a total Government expenditure on civil research of £30,453,000 in 1958–59 and £38,868,000 in 1960–61, £16,980,000 and £22,703,000, respectively, went to the Agricultural Research Council, the Medical Research Council, the Department of Scientific and Industrial Research and the Nature Conservancy.

Emphasizing that technological progress depends ultimately on the scientific work in the universities and technological institutions, the Advisory Council is once again concerned that British resources of highly qualified scientific man-power should be used as efficiently as possible in such institutions, and it believes that, to ensure this, further expenditure is required on improving equipment and facilities and in providing additional technicians. This may well be the more important with the further expansion of the universities and the establishment of new universities and colleges of technology, but it is also possible that the re-examination of teaching methods such as Prof. A. H. Cottrell and others have suggested could make a by no means negligible contribution to the efficient use of trained man-power. These are, of course, primarily matters for the universities and colleges themselves and for the professional institutions, and it is clear enough from the present report alone, and from what Lord Hailsham himself has said in the House of Lords, that the Advisory Council has no intention of endangering the autonomy of the universities. The present system of block grants for teaching and research through the University Grants Committee and of complementary earmarked grants for scientific research through the Research Councils appears to offer the minimum difficulties in administration and maximum freedom for the

universities; and the arrangements described in the Council's previous report for the periodic review and transfer of financial responsibilities for established research projects from the Research Councils to the University Grants Committee should make the system more effective.

Before discussing the survey in detail, the Council compares the United Kingdom expenditure on research and development in 1958 of £478 million, or 2·35 per cent of the gross national product, with the £3,971 million, or 2·74 per cent of the gross national product, expended in the United States. Whereas, however, in the United Kingdom the public sector accounts for 34·7 per cent of the cost of the work done, industry 57·1 per cent and the universities 4·8 per cent, in the United States the corresponding figures are 15·4, 75·3, 7·5 per cent, respectively. On the other hand, in the United Kingdom the public sector provides 68·5 per cent of the finance, industry 28·5 per cent and the universities 0·3 per cent, the corresponding figures for the United States being 61·0, 36·4 and 1·8 per cent, respectively. While the United States is devoting a somewhat larger proportion of its resources to research and development, it is probable that in both countries about 1·25 per cent of the gross national product is devoted to civil research and development work, and in this connexion the Advisory Council stresses the importance of using any opportunity which reductions in defence research and development may afford to increase the civil research effort in industry and elsewhere. It concludes further that a comparable scientific effort, in relation to the gross national production, with that of competitors should be maintained in Britain.

In regard to pure science, the Advisory Council's survey of the balance of effort leads it to the view that in pure mathematics Britain is losing ground, and that here the universities should give more attention to the provision of facilities for co-operative work. Oceanography and taxonomy have been relatively neglected, and in the section of the report which discusses the position of astronomy and seismology in some detail, the Council comments on the way in which British optical astronomy has lost considerable ground, partly in consequence of a low output of suitably trained specialists. Further steps are needed to bring astronomy to the notice of young physicists as a possible career, and while contemporary British resources in theoretical astronomy are substantial enough for an effective and relatively inexpensive contribution to British achievement and prestige, the proper deployment of these resources, which are scattered over a number of universities, is hampered by the lack of essential computing facilities. The provision of such large and expensive facilities may involve questions of university independence, and these are matters in which the universities may well be expected to take the initiative in co-operation, as in fact the Universities of Manchester and Liverpool have already done.

The Advisory Council endorses the recommendation of the British National Committee for Astronomy that the first priority for British astronomical activity in the southern hemisphere should be an immediate development of the potential resources of the Radcliffe Observatory; but on radioastronomy it makes no comment on the Jodrell Bank position and is content to express the hope that the two techniques, which are not alternatives, but complementary in the exploration of space, will be developed concurrently. The British weakness in seismology is particularly stressed, and if Britain is to regain her position in seismological research and provide the minimum background for participation in any international scheme for the inspection and control of nuclear explosions, seismological centres must be developed at one or two universities. Specifically the Advisory Council recommends that the existing activity at the University of Cambridge be expanded to provide such a centre or unit, with appropriate equipment facilities for routine and specialized experimental and theoretical work and provision for university teaching, and that a similar centre be created in the University of Edinburgh.

These recommendations regarding astronomy and seismology arise out of the Council's special examination of these fields rather than out of the general survey. The latter, however, directed attention to some fields in medical science where further research effort is desirable, such as mental illness, dental disease and social and industrial aspects of medicine. Some of the less-popular technologies also offer fruitful opportunities, and particular reference is made to a serious deficiency over the whole field of civil engineering. Here the Council recognizes that educational developments offer a real opportunity for a serious examination of the possibility of greater co-operation in the use of facilities between the universities and colleges of technology and Government establishments, but it also points to a few major topics where further work is needed. The Council had much evidence that engineering prospects are intimately bound up with the economic production of new materials—conducting, semiconducting, insulating, magnetic and structural—and the improvement of existing ones, particularly materials capable of operating at much higher temperatures.

This is a field demanding much-improved collaboration between chemists, physicists, mathematicians and metallurgists both in universities and in industry, while research into energy sources and their utilization also involves difficult problems alike in co-operation and in assessing the balance of effort. The Council considers that research effort on the utilization of coal should be strengthened, particularly on the development of processes for the complete gasification of coal, and it has asked the Minister of Power and the University Grants Committee to consider ways of strengthening studies in coal technology at universities or colleges of technology. The need for further application in industry of refined techniques of calculation and automatic controls is also stressed, as are the needs for work on the measurement and suppression of noise, research into

the environmental conditions and other aspects of important livestock groups, the metabolic diseases of sheep and cattle, the storage of fruit, and research into industrial ceramics to provide management with control techniques of appropriate precision. Finally, it comments on the significant absence of basic research in the scientific assessment of such major problems as the conservation and long-term utilization of British water-supplies, the basis for policies of land utilization, and it urges that new measures may be required to deal with basic research relating to the conservation of our natural resources.

This is one of the points concerning which the Council recommends some change in the organization of research. While the survey indicates that the general pattern is in broad outline satisfactory, one important gap in responsibility is apparent. There is no clear general responsibility for the conservation of our natural resources, whether of minerals, water, land-use, biological resources or fisheries. The responsibilities of the Nature Conservancy, and of other Departments concerned, cover only limited aspects, and the Council believes that there may be justification for a Research Council with central responsibilities for ensuring that, over the whole, scientific knowledge and research are brought to bear on all these issues. The problem is being examined in detail by the Council's Biology and Allied Sciences Committee.

Another point relating to the organization of research arises out of the high cost of some research projects, and has already been noted in relation to both astronomy and seismology. The general point is frankly faced by the Council, and the report points out that the attempt to pursue certain types of scientific activity in many different universities can so disperse and dilute the British effort that in the end she achieves much less than could be expected from the total expenditure involved. This is quite apart from considerations of man-power, and even if the universities were fully supplied with technicians on the scale desirable to avoid waste of highly trained man-power to which the Advisory Council has previously directed attention, there is still the possibility that large installations of equipment, which must be serviced by many specialized technicians and which has a high obsolescence-rate, may distort the pattern of a university and lead to a situation in which the direction of its research may be determined not by the scientific stature of the men available but by equipment available.

The Advisory Council cites nuclear physics as an example of these dangers, and believes that less dispersal of the British effort in the early stages of its post-war development would have given a greater return for our expenditure in this field. The situation has since been recognized by the creation of the National Institute for Research in Nuclear Physics, and while the Council notes with satisfaction recent developments in the regionalization of electronic computers and proposals for joint operation of nuclear reactors, it suggests that extension of the idea of such national institutes may require some adjustments of our scientific organization. Optical and radio astronomy, as well as space research, are other fields in which it is necessary to decide on the level of expenditure of resources and man-power that Britain is prepared to operate, and how dispersal of effort and unnecessary duplication of costly research facilities are best avoided. As alternative to a central institute available to workers in universities and similar institutions, it is suggested that such activities should be confined to one or two universities, as in fact it proposes for seismology.

The Advisory Council does not attempt to decide between these two alternatives, but it sees no other possibility if Britain is to participate effectively in such fields of research. Clearly the problem is one that should be engaging the active attention of the University Grants Committee as well as of the Research Councils; and the Advisory Council itself could well examine further the forms of organization and control appropriate to national institutes of this kind. Moreover, it may be necessary to extend the principle to the international plane, for in certain fields—the report instances space research, nuclear physics and oceanography—the point is fast being reached, if indeed it has not already been passed, at which international co-operation provides the only appropriate way of continuing effective work in these fields without subordinating the entire scientific effort of the United Kingdom to a few major programmes.

Finally, the Advisory Council observes that the problem is equally serious in industry. Fragmentation of the British industrial research effort can be a source of weakness, and of waste both in terms of money and of scientific man-power. Some degree of duplication in research may be desirable, and is indeed inevitable in the British economy with its multiplicity of independent industrial units; but it is notable that industrial leaders have of late been stressing the importance of co-operation in the attack on major problems of interest and importance to several industries. The Advisory Council points out further that there are to-day problems and projects of such magnitude in some fields that even large firms operating individually may only multiply, to no real purpose, research development and design work aimed at the same technical objectives.

No specific proposals are made for collaborative arrangements. The Advisory Council is content to remark that such co-ordination of effort is not merely essential but also possible and entirely compatible with a free economy. Without it Britain cannot hope to compete successfully in some of the newer fields of endeavour with other countries which are larger and wealthier, or which operate a political system in which industrial effort is co-ordinated centrally.

It may suffice here to note that the Advisory Council fully recognizes the bearing of education on the scale and effectiveness of the research effort, and that it welcomes many of the recommendations of the Crowther Report as likely to lead to education better suited to meet the scientific and technological

needs of Britain in the years ahead. This cogently argued and well-balanced report can only add to the stature and influence of the Advisory Council. It demonstrates that, in the Advisory Council for Scientific Policy, Britain now has a body capable of taking a comprehensive, balanced and authoritative view of the country's scientific effort, and assessing wisely the contributory factors. Its review shows clearly that there are still too many fallow fields and that there are also some fields in which activities could well become too large and distort the general pattern. The Council is clearly aware of the conditions which favour and encourage creative activity, and is concerned to do all that is possible to foster such conditions and to avoid any measures of adjusting the scientific effort which are detrimental to creative work. None the less, it does not hesitate where necessary to challenge the universities as well as industry, professional institutions and Government departments to the fresh thinking that may be required to shape existing arrangements or even institutions to new needs, and it is to be hoped that this sensible and balanced report will be closely studied by scientists and technologists and administrators whether in industry, in Government departments and public corporations, in research institutes or in universities and colleges of technology.

HISTORY AND PHILOSOPHY OF SCIENCE

Critical Problems in the History of Science

Proceedings of the Institute for the History of Science at the University of Wisconsin, September 1–11, 1957. Edited by Marshall Clagett. Pp. xiv + 555. (Madison, Wisconsin: University of Wisconsin Press, 1959.) 5 dollars.

THE conference reported in this volume is symptomatic of the great and accelerating attention given in the United States to the history and philosophy of science. The work of the earliest pioneers of these themes in that country, George Sarton, Chauncey Leake and Henry Sigerest, is bearing fruit in the establishment of many academic posts to which, alas, though not unnaturally, distinguished English exponents are being attracted as they observe through a second generation the lack of such posts in their own land. Sixteen papers besides invited commentaries were contributed to the conference.

In the opening paper, Prof. Rupert Hall, discussing the respective shares in the Scientific Revolution of the scholar and the craftsman, points out that during the seventeenth century the "medieval association of scientific activity with the universities was weakened though not disrupted" not only by the importance in science of men who were not academically trained but also by the shift of scientific activity from universities to the scientific societies and to circles basking in exalted patronage. Further interesting contributions on this theme are by Profs. Robert Merton and Francis Johnson, Dr. A. C. Crombie and Father J. T. Clark.

In a stimulating contribution on the "Role of Art in the Scientific Renaissance", Prof. Giorgio de Santillana shows how art and science joined in the crucially important theory of perspective evolved by the architect Brunelleschi (1377–1446). He notes that Brunelleschi was accepted by his peers as an intellectual, and in this context he shows the importance of the literary skill of Leon Battista Alberti (d. 1472).

Prof. E. J. Dijksterhuis gives a brilliant survey of the precursors of Newtonian mechanics. It is impossible to epitomize his amazingly clear account of the development of European mechanics before Newton, but this paper well repays careful study.

"Contra-Copernicus: a Critical Re-estimation of the Mathematical Planetary Theory of Ptolemy, Copernicus and Kepler", is by Prof. Derek Price. It is written with this writer's usual clarity and beautiful figures, with some abatement of the credit usually awarded to Copernicus.

A number of papers consider the influence on science of social and political developments in Europe. Prof. C. C. Gillispie has a learned discussion of the *Encyclopédie* and Jacobin philosophy. He considers that a certain arrogance on the part of French scientists was responsible for the movement to promote an unlearned "natural history" and for the forcible closure of the Paris Academy of Sciences. Dr. Pearce Williams finds some explanation of what he, following Prof. Guerlac, calls the anti-Newtonianism of the leaders of the French Revolution in the movement that he terms "Enlightened Stoicism". Reform was sought through moral regeneration. By 1792, Condorcet presented his scheme for universal education throughout France, based on a simplified science.

Prof. Thomas S. Kuhn considers the influence on the formulation of the doctrine of conservation of energy exercised by the discoveries of conservation in other kindred fields. Prof. I. B. Cohen gives a no less convincing and fascinating exposition of the discovery of the conservation of the electric charge. Prof. Carl B. Boyer emphasizes the importance of nineteenth century observation of chemical weight.

Turning to biology, Prof. J. W. Wilson suggests "Biology attains Maturity in the 19th century". Prof. J. C. Greene epitomizes the views and influence of Auguste Comte and Herbert Spencer. Prof. R. H. Shryock expresses the hope that biology has not yet reached maturity. Prof. Conway Zirkle maintains that there is no evidence that either Darwin or Wallace was influenced by Victorian political or economic *laissez-faire* or belief in the benefits of competition.

Prof. C. S. Smith describes "The Development of Ideas on the Structure of Metals". His paper, although technical, is beautifully lucid. He discusses the influence on metallurgy of the revival of interest in atomic theory. Dr. Marie Boas gives an interesting account of "Structure of Matter and Chemical Theory in the 17th and 18th centuries".

Into this galaxy of fascinating information and reflexion are inserted valuable papers recording pioneer experience in teaching the history and philosophy of science. Prof. Dorothy Stimson records the consistent success of such studies with the students at Goucher College; Prof. Henry Guerlac relates that engineering students at Cornell have been equally enthusiastic; Prof. Bernard Cohen gives a cheering historical sketch of the teaching of the history of

science at Harvard over a period of sixty-eight years; Dr. Boas follows with an account of her happy experience in giving courses open to all upper-class university students in an Arts and Science School.

Prof. Guerlac gives an eloquent and convincing exposition of the function of the study of the history and philosophy of science in promoting true education.

It should be added that exceptionally full bibliographies are attached to all the papers. Space permits no adequate account of the important material packed into this volume. Both the conference and the publication were sponsored financially by the National Science Foundation of the United States and by the Research Committee of the University of Wisconsin. DOROTHEA WALEY SINGER

ELECTRICAL CHARACTERISTICS OF THE EARTH'S STRATA

Overvoltage Research and Geophysical Applications

Edited by James R. Wait. (International Series of Monographs on Earth Sciences, Vol. 4.) Pp. viii + 158. (London and New York: Pergamon Press, 1959.) 55*s*. net.

MEASUREMENTS of the electrical characteristics of the Earth's strata indicate the existence of several interrelated phenomena, which have been discussed from time to time in the literature. One of the effects is the potential which can be observed between two non-polarizable electrodes immersed in a porous medium, after the interruption of an applied step function current. This induced potential has a considerable bearing on the transient and frequency response of the medium. However, the phenomenon has, with a few exceptions, received scant attention.

The monograph edited by J. R. Wait consists of a collection of papers on the various aspects of induced potential. Various hypotheses for the occurrence of the normal effect observable in all naturally occurring porous media are fully discussed, and results of experimental work designed to test these hypotheses are given.

The emphasis of the majority of the papers is given to the geophysical application of the abnormal overvoltage effect observed in a porous medium containing electrically conducting particles, that is, metallic ores.

Theories of the transient and frequency response characteristics of such media are suggested, and the results of both laboratory and field investigations are given and discussed in relation to the suggested theoretical treatments. A short but useful paper on the field equipment required for prospecting for metallic ore bodies by the overvoltage method is included.

Some of the hypotheses advanced and indeed some of the practical results reported do not altogether agree with other published data on the subject. These differences are, however, mainly in degree rather than in fundamental concept. There appears to be, for example, some discrepancy between the discussion of the variation of measured conductivity of porous media with frequency, when this is compared with earlier reports. This discrepancy may be real and, in fact, represent a difference in the response obtained from porous media with and without conducting particles.

The authors have given factual reports of the results of a concerted attack on the problem of the overvoltage phenomenon and its practical application to geophysical prospecting. The individual papers are well presented and the various discussions are logical and thought-provoking. The collection is well worth study by all research geophysicists, and should be read by anyone concerned with the flow of electrical current through Earth strata. P. THREADGOLD

NATURAL PRODUCTS

Konstitution und Vorkommen der organischen Pflanzenstoffe (exclusive Alkaloide)

Von Dr. Walter Karrer. (Lehrbücher und Monographien aus dem Gebiete der exakten Wissenschaften. Chemische Reihe, Band 12.) Pp. 1207. (Basel und Stuttgart: Birkhäuser Verlag, 1958.) 136 Swiss francs; 136 D.M.

NATURALLY occurring organic compounds have fascinated chemists for very many years. Their interest began with substances possessing some easily recognizable property, such as colour, smell, bitterness, or toxicity, but to-day it ranges through the whole spectrum of natural products. In spite of this interest and the current rapid developments in an understanding of the biogenesis of such compounds, there has been no up-to-date dictionary of natural products. Although monographs are available for some limited groups such as carbohydrates, alkaloids, steroids and carotenoids, in the case of many groups, or even individual compounds, the collection of comprehensive information has entailed a long and tedious literature search. Dr. Walter Karrer has now eased this difficulty to a considerable extent. He has collected together details of organic compounds of known, or apparently known, structure found in plants, other than alkaloids. Even with these limitations about 2,700 natural products are described, ranging from hydrocarbons through depsides, carotenoids and terpenes to nitriles, pyrimidines and nucleotides.

The structural formula of each compound is given, as well as details of its distribution in the plant world. Key references to the elucidation of structure and synthesis are also listed. The information given about those groups of compounds with which I am familiar is accurate and comprehensive, the literature being covered to 1956, and the author is to be congratulated on the immense task which he has successfully undertaken.

For those concerned with structural elucidation of natural products, with their pharmacological activity, or with the biosynthesis of organic compounds, the appearance of this volume emphasizes the need for an even more complete dictionary of all natural products. Many compounds have been isolated which are inadequately described in the literature or the structure of which is still unknown. Often the same compound is described under different names. If some chemist would collect together the information about these compounds with the same thoroughness that Dr. Karrer has shown in the present volume, he would perform an invaluable service.

T. G. HALSALL

MOLECULES IN CRYSTALS*

By Dr. DOROTHY HODGKIN, F.R.S.

Chemical Crystallography Laboratory, Oxford

On this occasion, I wish to describe the structures, as we see them to-day, of a number of very remarkable crystals. These would certainly have interested the early Fellows of the Royal Society and particularly perhaps Hooke and Boyle, both of whom carried out experiments on growing crystals, observed the shapes of their faces and speculated on the arrangement of corpuscles within them. In his "Micrographia", in 1664, Hooke drew pictures of alum crystals side by side with sheets of globular bodies in hexagonal and cubic arrays (Fig. 1) and commented: "I think, had I time and opportunity, I could make probable, that all these regular Figures that are so conspicuously *various* and *curious* . . . arise onely from three or four several positions or postures of Globular particles, and those the most plain, obvious and necessary conjunctions of such figur'd particles that are possible . . . by these kinds of texture or position of globular bodies, may you find out all the variety of regular shapes into which the smooth surfaces of *Alum* are form'd . . . nor does it hold in superficies but in solidity also, for it's obvious that a fourth *Globule* laid upon the third in this texture, composes a regular Tetrahedron, which is a very usual Figure of the *Crystals* of *Alum*".

Boyle imagined the integral parts of a body might have a variety of shapes, not only globular. Among the Qualifications that conduce to Fixity, he imagined would be "the ineptitude of the component corpuscles for avolation by means of their branchedness, irregular figures, crookedness or other inconvenient shape, which intangles the particles among one another and makes them difficult to be extricated".

The structure of alum is considerably more complicated than Hooke's drawings propose. As we know it now, it is based on a series of studies made by Cork, Beevers and Lipson, using X-rays, and most recently, by Bacon and Gardner, using neutron diffraction. Each unit cell contains 4 aluminium ions, 4 potassium ions, 48 water molecules, 8 sulphate ions. Remarkably enough, the relative positions of the positive ions in the crystal conform with Hooke's suggestions. But the intermolecular attractive forces which hold the units together are clearly more complicated than simple close packing. Around each trivalent ion are 6 water molecules, in a regular octahedron, each exactly oriented with the hydrogen atoms directed symmetrically away from the metal ion: and the metal to oxygen distance here is relatively short—1·94 Å. Around the monovalent ions, the six water molecules have a more open, irregular arrangement with oxygen–potassium 2·97 Å.; and between the oxygen atoms of the water molecules and sulphate ions various short contacts can be traced, the shortest being those where one hydrogen atom lies in the direct line between the two oxygen atoms. The whole atomic arrangement is seen to result from a delicate balancing of a number of interlocking chemical and physical and geometrical requirements.

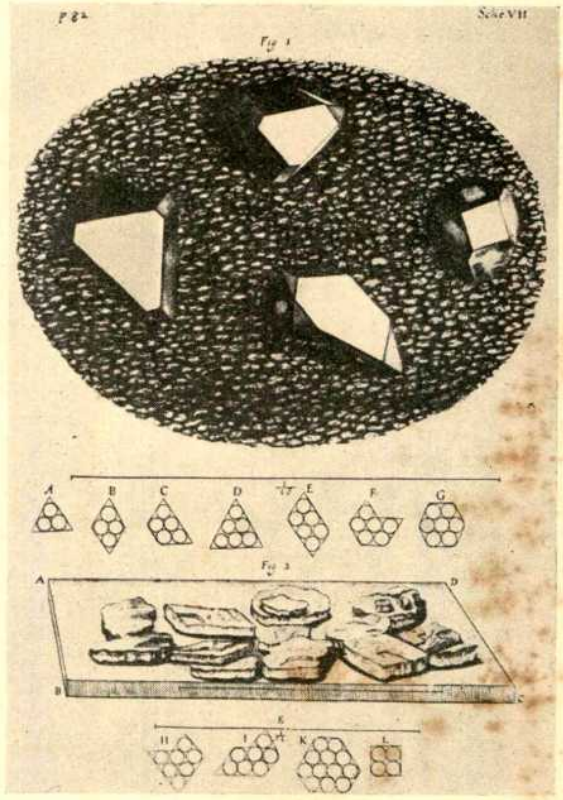

Fig. 1. Drawing from Hooke's "Micrographia" showing alum crystals and close-packed spheres. (*A*, *B*, *C*, *D*, Fig. 2 is an illustration to another section of the book)

The knowledge we have of the exact arrangement of the atoms in this and many other crystals has been obtained as a direct result of the discovery of X-ray diffraction of crystals by von Laue, Friedrich and Knipping, and its development as a tool for structure analysis by W. H. and W. L. Bragg nearly fifty years ago. It is particularly sad that Prof. von Laue died only some months ago—but also a particular pleasure to think that he must have known before his death of the latest and most spectacular results of his discovery—results with which Sir Lawrence Bragg has been almost as intimately associated as he was in the first solution of any crystal structure.

The impression that I wish to give is one almost of direct sight of the atoms in crystals, an impression which has followed particularly from the use of Fourier series in interpreting the diffraction effects. In 1915, W. H. Bragg pointed out that the periodic

* Substance of a Royal Society Tercentenary Lecture delivered on July 23.

variation of the medium in crystals could be analysed by Fourier's method into a series of harmonic terms, the existence of which was indicated by the series of spectra obtained by diffraction from a given set of crystal planes. The recombination of the observed harmonic terms in a Fourier synthesis is now usually carried out mathematically to provide a physical measurement of whatever periodic structure is responsible for the observed diffraction effect—the electron density, if X-rays are used, potential distribution in electron diffraction, nuclear scattering power in neutron diffraction. The formulæ involved may be given in the form

$$\rho_{xyz} = \frac{1}{V}\sum_{-\infty}^{\infty}\sum_{-\infty}^{\infty}\sum_{-\infty}^{\infty} |F_{hkl}| \cos(\theta - \alpha_{hkl}) \qquad (1)$$

$$\text{where } \theta = 2\pi\,(hx + ky + lz)$$

$$F^2_{hkl} = [\sum_n f_n \cos\theta_n]^2 + [\sum_n f_n \sin\theta_n]^2 \qquad (2)$$

$$\tan\alpha_{hkl} = \frac{\sum_n f_n \sin\theta_n}{\sum_n f_n \cos\theta_n} \qquad (3)$$

Here the first equation shows that ρ, the electron density in the case of X-ray scattering, can be found at a position xyz in the crystal cell by summing a series of which the coefficients of the terms $|F_{hkl}|$ are given by the measured intensities of the diffracted spectra. Both these intensities and the phase-angles α associated with them depend on the actual positions of the atoms in the crystal, as shown in the equations 2 and 3; while the intensities of the spectra may be directly measured on photographic films or by counters, the determination of the phase-angles presents more serious problems. Usually they are found through a series of approximations to the exact atomic distribution often involving trial structures and a variety of calculations, many of them also based on Fourier series; for example, F^2 series and series in which the phase-angles are calculated on some parts only of the structure, often with the coefficients modified by the subtraction of certain calculated atomic contributions.

The X-ray analysis of the alums happens to occupy a rather special place in the history of the crystallographic use of Fourier methods. In their investigation, it was first pointed out that by the study of an isomorphous series of crystals the phases as well as the amplitudes could be experimentally determined, and a direct picture of the atomic arrangement formed by Fourier synthesis without preliminary trial calculations. In the alums, the scattering power of the atoms can be changed by chemical substitution, for example, aluminium may be replaced by chromium, potassium by ammonium, rubidium, cæsium or thallium, sulphur by selenium; and a direct calculation of the one-dimensional electron density distribution between two planes in alum crystals was first made by Cork in 1927. The crystallographic situation here is very simple since the alum crystal structure is centro-symmetrical. But the formal equations are clearly soluble for the three-dimensional asymmetric case, given three or more isomorphous crystals, as has been effectively demonstrated in the solution of the most complicated crystals so far analysed.

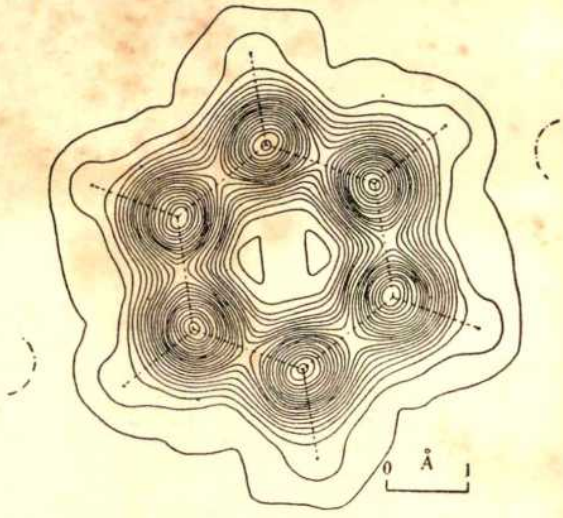

Fig. 2. Electron density in the plane of the benzene ring. Contour interval, 0·25e/Å.^{3} (from Cox, Cruikshank and Smith, *Proc. Roy. Soc.*, A, **247**, 1; 1958)

It has become common in the past few years with the advent of electronic computers to calculate the electron density in crystals in three dimensions. With simple crystals, these calculations can provide a highly exact picture both of the positions and of the modes of vibration of the atoms in the crystal. The analysis of benzene at $-3°$ by Cox, Cruikshank and Smith may be quoted as an example. The electron density in the plane of the benzene ring (Fig. 2) shows rather distorted peaks over the carbon atoms. If the density to be expected from spherical carbon atoms is subtracted from this pattern, we get difference peaks which show the positions of the hydrogen atoms and also indicate atomic movements—that the molecule, as a whole, is oscillating with a root mean square amplitude of approximately 7·9° about the six-fold axis. Such a large amplitude of oscillation is permitted by the non-directed character of the intermolecular forces and cog-wheel packing of the molecules in the crystal. In diketopiperazine crystals the situation is rather different. The molecules are hydrogen-bonded together in bands in the crystal; the atomic positions are very accurately defined to within 0·004 Å. through the X-ray analyses of Corey, Degeill and Marsh and electron diffraction studies by Vainstein. In the latest electron density maps calculated with data obtained with molybdenum $K\alpha$ X-radiation, the atomic maxima appear very sharp (Fig. 3). The contour interval is 8 times that on the benzene map, and the thermal parameters derived for each atom have been analysed by Dame Kathleen Lonsdale. It appears that in this crystal the chains of molecules linked by hydrogen bonds are behaving like bundles of sinuous and somewhat elastic ribbons. The easy movements are those by which the atoms move out of the plane of the ribbon, either by a translational or librational movement of the molecule as a whole. Translation of the molecule within the chain is slightly more difficult, and there seems very little oscillation about the normal to the ring system: by contrast with benzene, the root mean square amplitude of oscillation is here only 1·7°.

Once allowance has been made for thermal motion in interpreting electron-density maps, the deviations of the peaks from spherical symmetry seem extremely

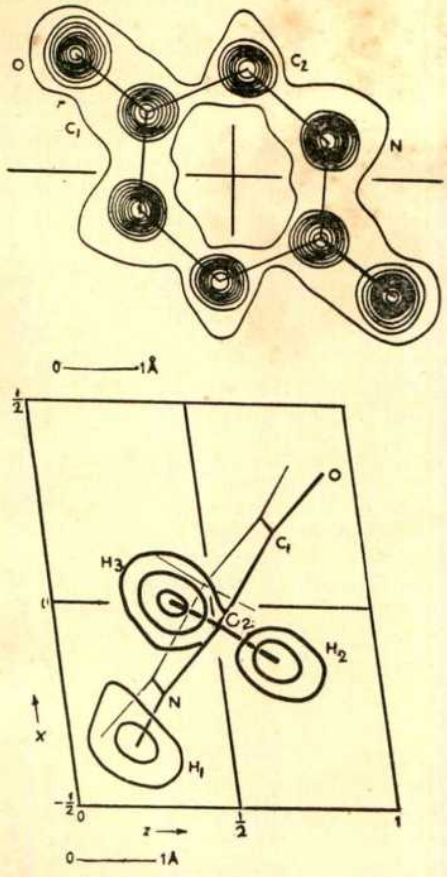

Fig. 3. Above, electron density in the plane of the ring in diketopiperazine. The contour interval is $2e/Å^3$ beginning with the 1-electron contour. Below, a composite drawing of the electron density over the hydrogen atoms. The contours are at intervals of $0{\cdot}25e/Å^3$ (from Degeill and Marsh, *Acta Cryst.*, **12**, 1007; 1959)

small: more accurate work at varying temperatures is required before these deviations can be taken very seriously as evidence of different varieties of chemical linking. Still, at the level of good approximate structure analysis, many interesting observations have been made. Some of these illustrate the ways in which molecules are restricted in their atomic arrangement, the flatness of aromatic or multiple-bonded systems, the staggered conformation of carbon chains, the tendency to form hydrogen bonds in certain preferred directions in relation with hydroxyl, amino and carbonyl groups. In oleic acid crystals, for example, Abrahamsson and Nahringbauer find long V-shaped molecules, with planar double bonds and staggered chains, associated through carboxyl groups. In *i*-erythritol—analysed by Powell and Bekoe—small compact molecules, with hydroxyl groups on each of four carbon atoms, are knit together by two systems of hydrogen bonds in a complex tetragonal arrangement. In hexagonal crystals, the molecules of the amino-acid, cystine, have a spiral arrangement about a six-fold screw axis —identity requires a lattice repeat interval of 56 Å. There are close hydrogen-bonded contacts between amino and carboxyl groups within one layer, the layers being linked by S–S bridges. Observations on crystals such as these provide a solid basis of facts in the light of which we can interpret data from more complex molecules.

The electron-density patterns obtained from these crystals are mostly derived by a series of approximations based on trial structures. These approximations are easier to interpret if one or two atoms in the molecule are relatively considerably heavier than the others. The heavy atom positions can then usually be found unambiguously and their scattering contributions used to initiate a series of approximate electron density calculations. The effects have been exploited in a large number of recent analyses aimed at the determination of the actual chemical structure of natural products, sterols, terpenes and alkaloids, a variety of molecules with fantastic names and fantastic condensed ring systems, calycanthine, limonin, *iso*clovene, mirœstrol—many others. Limonin, examined by J. M. Robertson and his students very recently, was effectively analysed twice over in the same crystal, since the derivative used, epilimonol iodoacetate, crystallizes with two non-crystallographically identical molecules per asymmetric unit. The character of the analysis may be illustrated by a half-way stage such as the third calculated three-dimensional electron density distribution (Fig. 4).

Here heavy peaks indicate atomic positions recognized earlier and used in calculating phase angles, small ones show newly appearing atomic sites—the relatively unknown are differently distributed in the two molecules. Both the detailed molecular structure revealed and the fitting of the molecules in the crystal make one astonished at the variety of complications present—differently sized and shaped ring systems and side-chains. An earlier example of a similar analysis—which grew out of Bernal's first attack on the sterol structures—is that of calciferol which, in the form of the iodonitrobenzoate, also has a very intricate crystal structure. Both these illustrate remarkably well the difficulties of crystal growing and melting which Boyle envisaged in relation to the "branchedness" of the building units.

Considered simply as an aid to X-ray analysis, heavy atoms seem to work best at a level at which

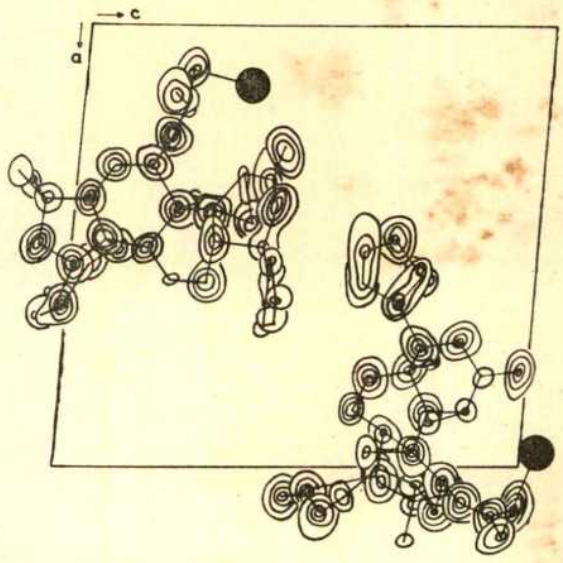

Fig. 4. Electron density contours taken from the third three-dimensional distribution calculated for epilimonol iodoacetate (after Arnott, Davie, Robertson, Sim and Watson, *Experientia*, **16**, 51; 1960)

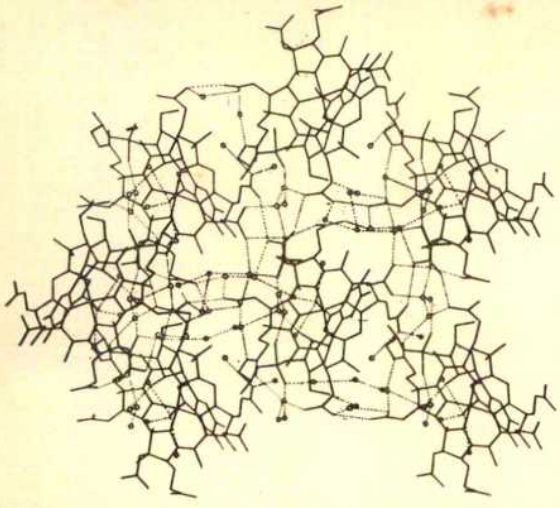

Fig. 5. Atomic positions in wet vitamin B_{12} crystals projected along *a*. The molecules in one layer are shown, together with a single molecule and the phosphate groups of molecules in the second layer. Small circles mark probable water molecule positions; dotted lines mark hydrogen bonds

their scattering power is roughly equal to that of all the other atoms present—for example, one bromine atom to about 24 carbon atoms, one iodine atom to 56 carbon atoms and so on—remembering that the scattering contribution is roughly proportional to the square of the atomic number. But much smaller relative differences can be exploited, as in the determination of the structure of vitamin B_{12}, where the heaviest atom, cobalt, contributes only one-tenth of the total scattering effect. Here the finding even of the exact molecular formula, $C_{63}H_{88}O_{14}N_{14}P\,Co$, depended on the gradual sorting of the atomic positions from various approximate electron density maps until it became clear which atoms belonged to the vitamin molecule itself, which to the surrounding water of crystallization. The knowledge from parallel chemical research that a benziminazole, sugar and phosphate group were parts of the molecule, greatly assisted the sorting process. But their relative positions in the molecule and the whole of the structure of the porphyrin-like nucleus followed from the X-ray analysis alone.

The vitamin B_{12} molecule proves to be quite compact, organized around the two planes of the inner porphyrin-like nucleus and the benziminazole group. Its geometrical form can be illustrated by a calculated projection of all of the atomic positions on the plane passing through the cobalt atom and four inner nitrogen atoms of the nucleus. From this projection it is clear that the benziminazole ring lies across the nucleus in a position mainly determined by packing considerations; it is also tilted about 10° from the direct normal to the projection plane and the nucleus is a little buckled where the two rings make contact. The different amide side-chains lead off from the nucleus in generally staggered arrangements; small deviations from these appear to be due to conflict with the requirements of intermolecular contacts, particularly through hydrogen bonds.

In outline the crystal structure is simple (Fig. 5). The roughly spherical molecules are arranged in approximately hexagonally close-packed layers, the two layers in each crystal unit being slid a little distance from the formal positions required by close-packing, with the spaces between the layers occupied by water molecules. But in detail, the atomic arrangement is very intricate, a consequence of the exact molecular geometry. In wet B_{12}, where the crystals are suspended in their mother liquor, the acetamide and propionamide groups all make direct intermolecular hydrogen-bonded contacts—the B_{12} molecules are in contact with one another on every side. Between them, the water molecules, approximately 22 per B_{12} molecule, make additional hydrogen bonds with the active groups, particularly with the amide and phosphate groups and with one another. Along particular lines in the crystal structure, water is continuous from one side of the crystal to another and is probably trickling through it during X-ray photography in narrow streams, one molecule deep. As Sir Francis Simon suspected when he examined a model of the structure, the atomic arrangement is not the same in every unit cell throughout the crystal and, as the crystals are picked out of their mother liquor, a somewhat irregular transformation occurs. A few water molecules leave every unit cell, the B_{12} molecules slightly change their relative positions, two amide groups swing round carbon–carbon bonds and check the flow of water and there results a new, more imperfect but still largely crystalline molecular arrangement. The electron density calculated throughout the water molecule region in the air-

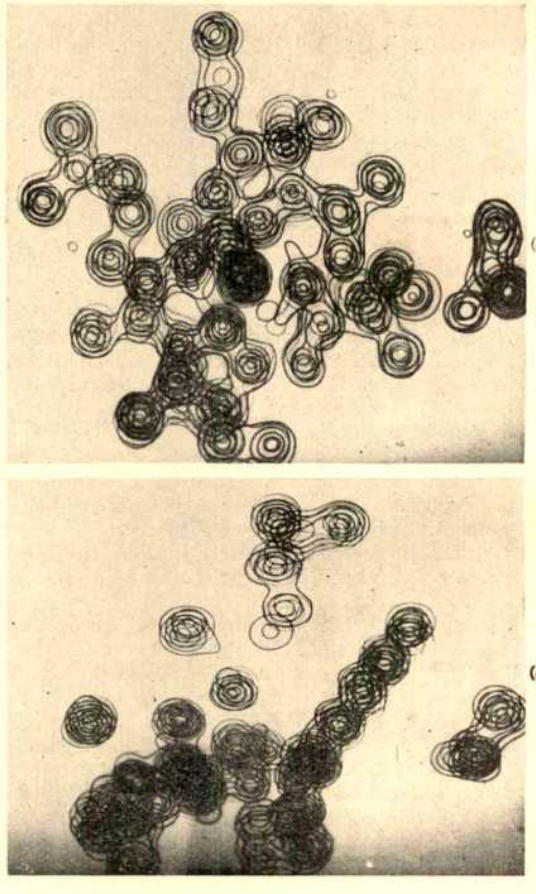

Fig. 6. Superimposed sheets showing the electron density calculated over the molecule in wet vitamin B_{12} crystals

a, The corrin nucleus and its surroundings; *b*, the benziminazole nucleus, seen edge on, and its surroundings

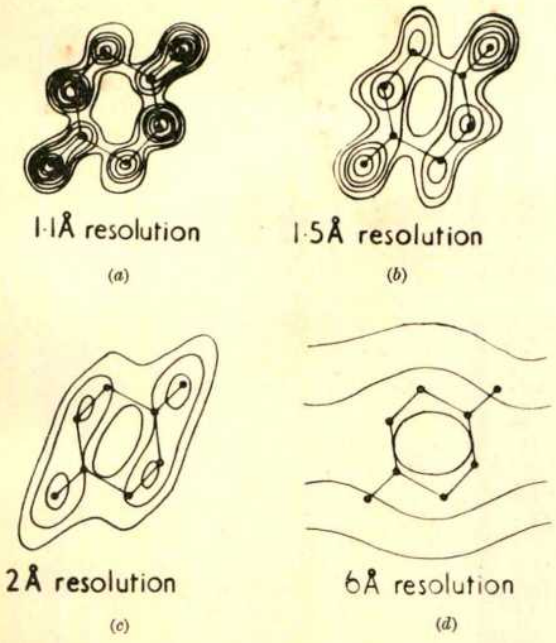

Fig. 7. Electron density in diketopiperazine calculated with reflexions limited at different spacings

dried crystals illustrates different degrees of order within the crystal pattern. Some water molecules, such as those hydrogen bonded to the phosphate oxygen atoms, are represented by high peaks ; others by low ridges which seem to represent no more than the regions in which moving water molecules have been stranded in different unit cells as the crystals dry.

The atomic positions in the electron density maps for B_{12}, though distinct, are not so well defined as those shown earlier—a consequence of the smaller number of observable X-ray reflexions (spacing limit, 1·1 Å.) which in turn may be due to irregularities in the crystal introduced by the moving water molecules (Fig. 6). As the spacing limit is still further reduced the electron density pattern becomes increasingly blurred—the appearance of diketopiperazine in Fig. 7, calculated with different numbers of X-ray reflexions, shows the effect very clearly. The first drawing corresponds with the limit of reflexions observed for B_{12}, the second and third to limits of 1·5 and 2·0 Å. respectively, the fourth to 6 Å. At the fourth all individual atomic definition has disappeared. But at the third, although the pattern is much blurred, it is easy to recognize the molecule provided one knows approximately what to look for.

Diketopiperazine as an example of atomic definition, and these particular cut-off limitations on our view of atomic positions, have been chosen to illustrate our evidence on the structure of the protein crystals, myoglobin and hæmoglobin. The molecules here are twelve to fifty times as large as B_{12} and composed of amino-acid residues linked in peptide chains. Many earlier lines of evidence indicated that within these molecules the peptide chain must be composed into a structure that had itself something of the character of a crystal lattice. Lindeström-Lang described in imagination a protein molecule as itself a small crystal, in equilibrium with the surrounding medium, with the peptide chains within it knitted together by forces well known from macrocrystals—van der Waals' forces and hydrogen bonds. It was Astbury who recognized that X-ray diffraction effects from many proteins suggested the chains were present in a specifically folded form, the α-fold for which Pauling, Branson and Corey proposed in 1951 a particular chain configuration, the α helix, following the long series of exact peptide structure X-ray analyses which began with diketopiperazine. To-day it is possible to see within myoglobin crystals the peptide chain and its configuration—indeed to visualize the positions of some 1,200 atoms as well as the 8 which occur in Fig. 7*c* ; while in hæmoglobin the peptide chain is as clearly outlined as the molecule as a whole is defined in Fig. 7*d*. This result has been reached through the very remarkable series of researches of Perutz, Kendrew, and their collaborators at Cambridge, who have exploited certain features of protein crystals to make a whole series of accurately isomorphous crystal structures.

Protein crystals were early observed occurring naturally in plant and animal tissues ; one of the first described in the literature was the hæmoglobin of the earthworm (Hünefeld 1840), which crystallizes spontaneously in blood left to dry on slides. Early too, in the middle of the nineteenth century, one of the important properties of these crystals was recognized by Schimper—that they contain large volumes of water of crystallization penetrable by ions and by quite large molecules such as organic dyes without apparent disturbance of the crystal lattice. This property can be used to introduce heavy atoms into the crystal in order to make isomorphous derivatives of the proteins for X-ray analysis. The first such heavy atom isomorphously introduced, mercury in sodium *p*-chloromercury benzoate, was chemically attached by the SH groups in hæmoglobin : others have been found to enter and lodge in definite positions in the crystal lattice by crystallizing the proteins in the presence of heavy atom-containing ions or molecules and by soaking them in appropriately buffered dilute solutions of the reagents. The molecules which have been shown to lodge in hæmoglobin and myoglobin are a varied collection—*p*-chloromercury benzene sulphonic acid, mercuridiammine and aurichloride derivatives, *p*-iodonitrosobenzene, which reacts with the iron atom in the hæm group of myoglobin, among others. Measurements of the intensities of some 10,000 X-ray reflexions from each of five different myoglobin derivatives and of several hundred reflexions for six different hæmoglobin crystals have been made; and with the F_{hkl} values derived for these the full potentialities of equations (1) (2) and (3) have been exploited to derive phase angles and calculate directly in three dimensions the electron density in crystals of sperm whale myoglobin and horse methæmoglobin.

So far, two three-dimensional electron density distributions have been calculated for the sperm-whale myoglobin crystals. The first of these, at 6 Å. resolution, shows the main back-bone structure of the molecule, a series of rod-shaped units linked together by strands of density and surrounding a rather heavy maximum, clearly the iron atom of the hæm group. At 2 Å. resolution the rods and strands break up and, to an astonishing degree, the calculated density pattern defines the whole of the atomic distribution in myoglobin (Fig. 8*a*). One can see,

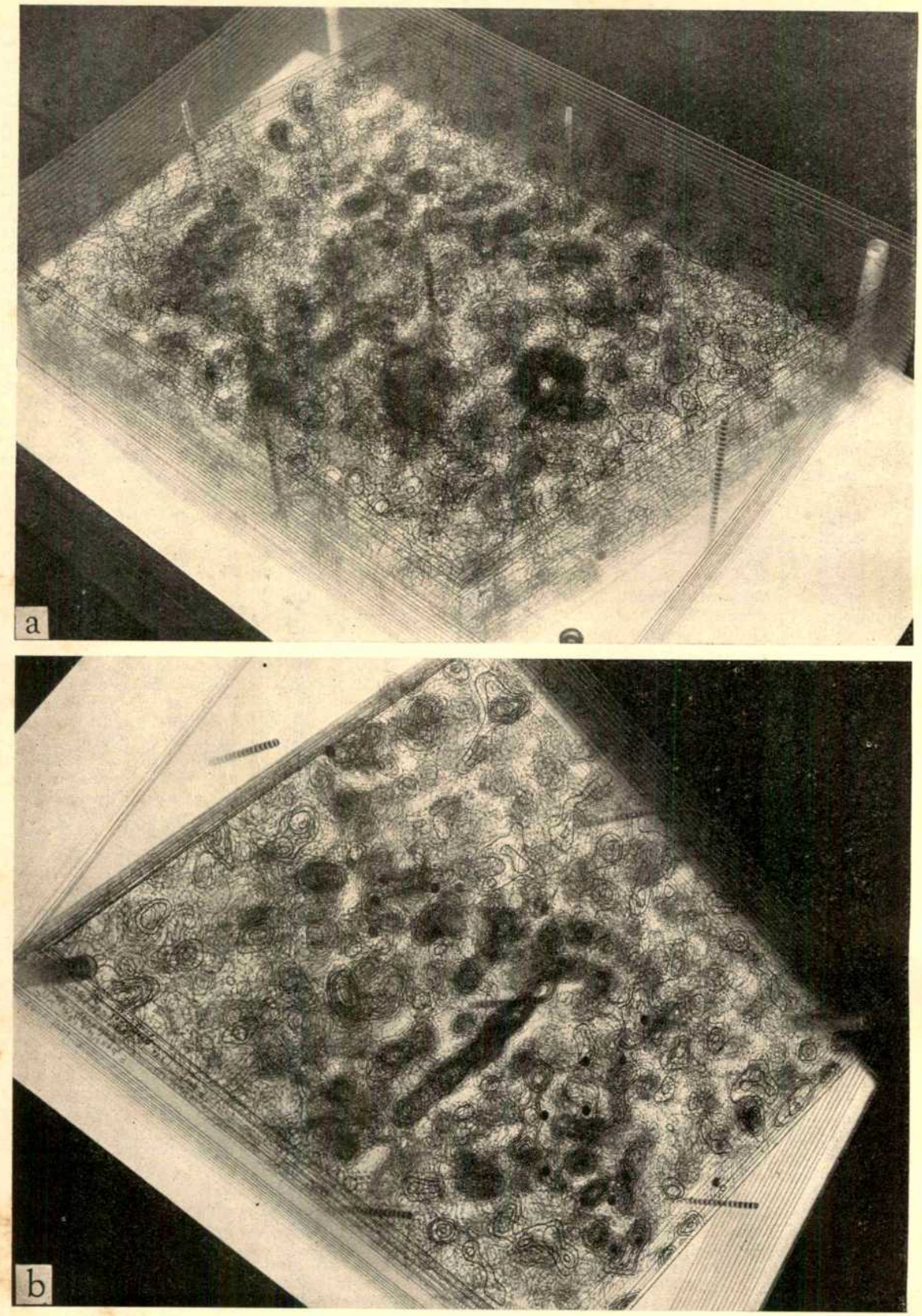

Fig. 8. Electron density calculated at 2 Å. resolution for myoglobin. The contour intervals are at 10·32e/Å.^{3} with the first contour dotted, the electron density contours being drawn on sheets stacked together. *a*, To the right, one is looking down an α-helix, clearly marked by the concentration of density around a hole of low density ; *b*, the model tilted to show the hæm group on edge

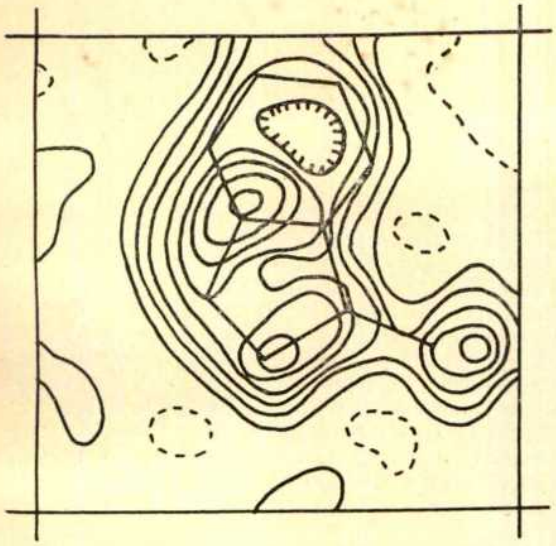

Fig. 9. Electron density contours defining a tryptophan residue in myoglobin. Contours at 1/5e/Å.[3]

within each rod-shaped unit, the peptide chain wound in precisely the configuration required in a right-handed α-helix; there are in all eight distinct stretches of α-helix of very varying numbers of residues—one 24, one 19, one 18, two 16, one 8, two 7 residues long. These lie generally at considerable angles to one another and are linked either directly or by small stretches of open chain—one, two, three or more residues long. Projecting from the main chains are the different amino-acid side-chains and these too are surprisingly recognizable—the very flat aromatic units, phenylalanine and tryptophan (Fig. 9), for example, are easily distinguished from branched valine or extended staggered leucine; a terminal atom turning back towards the peptide backbone or to an isolated peak—a water molecule—as if to form a hydrogen bond helps to identify hydroxyl groups as in serine or threonine. Nearly the whole of the sequence of 153 amino-acid residue in the molecule can be traced—and much of it has already been checked with parallel chemical studies of Edmondson. The hæm group itself is very clear (Fig. 8*b*). On one side of it there is a single peak, probably a water molecule, attached to the iron atom in the same way as the water molecules to the chromium or aluminium ion in the alums. On the other side is a histidine group, corresponding with the benziminazole group in vitamin B_{12}—and like it arranged with its plane at a general angle, about 10°, to the nearest Fe–N bond.

There are main chains—as suspected earlier—lying on either side of the hæm group and from these project other residues, mainly aromatic, tyrosine, phenylalanine, proline, and one other histidine residue. The molecules make contact with one another on every side in the crystal, directly and through water molecule bridges; they enclose channels through which smaller molecules and ions can move—carrying the heavy atoms with them. The spaces between and within them look ragged to one's eye. But clearly to approaching reactants they must offer specific attractions. So far as one can see, most of the heavy atom-containing molecules introduced are not chemically attached to particular residues but individually trapped in clefts of various shapes and sizes within and between the molecules.

While in each small region of the myoglobin crystal one can see operating the same stereochemical conditions that determine atomic arrangement in smaller crystals, it is much more difficult to recognize the principles that determine the pattern of chain fitting into the molecule as a whole. Yet principles there must be, complex as the pattern is. With small variations and at low resolution only, similar patterns have been observed both in seal myoglobin and horse methæmoglobin. The crystal structure of hæmoglobin is particularly interesting. Piecing together the low ridges of electron density observed in the three-dimensional electron density distribution, Perutz has found that each molecule is composed of four myoglobin-like molecules, packed together in an irregular tetrahedron. One might compare the packing here with Hooke's four globules were it not for the precise and intricate way in which chain locks into chain in the molecule as a whole. The iron atoms in the four hæm groups are found to be between 25 and 35 Å. apart. Already one can see detailed chemical implications of the structure. While their situation in clefts between chains provides a ready explanation for the slow reaction that has been observed of the iron atoms with bulky reactants, they seem to be rather far apart for any direct interaction. Possibly changes in the rate constants as oxygen is added arise from a general loosening of the molecule as reaction proceeds.

At this point it would be possible to discuss the building up of units of the size of hæmoglobin into still more complex molecules and crystals such as can be seen among the viruses. Poliomyelitis virus, for example, has been crystallized and gives very beautiful X-ray photographs. From these, Dr. Klug has deduced that the virus molecule is spherical and has an arrangement of sub-units over its surface which approximates to cubic symmetry. One of the formally possible arrangements seems very likely from the look of the electron microscope pictures. Others, still more complicated, have been found for other viruses.

In each of these enormous molecules there must be, at an atomic level, the same kind of intricate fitting together of individual atoms observed in simpler systems; and this leads us back to ask more intimate questions about the way in which the different molecules react with their surroundings. What, for example, is there in the chemistry of cobalt and iron that makes them specifically suitable for the biological reactions of vitamin B_{12} and hæm? In other fields of chemistry, new and most curious types of compound have been discovered, involving both cobalt and iron in hitherto unsuspected types of binding. The versatility of the chemical elements in their relations with one another is proving to be much greater than was supposed even a few years ago.

Looking back through history, one finds oneself impressed by the many characteristics of the molecular structures here described which were correctly inferred or imagined in the past, often from very indirect evidence. Yet these structures, as we have found them to be in detail, also contain new and surprising and undreamed-of features. The impact of the exact knowledge we now have is tremendous. It changes our whole outlook.

THE MANCHESTER LITERARY AND PHILOSOPHICAL SOCIETY

THE new buildings of the Manchester Literary and Philosophical Society in George Street, Manchester, were formally opened by Sir Cyril Hinshelwood, president of the Royal Society, on September 12 in the presence of the Lord Mayor of Manchester, who brought civic greetings and good wishes for the new venture. Prof. H. Lipson, president of the Society, who presided, referred to the past of the Society, which was indeed founded in 1781; but its premises with its irreplaceable library and records were destroyed by bombing in December 1940. He then commented that, although the Society now has its own building again, no society can live on its past. The membership of about 350 is little greater than in the time of Dalton and Joule, and Prof. Lipson hoped it would now increase and be maintained. The Society has a part to play in the life of Manchester that the University itself cannot hope to do.

Sir Cyril Hinshelwood, who had stoutly vindicated the function of the scientific society or academy in the conditions of to-day in his tercentenary address to the Royal Society, did not pursue that theme on this occasion; but, picking out the title of the Society and its original objective, "the advancement of literature and science", proceeded to discuss the arts and the sciences and, as he put it, to "roam destructively about, hacking at some of the useless conventional hedges which divide up liberal studies". It would appear, he began, that the division between the much-discussed 'Two Cultures' is not recognized in the Society, and the refusal to do so should be applauded and upheld: the dichotomy in question is largely illusory, but the illusion, in so far as it is believed or acted on, can do great mischief. So too can the false dichotomy between pure and applied science, and Sir Cyril suggested that it would be more sensible if people who took an intelligent interest in any of these things considered rather what they have in common than matters of difference. Inquiring further, Sir Cyril suggested that the philosopher, in the widest possible sense of the word, seeks some coherent vision of the world, something deemed worth while in its own right and worth the cultivation of skill and the exercise of effort to obtain. This, with the satisfaction of an urge to create, covers a large part of the liberal or philosophical or educated approach to existence, and the manifold ways in which it can find expression are only variations on the fundamental themes. The real antithesis to the liberal attitude lies in such things as the pursuit of power for its own sake, the accumulation of wealth except as a means to an end, or the basing of moral judgments on self-righteousness and prejudice.

Rejecting the view that the sciences deal with things and the arts with people, Sir Cyril insisted that both science and art are concerned with life, with living; the barriers between them are artificial, and in each alike there is a place for observation and experiment, for imagination and creative powers. Scientific imagination does not differ from any other kind and is called into play in science at least as often as elsewhere. Nor is the æsthetic element without an important role in science, though less commonly recognized, and to try to draw a distinction between the natural sciences and some of the arts in terms of objectivity can be equally misleading. Science is more than the simple enumeration of the facts of Nature: it is the ordering of these facts into patterns which are felt to be significant and satisfying, which can be interpreted and explained, and both involve subjective judgments. The acceptance or non-acceptance of a physical principle as a fundamental law of Nature must in the end rest largely on an æsthetic judgment.

Even in abstract art, Sir Cyril thought the analogy and affinity with pure mathematics are suggestive, nor did he think curiosity and the excitement of discovery operate differently or to different degrees in the arts and in the sciences. It is the weakest kind of sentimentality to make enjoyment of poetic images dependent on some desperate determination to accept them literally or to shun all other knowledge. Passing over the problems raised by history, whether it is a science or simply the register of the crimes, follies and misfortunes of mankind and its strivings and virtues, Sir Cyril commented that history does not teach us much about the handling of men. The sympathy and imagination needed to understand motives and feelings, the wisdom and experience to judge effect are generated not by the study of history but by the processes of real life. The real value of history, like that of science, is the ordering of complex arrays of facts into patterns to give a coherent though never wholly objective view of the world, and in both, as in art, the exercise of a strenuous and disciplined technique is essential.

Before considering technology, Sir Cyril made the comment in passing that there is no greater mistake, in science or in the fine arts, than to under-value manual craftsmanship, and in some respects the educational system of Britain seems designed to divert some with potentially first-rate manual skill into being second- or third-rate mental workers. At every stage of their development, fundamental science and technology have been interdependent. To-day no technological institute can dispense with the best theoretical equipment; but no laboratory devoted to pure science can hope to advance far without the finest technological assistance, and governments, industries and universities have still to find the best solution of the problems of organization which this situation presents. Moreover, many of the fundamental laws of physics confront us with metaphysical problems such as the nature of space and time, of causality and determinism, about which it is easy for one untrained in philosophical thought to make very unwise statements. Conversely, the philosopher who deals with these matters is in grave danger of spinning words in a vacuum, if not of perpetrating blunders, if he does so without know-

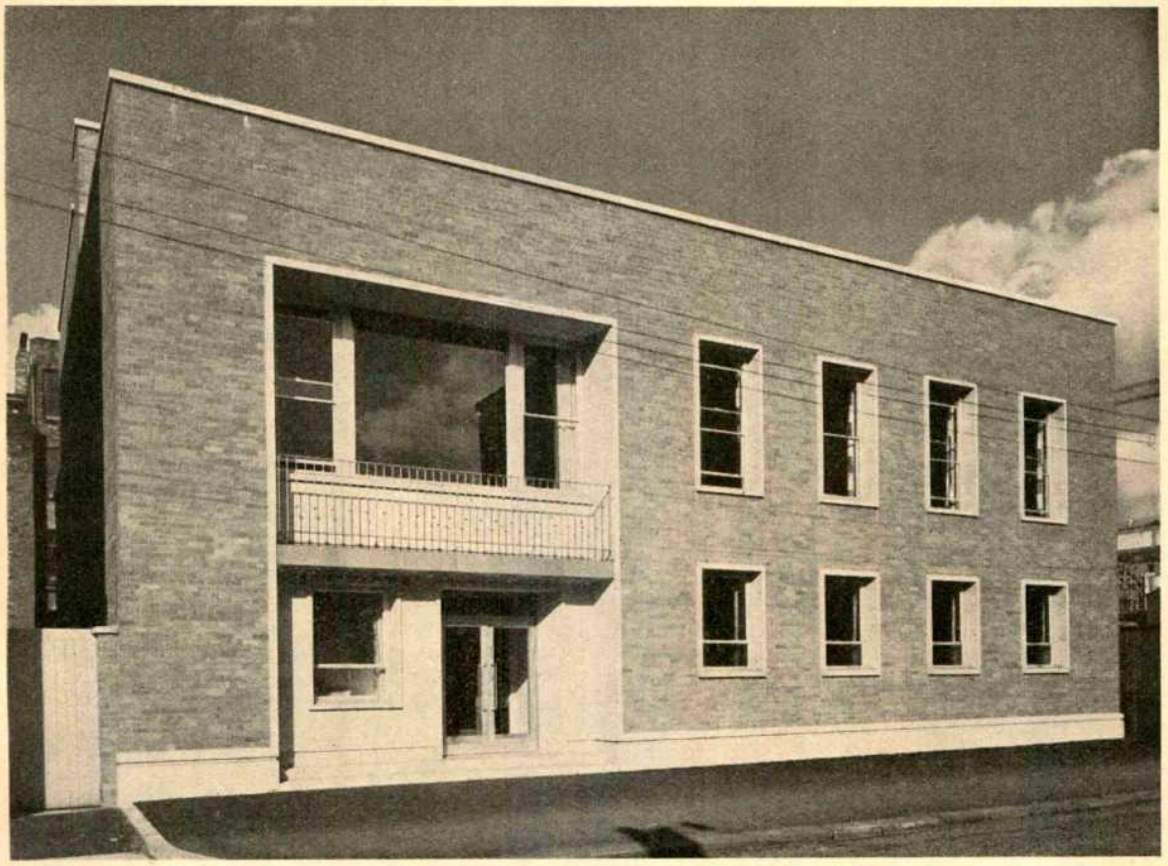

Fig. 1. New meeting house of the Manchester Literary and Philosophical Society

ledge of what physics has revealed. Biology, too, needs an occasional injection of philosophy and in the last resort physicists, philosophers, biologists, psychologists and even moralists ignore one another at their cost when confronted with some of the deepest problems of existence.

Finally, concluded Sir Cyril, the liberal arts and sciences have in common that they seek a coherent vision of the world, and that they all demand a highly disciplined technique. They are not inherently superior or inferior to one another, and the actual content of a particular study has little influence on the development of personality. Only real experience of the world exerts such influence, and it is the liberal approach rather than the choice itself that matters. Sir Cyril qualified this declaration of independence—to follow one's own bent and to respect others who follow theirs—by urging that arts and sciences should be cultivated side by side. They are allies, not rivals or antagonists; and he rejected the idea that the pressure of modern life and the demands of specialization make it impossible for the scientist to know something of literature and the arts man to know something of science. What matters in the end is the atmosphere, the attitude and the approach. The right ethos is likely to be found, he said, in the Manchester Literary and Philosophical Society, and he hoped it would be maintained and spread far and wide.

After a vote of thanks to Sir Cyril moved by Lord Simon of Wythenshawe, and conferment of honorary membership on Sir Cyril, the building was opened for inspection, and members of the Society may justly feel that the dignity and spaciousness which the architects, Messrs. Francis Jones and Sons of Manchester, have brought to their new home admirably fit it for the function which Sir Cyril commended. Besides the main lecture theatre on the ground floor, seating about 200, in which the opening meeting was held, with comfortable seating, good acoustics, and all the devices needed by a contemporary lecturer, it has on the first floor a smaller lecture theatre for more informal meetings of about 70, which can be arranged for social meetings also, and the Dalton Room, opening off which is the members' common room. The Dalton Room, which also serves as the council room, houses a small reference library and a collection of relics, mementoes and books relating to the history of the Society and its members, while the periodicals and other publications received from all over the world will be available in the common room, where light refreshments will be served. Although the Dalton Room holds pride of place, the whole building is light and appropriate to its contemporary purposes, and the equipment and furnishings are in keeping. Great credit is reflected on all responsible for the detailed planning and its execution.

OBITUARIES

Prof. F. J. M. Stratton, O.B.E., F.R.S.

A GREAT many friends all over the world will have learned with regret of the death on September 2 of F. J. M. Stratton; 'Professor' to some, 'Colonel' to others, 'Chubby' to many.

Frederick John Marrian Stratton was born in Birmingham on October 16, 1881. He was educated at King Edward's Grammar School, at Mason University College (afterwards University of Birmingham) and at Gonville and Caius College, Cambridge. He was third Wrangler in 1904, Isaac Newton Student in 1905, and Smith's Prizeman in 1906. In the years before 1914 he was a mathematics lecturer at Caius College and also assistant director of the Solar Physics Observatory, Cambridge, under H. F. Newall. His early papers covered a wide range of astronomy, including celestial mechanics, but the appearance of Nova Geminorum (1912) focused his attention on what proved to be a problem of life-long interest. In 1914 he had gone to the Crimea with Newall, intending to observe the total solar eclipse of August 21, but on the outbreak of war he hurried back to England and joined the Army immediately. He served with great distinction in France and was awarded the D.S.O. and the Légion d'Honneur.

The First World War was the first of the great upheavals of this century and the one for which the world was least prepared. At its end, Stratton returned to Caius College, as senior tutor, to face what was a difficult time of readjustment for the University at Cambridge, as much as for Britain as a whole. If one may judge by the remarks of his pupils it was a job for which his personality and experience admirably suited him, and which he carried out with much success. During this period he continued to give lectures on astronomy, among them one of the first general courses on astrophysics to be given in Britain. Somehow he also found time to go to Sumatra for the 1926 total solar eclipse, where with C. R. Davidson he made successful observations of the chromospheric spectrum.

On Newall's retirement in 1928, Stratton was appointed professor of astrophysics and director of the Solar Physics Observatory, relinquishing his tutorship at Caius. He held this post until 1947, although his tenure was interrupted, first by a serious illness in 1931 and later much more extensively by the Second World War. This period of his life was notable for the encouragement and help he gave to a whole generation of younger astronomers, many of whom still remember him with gratitude. He organized three more eclipse expeditions, to Siam, Canada and Japan, but was dogged by bad luck with the weather. Only in Japan, in 1936, were results of any scientific value possible. Even then the success was only partial, the Sun being covered by a cloud almost at the instant of second contact. However, members of his team made good measurements of wave-lengths in the spectrum from very near the Sun's limb, and obtained chromospheric spectrograms, study of which by Thackeray and by Woolley stimulated a good deal of later work.

In 1934, Nova Herculis appeared and, despite the inadequate equipment of the Solar Physics Observatory at Cambridge, Stratton and his staff during the next few months obtained a remarkable record of the spectrum changes of what turned out to be an extremely interesting star. Work on this spectrum absorbed much of his energies for several years, culminating in the production, with W. H. Manning, of the "Atlas of the Spectrum of Nova Herculis", using material made available from all over the world. This is still one of the most complete records we have of a nova outburst.

In 1939, at the outbreak of war, Stratton was bitterly disappointed at the refusal of the British Army to allow him to undertake active service again (at the age of fifty-seven), but nothing would stand in the way of his giving service of some kind. So the war years found him travelling extensively, in Canada, Australia, India and elsewhere, on duties for the Royal Corps of Signals. At the conclusion of the War, he had only two more years as professor of astrophysics, and in the conditions then prevailing in England, he realized he could do little to get back into active astronomy. He did, however, complete an interesting history of the Cambridge Observatories up to 1947. After his retirement he was deputy scientific adviser to the Army Council for two years and continued to serve on innumerable committees.

To celebrate his seventieth birthday, some of his pupils undertook, with Dr. A. Beer as editor, to produce what was to have been a *Festschrift*, but which expanded, as more and more of his friends came to hear of it, into two thick volumes, "Vistas in Astronomy". Indeed, the publication quite outgrew its original purpose, no doubt causing Stratton some amusement as well as gratification, and a third volume appeared, while yet others are still in preparation.

Stratton's official posts formed only a part of his activities. During 1925–35 he was general secretary of the International Astronomical Union, and did much to foster what was one of the earliest and most successful of the international scientific unions. He was also general secretary of the International Council of Scientific Unions from 1937 until 1952, and general secretary of the British Association, 1930–35. He was president of the Royal Astronomical Society, 1933–35, and its foreign secretary during 1945–55. He was honorary secretary of the Society for Visiting Scientists during 1948–55. He was president of Caius College, 1946–48, and at the time of his death was its senior Fellow. He served as president of the Society for Psychical Research, 1953–55. He was a life-long supporter of the Unitarian Church and was ever active on behalf of ex-servicemen's societies and causes. In the early 1930's he gave much help to refugee scientists from Central Europe. He was elected to the Royal Society in 1947.

Until his last years, Stratton lived life at the double. He thought fast, talked fast, decided fast, and in his younger days moved fast. Despite great sociableness and much hospitality, he was not an easy man to get to know really well, in part because he tended to keep his life in watertight compartments. He made great contributions to science and learning, chiefly by help and encouragement to younger men,

and not merely in Great Britain alone. A bachelor, he was completely devoted to his College, his pupils, to astronomy and especially to the International Astronomical Union, to his comrades of the First World War, and to his duty wherever he thought it to lie. Personal convenience, comfort or profit came very low indeed on his scale of priorities. He was one of the most generous men I have ever met, and one of the most modest. Astronomer, soldier, don, Unitarian, internationalist, he has left the world greatly in his debt.

R. O. REDMAN

AMONG young intellectuals in the universities, in the years before the First World War, it was commonly regarded as a sign of feebleness of intellect to believe that war was conceivably possible; and indeed as a mark of moral obliquity to take any personal steps to meet such an emergency. Fortunately a substantial minority, in reality no less intelligent, paid rather little attention to the intellectual and moral stigma; and the following short story of a small group of them at Cambridge describes one of the earliest contributions of young scientific men to national preparedness for war.

In 1908, under the Haldane Scheme for the Territorial Army, the Officers Training Corps of the Universities took the place of the earlier Volunteers. In Cambridge, in addition to the previous battalion of infantry, units were established of cavalry, artillery, engineers and medicals. Two years later, under the imaginative leadership of F. J. M. Stratton, a Signal Company was started and before long a wireless telegraph section was formed as part of it. Encouraged by Bertram Hopkinson, professor of engineering, who lent a room in his laboratory, the wireless section began work on the design of sets for field work and it drew in a remarkable group (as it proved) of young scientists for the task. It was not possible in those days to go and buy components from dealers, and radio valves did not exist. Everything had to be built up in workshop, laboratory, or tent, by members of the section itself. Since sets had to be portable, a generator was designed to be fitted to a bicycle, and during 'operations' a member of the section pedalled steadily, if wearily, to provide power for transmission. When communication failed, for example, between Farnborough Common and Eelmore Hill, it was re-established by flag and/or bicycle.

A photograph exists showing the ten members of the section in 1912, together with Captain Stratton commanding the Signal Company and a portable radio set complete with antenna. In it, among others, are Lance Corporal Henry Thirkill, Lance Corporal T. L. Eckersley, Private Harold Spencer Jones and Second Lieutenant A. V. Hill. Those were early days. By 1914 the wireless section had expanded considerably, and since no reserve of regular W/T officers existed when the War broke out, it was natural that members of the section should be drawn into field wireless. In fact, the section provided senior wireless officers for four armies. After the War, the Signal Company was more generously treated by the War Office, and a special research group was formed inside the wireless section.

Prof. (alias Lieut.-Colonel) Stratton recalled that, among the members of his Signal Company, the following could be counted: several who went into industry, one of whom was scientific adviser to Marconi's for twenty-seven years; four vice-chancellors and five masters of Cambridge colleges; nine professors; nine Fellows of the Royal Society and three Nobel Laureates; one director of scientific research, Admiralty; one chief engineer of posts and telegraphs, India; one secretary of the World Meteorological Organization; three successive secretaries-general of the International Council of Scientific Unions; one Astronomer Royal; two major-generals; [one D.S.O.]; one bishop; one Colonial chief justice; one M.P.; and one Olympic gold medallist. This list, as its author admitted, was rather a fraud, since on the average each person in it occurred twice. Nevertheless, it is rather impressive, particularly when one remembers that two-thirds of these people served in the Signal Company during its initial years 1910–14.

A. V. HILL

Dr. J. Brooks, O.B.E.

DR. JACK BROOKS, principal scientific officer at the Low Temperature Research Station, who died in Cambridge on October 2, was in charge of the work on eggs and poultry.

Brooks joined the scientific staff of the Low Temperature Research Station in 1928 from the Muspratt Laboratory of Physical and Electro-Chemistry of the University of Liverpool, at the invitation of the late Sir William Hardy. From the outset of his career he was an individual worker, belonging to the less-common class of investigator who prefers to do most things for himself in the laboratory. Before the War Brooks made a name for himself in fundamental research, especially in the field of hæmatin pigments. Quite early in his career he was publishing work in the *Proceedings of the Royal Society* and the *Biochemical Journal*, and up to the outbreak of war he continued to produce a steady series of papers in his particular field of physical chemistry applied to biological systems. He then showed himself equally capable at quite the highest level in applying theoretical results to immediate practical objectives, namely, the dehydration of egg and the storage of dried material.

Brooks held an established position as the leading Government consultant in Great Britain on all matters concerned with the handling and storing of eggs. During the period 1943–47 he was lent to the then Ministry of Food for various periods, in the course of which he visited the Argentine, United States, Canada and Australia in connexion with the Ministry's programme for the manufacture of dried egg and, afterwards, for full-scale trials of sugar-dried egg production. Later he again visited Australia as a member of the British Food Mission. After the War the emphasis of Brooks's work turned from dried to shell eggs, and again his knowledge, skill and personality were called on by the Ministry of Food to help in the solution of problems in countries exporting eggs to Britain. In 1948 and again in 1950, he visited Poland in response to a request from the Polish Government for help in finding a solution to difficulties which had arisen in the preparation of frozen pasteurized egg in fulfilment of orders placed by the Ministry of Food. Brooks was the only person in Britain possessing the specialized knowledge for this task, and he was able to discover the cause of the trouble and suggest a solution completely satisfactory both to the Polish Government and the Ministry.

Although such calls for Brooks's services seriously interrupted his supervision of laboratory investigations, he continued to exercise a firm control over

these and to initiate and maintain lines of research which have been successful in several directions. Some of these lines, such as the storage of oiled eggs, had immediate industrial application. Others were aimed at discovering the mechanism of deteriorative changes which occur during prolonged storage such as, for example, the thinning of the white, the weakening of the yolk membrane, and the production of undesirable changes in flavour due to enzymic oxidation. These were all problems needing deep exploration and a capacity for skilful research of the most fundamental nature. But for his deflexion from 1940 onwards to the more applied aspects of his work, Brooks would almost certainly have established for himself as high a reputation in academic circles as he enjoyed in responsible quarters for his technical skill and knowledge of matters pertaining to eggs.

E. C. Bate-Smith

NEWS and VIEWS

Air Ministry Appointments : Mr. Hayne Constant, C.B., C.B.E., F.R.S.

Mr. Hayne Constant has been appointed Scientific Adviser, Air Ministry. As a Fellow of the Royal Society and a member of the Aeronautical Research Council, and as director of the National Gas Turbine Establishment, Pyestock, he has for many years been closely connected with forward thinking in the aeronautical field. Born in 1904 at Gravesend, Kent, he went up to Queens' College, Cambridge, as a scholar in 1924 and graduated with first-class honours in the Mechanical Science Tripos in 1927. After a year's postgraduate research he entered the Royal Aircraft Establishment, and, after work on aircraft vibration and the performance of engines on weak mixtures, he pioneered work on the axial jet engine. His career has been mainly devoted to the advancement of the gas turbine as a prime mover, particularly for aircraft, in which sphere there has been such enormous advance in the past twenty years. In 1941, Hayne Constant was head of the Engine Department of the Royal Aircraft Establishment. In 1944, he linked forces with the Power Jets Whittle team as Power Jets, Research and Development, Ltd., and when that body became the National Gas Turbine Establishment he was deputy director. In 1948, he was elected a Fellow of the Royal Society and in the same year he succeeded Dr. (now Sir Harold) Roxbee Cox as director. In this capacity he was responsible not only for research but also for the centralization of the National Gas Turbine Establishment, bringing the Whetstone (Leicester) Whittle group to Pyestock, and the development of Pyestock into the biggest centre in Britain for gas turbine and ramjet test plant, including the Engine Test Facility. He received the Busk Memorial Prize of the Royal Aeronautical Society in 1932, and the Clayton Memorial Prize of the Institution of Mechanical Engineers in 1947. He was, from its inception in the war years, a member of the Gas Turbine Collaboration Committee with senior representatives of the British aero-engine industry. His views of, and predictions for, the gas turbine are published in his book "Gas Turbines and Their Problems", and in lectures and papers in many scientific and technical journals.

Mr. R. H. Weir, C.B.

Mr. Robert Hendry Weir has been appointed director of the National Gas Turbine Establishment in succession to Mr. H. Constant. Mr. Weir, who has been principal director and director general of engine research and development since January 1, 1954, was born in 1912 and educated at Allan Glens School, Glasgow, and the University of Glasgow, where he graduated B.Sc. with first-class honours in mechanical engineering in 1933. After an apprenticeship with Wm. Denny and Bros. Ltd., Dumbarton, he joined the Royal Aircraft Establishment in November 1933, where he was a member of the Engine Department until January 1939. He was then transferred to a post at headquarters in London, where he was engaged on aero-engine performance and work on pressurized cabins until December 1940. His next posting was to the Aircraft and Armament Experimental Establishment, Boscombe Down, where he spent a period of eighteen months on aero-engine liaison duties, and then transferred back to Engine Research and Development Headquarters in July 1942, for special duties on gas turbines. Mr. Weir was appointed director of industrial gas turbines in February 1950, and director of engine research and development in August 1952. He was made principal director of engine research and development in January 1954, which post was re-named director general of engine research and development in January 1959.

Ministry of Health : Sir John Charles, K.C.B.

Sir John Charles, chief medical officer of the Ministry of Health, Ministry of Education and Home Office, is retiring on November 30. He is a graduate of the University of Durham, and achieved a high reputation as medical officer of health, Newcastle on Tyne. In addition to competent administration, he made important epidemiological, nutritional and public health inquiries. During the Second World War he was appointed a deputy chief medical officer of the Ministry of Health and in 1950 became chief medical officer. In Sir John's ten years of office he has given much attention to the development and consolidation of the National Health Service. He has seen a further notable decline in tuberculosis and diphtheria, and has encouraged effective vaccination against poliomyelitis. Among many other subjects which have engaged his attention are the mental health services under the new Act, the dental services, care of the aged and the progress of maternity and child welfare work. Sir John has visited various parts of the world in the interests of international health, being also chairman of the Executive Board of World Health Organization and president of the twelfth World Health Assembly. He gave the Bradshaw Lecture in 1948 and the Harveian Oration in 1955 to the Royal College of Physicians. He can look back with satisfaction on his tenure of office as medical adviser to three departments of State ; and in his retirement

may find time for further studies in medical history, which is one of his interests.

Dr. G. E. Godber, C.B.

Dr. George Edward Godber has been recently appointed to succeed Sir John Charles, with effect from December 1. Dr. Godber was educated at Bedford School and New College, Oxford, where he read physiology, and at the London Hospital. After qualifying, he served for twelve months as house physician in the professorial unit under Sir Arthur Ellis. Subsequent to gaining some experience of general practice and of local government service in Surrey, he joined the staff of the Ministry of Health in 1939 at the age of thirty. His first assignments there were concerned with the reception of evacuees in the reception areas and with the other early wartime responsibilities which fell to be discharged by the Ministry. Later he was responsible with the late Sir Leonard Parsons and Mr. Clayton Fryers for carrying out the combined Ministry of Health and Nuffield Foundation survey of hospitals in the Sheffield Region. Returning to Whitehall, he was concerned in association with other members of the Ministry's lay and medical staff in the various preparations which culminated in the launching of the National Health Service on July 5, 1948. Since he was appointed as deputy chief medical officer, his chief responsibilities have continued to lie with the several branches of the health service, and he has been active in collaborating both with the College of General Practitioners and the Society of Medical Officers of Health. He has been and continues a vigorous advocate of home care of the sick wherever practicable, and of active co-operation between general practitioners, local health authorities and the hospital and specialist services.

The Royal Society of Edinburgh: Officers for 1960-61

At a statutory meeting of the Royal Society of Edinburgh held on October 24, the following officers and members of Council were elected: *President*, Prof. E. L. Hirst; *Vice-Presidents*, Prof. T. Neville George, Prof. J. R. Matthews, Dr. T. R. Bolam, Dr. Douglas Guthrie, Dr. A. W. Greenwood, Prof. R. A. Rankin; *General Secretary*, Prof. Norman Feather; *Secretaries to Ordinary Meetings*, Dr. Mowbray Ritchie, Prof. A. E. Ritchie; *Treasurer*, Dr. J. R. Peddie; *Curator of Library and Museum*, Dr. R. Schlapp; *Members of Council*, Prof. E. G. Cullwick, Prof. G. Pontecorvo, Prof. M. M. Swann, Prof. V. C. Wynne-Edwards, Prof. H. A. Brück, Dr. H. R. Fletcher, Prof. G. L. Montgomery, Prof. W. L. Weipers, Prof. J. H. Burnett, Prof. C. F. Davidson, Prof. D. C. Pack, Dr. A. B. Stewart.

Applications of Electricity in Aircraft

The Councils of the Institution of Electrical Engineers and of the Royal Aeronautical Society have recognized the growing need to provide a forum wherein engineers engaged respectively in the fields of electrical engineering and of aircraft construction can meet to discuss problems and new ideas affecting their common interest in aircraft electrical engineering. A Joint Committee, of which Prof. G. A. Whitfield, of the College of Aeronautics, Cranfield, is the chairman, was recently formed by the two organizations to consider ways and means of stimulating discussion of these matters, and it has now been agreed that this can best be done by arranging for joint meetings of the two organizations in London and for the formation of joint groups in the provinces. It is intended that meetings of the joint groups should be informal and in the nature of colloquia, designed to interest technicians as well as aeronautical and electrical engineers. In order to launch the scheme there will be an inaugural meeting at the Institution of Electrical Engineers, Savoy Place, London, W.C.2, on November 11, at 5.30 p.m., when Viscount Caldecote will deliver a lecture on "The Future of 'Electrics' and 'Electronics' in Aircraft and Guided Missiles".

Department of Scientific and Industrial Research: Report on Shipbuilding

In answer to questions in the House of Commons on October 27, regarding the publication of the Council for Scientific and Industrial Research's report on shipbuilding, Sir David Eccles, as representing the Minister for Science, said that the report was the subject of confidential discussions between the Council and representatives of the Ministry of Transport and the industry. The question of publication, which was one for the Council, would not arise so long as these discussions were in progress, but the Council intended to publish a statement as soon as these discussions were concluded. In reply to a further question, Sir David said that the current grant to the Parsons and Marine Engineering Turbine Research and Development Association amounted to £70,000 in consideration of the £210,000 raised by the industry, and the grant for next year would be on the same terms.

Russian Chemical Reviews

The Russian *Uspekhi Khimii* is being published in translation as *Russian Chemical Reviews* by the Chemical Society with the support of the Department of Scientific and Industrial Research. The first issue has appeared and contains four review articles, on the chemical action of ultrasonic waves on macromolecules, developments in the chlorination of saturated hydrocarbons, the hydrides of the rare-earth metals, and the chemistry of quinuclidine derivatives. These are excellent surveys of the subjects, with extensive references to papers in Russian and other languages, and the translation appears to have been very well done. The translation is described as cover-to-cover, but reviews in the original which are translations from foreign periodicals are, with few exceptions (for example, Chinese sources), not included. The subscription rates are £12 (United States 36 dollars), with a reduced rate for libraries of universities and technical colleges of £9 (27 dollars) per annum, including postage. Orders should be sent to Cleaver-Hume Press, Ltd., 31 Wright's Lane, London, W.8.

Checking Accidents in Factories

Under the title "Guide to Statistics collected by H.M. Factory Inspectorate" the Ministry of Labour has issued a booklet giving details of the methods of collection and compilation of the statistics, and of the systems of coding and classification which permit analysis of further information as and when required (Pp. i+41. (London: H.M. Stationery Office, 1960.) 4*s*. net). These statistics are based on the reports of accidents made by occupiers of factories and by certain other employers in accordance with

Section 64 of the Factories Act, 1937. The circumstances in which reports are required are detailed, and copies of the prescribed forms are appended to the booklet and also of the tables used for classifying the information. The booklet describes in detail how this information is examined, classified and given a coding to permit subsequent analysis.

Grants for Field Work in Natural History

GROUPS of local naturalists often find themselves held up for lack of specialist advice on how to tackle their problems. To help its members, the Council for Nature approached the Carnegie U.K. Trust, which has now agreed to set aside a fund from which it will make grants to approved societies for assistance with field work. These grants will be made on recommendations submitted by the Council for Nature and will be contributions towards expenditure incurred in carrying out specific projects that give amateurs experience of field work in natural history under skilled direction. Approved expenditure is likely to include fees paid to experts for instruction and leadership, the incidental expenses of such people and the cost of essential equipment subject to certain conditions. Grants will not be available for the expenses incurred by members of societies taking part in any scheme or for the general support of a society. Full particulars of the conditions for the award of grants can be obtained from the Carnegie U.K. Trust, Comely Park House, Dunfermline, Fife, or from the Council for Nature, 41 Queen's Gate, London, S.W.7.

The Wellcome Trust: Grants for Medical Research

DURING the six months from March 1 to August 31 the Wellcome Trustees accepted the following applications for major grants to assist medical research. Together with smaller grants totalling £41,000, and Wellcome research travel grants, totalling £17,000, the allocations by the Trustees in this period exceeded £420,000. The grants were allocated as follows: £50,000 to the Middlesex Hospital Medical School, University of London (Prof. C. A. Keele), for a suite of Wellcome Research Laboratories in the Pharmacology Department of the new Medical School building; £50,000 to the Massachusetts General Hospital, Boston, to establish a Wellcome research professorship for ten years; £61,000 to the Medical Research Council, to construct a laboratory and housing accommodation for an Epidemiological Research Unit in Jamaica, also £60,000 to provide five Sir Henry Wellcome research travelling fellowships for five years; £40,000 to McGill University, Montreal, Canada, to extend the support of the Wellcome Research Department of Anæsthesia for a further five years; £17,000 to the University of Pennsylvania, to extend the support of the Wellcome associate professorship of research in anæsthesiology for a further three years; £16,000 to Trinity College, Dublin (Mr. K. M. Shaw), to construct and equip an experimental surgery unit and an animal house; £16,300 to the University of Oxford (Sir George Pickering), to construct an animal house for the use of workers in the Department of the regius professor of medicine; £6,000 to the Postgraduate Medical School, University of London (Prof. J. McMichael), to equip a cardiac catheterization research laboratory in the Department of Medicine; £10,000 to the University of Birmingham, Department of Biochemistry (Prof. S. V. Perry), for equipment to investigate the nature and functions of the proteins of brain and muscle; £5,500 to St. Mary's Hospital Medical School, University of London (Prof. R. R. Porter), for an analytical ultracentrifuge to investigate the structure of antigens and antibodies.

In addition the Trustees made grants totalling £21,800 for special research apparatus of various kinds to Prof. R. Woolmer, Department of Anæsthesia, Royal College of Surgeons of England; Dr. G. A. Kerkut, University of Southampton; Mr. H. A. Sissons, Institute of Orthopædics, University of London; the Agricultural Research Council's Virus Research Unit, Cambridge; Dr. K. S. Dodgson, Department of Biochemistry, University College of South Wales and Monmouthshire; Prof. O. L. Wade, The Queen's University, Belfast; Prof. G. A. H. Buttle, School of Pharmacy, University of London; Prof. J. W. Howie, University of Glasgow; and Prof. H. Heller, University of Bristol. A grant of £1,000 to purchase special equipment for high-altitude research was made to Dr. L. G. C. E. Pugh, physiologist to the Himalayan Scientific and Mountaineering Expedition, 1960–61.

Announcements

PROF. ARNE TISELIUS, of the University of Uppsala, Nobel laureate in chemistry (1948), has been appointed president of the Nobel Foundation.

THE Medical Research Council has recently established the following new research units: the Gastroenterology Research Unit at the Central Middlesex Hospital under the direction of Dr. E. N. Rowlands; and the Unit for Research on the Chemical Pathology of Mental Disorders in the Department of Physiology, University of Birmingham, under the honorary direction of Prof. I. E. Bush.

THE Institute of Biology, with the support of the Eugenics Society, has instituted an annual Darwin Memorial Lecture in human biology. The first lecture will be given by Dr. C. E. Ford of the Medical Research Council's Radiobiological Research Unit on "The Cytogenetics of Sex in Man". The lecture will be given in the lecture hall of the British Museum (Natural History), Cromwell Road, S.W.7, at 5.15 p.m. on November 23 and is open to the public.

THE annual exhibition of the Institute of Physics and the Physical Society will be held at the Royal Horticultural Society's Old and New Halls, Westminster, London, S.W.1, during January 16–20, 1961. During the exhibition, the following discourses and demonstration lectures will be given in the New Hall: January 17, "Hydrodynamics Research", by F. S. Burt (Admiralty Research Laboratory); January 18, "The Physics of the Ocean", by Dr. G. E. R. Deacon (National Institute of Oceanography); January 19; "Some Physical Problems in Travelling at Supersonic Speed", by Dr. F. P. Bowden (Laboratory for the Physics and Chemistry of Solids, Cambridge). Further information and tickets can be obtained from the Institute of Physics and the Physical Society, 47 Belgrave Square, London, S.W.1.

ERRATUM. We regret that in the communication entitled "Evidence for the Identity of Natriferin, the Frog Water-Balance Principle and Arginine Vasotocin", by Prof. Wilbur H. Sawyer, in *Nature* of September 17, p. 1030, there is a mistake in the table; the right-hand heading should read: "Activities (U./mgm. dry weight)".

SCIENCE BY THE UPPER FORM IN SCHOOLS

At the annual meeting of the British Association for the Advancement of Science the section devoted to matters of general scientific interest, Section X (Assembly of Corresponding Societies), has for some years provided an opportunity for sixth-form scientists in local grammar and public schools to present papers on scientific studies carried out as a result of group or individual investigation. One whole morning session is set aside to allow the presentation of four topics, and large adult audiences flock to listen to the young embryo scientists.

This year at Cardiff, "Science by the Upper Form" was represented by Robert Riden, of Cardiff High School for Boys, who read a paper on "The Caves of South Wales"; Colin Rees, of Cathays High School for Boys, who discussed "The Increase of Herring Gulls at Worms Head, Gower, and its Effects on the Razor Bill and Guillemot Populations"; Glanffrwd Phillips and Clive Davies, of Ferndale Grammar School, Glamorgan, who presented a joint report on investigations into the presence of "*Craspedacusta sowerbii*—Fresh Water Medusa of Microhydra" in Darran Lake, Ferndale, and by Roger Williams, of Tredegar Grammar School, Monmouth, who surveyed the vast subject of "Astronomy" in half an hour.

Each talk was admirably illustrated with slides or projected photographs as well as by other visual material.

Robert Riden gave a vivid account of his adventures in exploring a number of caves of different types which border the South Wales Coalfield. He indicated their relationship to the geology of the coalfield, gave details of their structure and physical grandeur, with particular reference to three to be found in Breconshire, in Carmarthenshire and in Gower, and showed how young people with a spirit of adventure and a disregard for the discomforts to be faced could carry out much useful exploration underground, providing their expeditions were properly organized.

Colin Rees, with the help of some delightful coloured slides, exposed the ruthless habits of the herring gull on Worms Head in the Gower Peninsula. He unfolded an interesting story of variations in the population of bird life on the headland over the past twenty years, beginning with the rapid decline of the gull population during the war years due to human raids on the eggs as an additional item of food until rationing came to an end in 1947. The eggs of razor bills and guillemots escaped as they nested on the inaccessible cliff face, so that these birds multiplied at the expense of the herring gulls. But when the eggs of the herring gull were no longer in demand it reasserted itself very rapidly, laying, as it does, three times as many eggs a year and nesting wherever it can at the expense of the razor bills and guillemots, until herring gulls were once more swarming over the headland by 1959. To-day, Colin Rees stated, there are 150 pairs of herring gull to about 100 pairs of guillemots and 50 pairs of razor bills—he considered that the herring gull would go on increasing while the others would remain in equilibrium. He gave some interesting information about the feeding and nesting habits of the various birds, discussed the dangers of oil pollution, and showed how the prolonged and intensive study of one particular area of a coastline can bring much valuable information about the habits in general of certain birds, the inter-relationships between the species, and the effects of human interference on their lives and numbers.

The third topic of the morning concerning the fresh-water medusæ found in 1959 in the Darran Lake, Ferndale, was illustrated by some excellent diagrams prepared by Pamela Evans and Moira Morgan of the same school as the speakers, Glanffrwd Phillips and Clive Davies. There was evidence throughout of careful preparation and good group organization by the senior biology mistress, Miss M. G. Lewis, who had also been responsible for the investigations in the field. The paper gave an account of the discovery of small, transparent jelly-fish-like creatures in the Lake near the school at the height of the very dry summer of 1959. At first thought to be sea urchins, the creatures were eventually identified as medusæ of *Microhydra*. Evidence was found of their previous location in other parts of Britain on rather rare occasions, always associated with hot, dry summers, but no clues could be discovered to account for their appearance at Ferndale in spite of much careful investigation of all the relevant factors. The series of slides revealed the wonders of the structure and variations in the shape of the medusæ and showed how they reproduced by forming simple buds. Microscopic specimens were also available for examination. It was a well-presented topic, indicating how much useful research can be carried out as the result of the chance discovery of one small strange creature in a lake.

The final paper was a discourse on "Astronomy" by Roger Williams. It was a quite masterly survey of this vast subject within the short time at his disposal and ranged from the history of the science to the analysis of the rival theories of the origin of the universe—"the explosive hypothesis" and the theory of continuous creation. Without being drawn into any religious controversy, Roger Williams pointed out that it is "no more absurd to postulate the supernatural as always creating than to contain the creative act to a single instant". He went on to consider the techniques at the disposal of the modern astronomer, referred to the importance of the work of the amateur, and thought that while inter-planetary exploration by man could not be far away it was not likely to provide us with many new clues as to the origins and structure of the universe. The pursuit of research into its mysteries will long remain of the utmost import to the pure astronomer, but Roger Williams concluded that the problem of what to believe and what not to believe must always remain a matter for the individual, unmodified by scientific knowledge.

Thus the session, "Science by the Upper Form", ended on a philosophical note. It is good to know that some sixth formers not only study their text-books, and listen to the experts, but also carry out their own investigations and learn to think for themselves. In encouraging these habits among our young scientists still at school, the British Association in this and many other ways is doing a notable work for the better understanding of science by the younger generation. "Science by the Upper Form" to-day may be the basis for scientific advancement to-morrow.

G. S. Campbell

THE TENTH CANADIAN HIGH POLYMER FORUM

ON September 7, some 170 scientists drawn mainly from Canada and the United States began a two and a half day conference on natural and synthetic macromolecules, under the general chairmanship of Dr. L. A. McLeod. As Dr. Sivertz reminded the conference, the study of high polymers in Canada, which was already important in relation to the large pulp and paper industry, received further impetus when, in 1942, Canada became a joint partner with the United States in the manufacture of synthetic rubber. A small working party drawn from the universities and industry was then set up, and from this developed open conferences and finally the Canadian High Polymer Forum was constituted and held its first meeting in 1949. Since that date meetings have been held at almost yearly intervals, and these have been characterized by informal and intimate discussion of contributed papers on a variety of topics. The meeting reported on here was the tenth in the series, and among other activities was marked by a banquet at which the mood of the principal speakers combined reminiscence with planning for the future.

Perhaps an outsider may be permitted to say that the meetings have not only served their regional and national purpose with particular success but have also been of wider value and importance, and that it is therefore entirely appropriate that the Canadian High Polymer Forum should be host to the International Symposium on Macromolecular Chemistry at Montreal on July 27–August 1, 1961. The relative merits of the small discussion group and the large conference with unrestricted membership have often been argued[1] and it will not be surprising if on the basis of its experience of earlier forums the organizing committee attempts to preserve the advantages of the former at the Montreal meeting. The eleventh Forum will not be held until the autumn of 1962 or the spring of 1963.

Twenty-four papers, all of which cannot be mentioned here, were presented at the tenth Forum. Five of these were concerned with ionic polymerization of unsaturated hydrocarbons. From these it appeared that rate constants for some of the individual steps in both cationic and anionic polymerization are now becoming available and it should not be long before coherent kinetic and mechanistic patterns emerge. Thus Dr. P. H. Plesch gave a value for k_p for the titanium chloride catalysed polymerization of *iso*butene in methylene chloride at − 60° C. and values of the Arrhenius parameters of the spontaneous termination, monomer transfer and water transfer reactions relative to those for the propagation reaction, from which it appeared that monomer transfer is the last chain-breaking reaction to survive at low temperatures. Dr. A. M. Eastham gave an account of interesting attempts to study the initiation reaction free from the complications of propagation by an investigation of the kinetics of the geometrical isomerization of but-2-ene in ethylene dichloride induced by boron trifluoride–methanol mixtures. The results seem to show rather surprisingly that an adduct of but-2-ene, methanol and two molecules of boron trifluoride may be involved. In a rare, but most welcome, contribution from one of the pioneers (R. M. Thomas) of cationic polymerization three new important findings were reported. The first was a medium for achieving liquid-phase cationic polymerization of *iso*butene at − 185°, the second the demonstration by carbon-14 tracer techniques of solvent-fragment incorporation in the polymer and the third was the existence of an 'inversion' temperature of about − 45°, above which the degree of polymerization of poly*iso*butene produced by aluminium chloride catalysis increases with monomer concentration and below which it decreases. This last result provoked much discussion, and mechanisms of chain termination involving two monomer molecules were advanced Prof. M. Szwarc described a capillary flow method involving contact times in the range 0·2–1·5 sec. for measuring the k_p for anionic polymerization of styrene in tetrahydrofuran solution with Na^+ as the counter ion, and also the preliminary results obtained, together with the relative efficiency of water and methyl iodide as chain terminators. An elegant spectrophotometric method for measuring the relatively slow reaction of lithium butyl with styrene was described by Drs. S. Bywater and D. J. Worsfold. The definite but unexpected result was obtained that, contrary to earlier work, the rate of the initiation reaction is proportional to $[\text{styrene}]^{1\cdot0}$ $[\text{Li Bu}]^{0\cdot15}$, whereas the rate of propagation is proportional to $[\text{styrene}]^{1\cdot0}$ $[\text{Bu (styrene)}_n^- \text{ Li}^+]^{0\cdot5}$. It seems that a six-fold aggregate of lithium butyl and bimolecular association of growing $\text{Bu (styrene)}_n^- \text{ Li}^+$ ion pairs must be involved in reactions in the lithium butyl catalysed polymerization of styrene. The latter association was much discussed in relation to earlier and later contributions (especially that of N. Nikolov) and generally agreed to be important in more concentrated solutions.

Free-radical processes received due measure of attention particularly in relation to unusual phenomena in solid systems. Thus the effect of sulphur-containing antioxidants is promoted not only by carbon black but also by polyacenes, diphenylpolyenes and substances capable of generating quinonoid structures. The effect was ascribed by the Bell Telephone Laboratory workers to formation of π-bond complexes between the promoter as acceptor and thiyl radicals as donors, thereby reducing the reactivity of the latter as hydrogen abstracting agents. Dr. R. J. Ceresa showed that the kinetics of the swelling of chemically cross-linked or molecularly entangled polymers by vapours followed similar courses, showing discontinuities to be associated with mechanical rupture of chains or the cross-links since the use of vinyl monomers as swelling agents leads to the formation of block copolymers. The hitherto somewhat puzzling phenomena connected with the polymerization of vinyl monomers in aqueous solution were discussed, and shown to be approaching rational codification based on the mutual compatibilities and the water solubilities of monomer and polymer, and the susceptibility of soluble polyradicals to oxidative and reductive termination by ions of metals of variable valency. The rate constants of the growth and termination processes of the soluble

radicals are not too dissimilar from those in non-aqueous media and are quite independent of those of any longer-lived radicals in suspended polymer particles.

Full characterization of a solution of a polymer requires a knowledge of the structure, sizes and shapes of all the polymer molecules present and of its equilibrium properties as manifested in partial molal values of thermodynamic functions of solvent and solute. Many of the papers were concerned with this topic in one or other form. One, by Drs. W. H. Beattie and J. T. Bailey, was a timely cautionary reminder, generally acknowledged, of the need for a sharpening of our perception of the significance of the number, weight, Z and $Z + 1$ averages obtained from light scattering. Another, by Dr. W. Cooper and his associates of the Dunlop Rubber Co., Ltd., showed that second-order virial coefficients obtained from light scattering measurements on polybutadiene are strongly dependent on chain branching and revealed that the branch points are preferentially susceptible to mechanical breakdown. One of the most exciting contributions was that in which Prof. W. Heller of Wayne State University described his attempts to "walk around" macromolecular particles oriented in a streaming solution by observing the light which they scatter when illuminated from chosen directions. Already this fascinating but technically very difficult approach has not only indicated the shape of rigid particles but has also given insight into molecular elasticity by providing indications of the change of shape of flexible coiled macromolecules under the influence of shearing forces. If this method could possibly be extended to the use of polarized light an immensely powerful tool would become available. A further paper on polymer solutions by Dr. B. E. Conway dealt with the thermodynamics of the polar system polyoxypropylene glycol in methanol. The decrease in hydroxyl content with increase in molecular weight of the polyoxypropylene glycol leads to a change of sign in the heat of mixing; the experimental entropies and free energies of mixing can be accounted for by the Munster theory, which takes into account specific solvent orientation effects.

A number of the authors described the application of new experimental techniques to the solution of polymer problems. Dr. L. A. McLeod has fractionated elastomers such as *cis*-1,4-polybutadiene using elution chromatography, and Dr. Bacon Ke showed that differential thermal analysis is not only useful in determining transition temperatures and heats of fusion of simple polyamides but may also give information concerning the structures of copolymers. Dr. W. Prins described a versatile osmometer which is capable, among other things, of measuring the de-swelling of polyelectrolyte gels. In this application the gel and solvent are separated by a porous stainless steel disk of porosity 5–65μ, and the change in gel volume is measured when pressures of up to 200 atmospheres are applied to the gel phase.

Some interesting developments in the field of new polymers and copolymers were described. The strong and highly extensible elastomers produced by the incorporation of 2,4-toluene diamine in copolymers of polyoxypropylene glycol and 2,4-toluene di*iso*cyanate were discussed by A. J. Havlik of the California Institute of Technology. Poly (5-methyl, 3-vinyl, oxazolidine-2-one), of which the surprising properties in water were reported by W. E. Walles at the ninth Forum, forms strong complexes with a wide variety of organic compounds. The complex with phenol in which one phenol molecule may be bound per monomer unit in the polymer owes its strength to hydrogen bonding, but more unusual are the fairly strong complexes of the polyoxazolidinone with methyl bromide and bromine.

It is a tradition of these meetings to have a guest speaker who delivers the Conference lecture. This year the speaker was Prof. F. S. Dainton and his topic was "Why Polymerization Occurs". The central theme was that addition polymerization, which is usually regarded only from the point of view of the kineticist, is merely the aggregation of freely translating monomer molecules into larger molecules in which the basic units are joined by primary chemical valencies. Except in the nature and strength of the inter-unit linkage it is thus entirely analogous to physical aggregation processes such as condensation and crystallization and like these can be examined thermodynamically. The now familiar[2] notions of 'ceiling' and 'floor' temperatures, monomer–polymer equilibria and metastability phenomena were treated by the lecturer in relation to a wide range of systems Recent calorimetric values of heats of polymerization and the entropies of polymers were used to illustrate the large effects on the heats and the minor effects on the entropies of polymerization of certain structural groupings in the monomer.

F. S. DAINTON
K. E. RUSSELL

[1] *Nature*, 184, 835 (1959); 186, 283 (1960).
[2] See Dainton, F. S., and Ivin, K. J., *Quart. Rev.*, 12, 61 (1958).

PHILOSOPHY OF SCIENCE

THE British Society for the Philosophy of Science held its fifth annual conference at Wills Hall, University of Bristol, during September 23–25. The four formal meetings and discussions, organized by Dr. Mary Hesse (Cambridge), were attended by fifty members and guests.

At the first meeting, with Prof. H. Heilbronn (Bristol) in the chair, two papers on the relation between pure and applied mathematics were read. Accepting the views of Frege, Cantor and others that the concepts of pure mathematics are exact, and of Waismann and others that empirical concepts are inexact, Prof. S. Korner (Bristol) introduced a new generalized logic which embraced relations not only between exact concepts but also between inexact concepts and between exact and inexact concepts. He showed that 'purely exact' and 'internally inexact' concepts, as he defined them, could be identified with pure mathematical and empirical concepts respectively, and that they were logically unconnected. He thus described the application of mathematics as a threefold process: inexact empirical concepts are

replaced by exact concepts, exact conclusions are then deduced and, finally, the exact mathematical concepts are replaced by empirical concepts.

Prof. R. L. Goodstein (Leicester) traced the evolution of formal systems, using the development of geometry, mechanics and arithmetic to exemplify his thesis. The stages of evolution were successively the formulation and application of rules, the discovery of relations between rules and development of the concept of proof, the analysis of the rules of proof (metamathematics) and, finally, formal codification of metamathematics. He concluded that in applying mathematics we retrace its evolutionary development, replacing theorems by statements of observation. A mathematical proposition thus has a dual role. The ensuing lively discussion centred on the part to be taken by Korner's generalized logic in clarifying the problem, and on the strangeness of the fact that the exact concepts of pure mathematics could sometimes be successfully applied to the 'open-textured' concepts of empirical science.

Echoes of this first discussion were heard next morning when the theme was the relation between universality and necessity. Mr. W. C. Kneale (Exeter College, Oxford) gave a critical historical review of the question whether necessity can be defined by reference to universality. He traced three attempts at such definition: that, derived from Hume, in which necessity appears as a by-product of arguments the major premises of which are universal statements about Nature; that, derived from Bolzano and recently revived by Tarski, in which necessity is based on the universal validity of patterns of argument in which the only essential words are logical; and that, propounded by Popper in an appendix to "The Logic of Scientific Discovery", in which a Leibnizian reference to possible worlds seems to be related to a modified Bolzano–Tarski theory. Having explained the difficulties he found in all these reductionist programmes, Kneale advanced his own views that formal logic is pure theory of necessitation, that necessity is a fundamental notion, and that (with Wittgenstein) "all necessity is logical".

The second paper was given by Dr. I. Lakatos (London School of Economics), who first analysed the differences between the arguments of Popper and Kneale on both the ontological and epistemological planes. His witty theological formulation of the controversy, in which he sided more with Popper than with Kneale, included the startling credo that "the natural laws uttered by God were of infinite length" (and that therefore all universal statements, whether contingent or necessary, are false) and then he summarily dismissed the controversy as metaphysical and therefore meaningless. As a fallibilist, not only in science but also in logic and mathematics also, he could only regard both Popper and Kneale as mistaken in their "epistemological optimism", different though the forms of their optimism might be.

The chairman, Mr. J. W. N. Watkins (London School of Economics), then offered for discussion a model neatly designed to emphasize the conflicting views that had been propounded. In discussion, attempts were made to clarify the relation between logical and physical necessity. Do they form a linear continuum? Or are they homogeneous? But before complete clarification had been achieved, Dr. Lakatos silenced all further discussion by proving that any proof refutes the proposition it proves!

After strenuous discussion of closely knit philosophical arguments, the members turned with relief and pleasure to view the intriguing optical devices used by Mrs. M. L. J. Abercrombie (Guy's Hospital) to illustrate her paper on learning to perceive. The chairman was Prof. J. E. Harris (Bristol). Mrs. Abercrombie explained that perception is a process of interaction between the observer's sensory input and his store of previously acquired information. In this interaction only parts of the total information available are used by the observer, selection being made both from the field observed (clues) and from the store (schemata). The observer makes a guess about what he perceives, acts on his guess and modifies it as other clues and other relevant schemata interact. She described how training to improve perception is possible by reference to her recent experiments in training medical students to improve their skill in diagnosis.

The second paper was given by Dr. M. H. Pirenne (Oxford), who described his experiments to determine the threshold intensity of light visible to the human eye. The physical and psychological factors impeding exact measurements were explained. The subject's eye had to be fixed and adapted to darkness; the subject had to be willing to co-operate and to be trained and tested for reliability. Difficulties were caused by day-to-day variation of response and by the phenomenon of 'subjective light'. There was not a sharp transition from visibility to invisibility as the energy of a light-flash was decreased, and the threshold was defined by an arbitrary statistical measure in the range of critical intensities. His results showed that the human eye could detect flashes of about 100 quanta in the narrow band of blue-green wave-lengths to which the periphery of the retina was most sensitive. Of these 100 quanta in the light-flash, only about 10 reached the retina and were there distributed among about 500 rods.

Discussion of these two papers was divided between questions of methodology and the implications of the empirical observations reported on current theories of perception. There seemed to be little evidence of, or need for, the pure sense-datum required in some theories.

At the final meeting, with Prof. M. H. L. Pryce in the chair, two theoretical physicists discussed the relation between methods of investigation and the characteristics of physical laws. In the first paper, Dr. D. Bohm (Bristol) criticized current views of the role of hypotheses in science. Implicit in Popper's view that scientific hypotheses could only be falsified was the assumption that questions giving answers in the form 'yes' or 'no' could always be put to Nature. But at the boundary of new scientific domains we knew the relevant questions only when the answers were already known. He also criticized the emphasis given to prediction and retrodiction in accounts of scientific method and expressed dismay at the degree of specialization enforced on scientists by the overwhelming mass of data which confronts them. It was important to establish a sound natural philosophy if the full potential of scientific method was to be realized.

The second paper, by Dr. P. W. Higgs (University College, London), reviewed the present untidy field of particle physics and discussed some of the implicit assumptions in this field that theoretical physicists were beginning to question. In particular, the effect of the gravitational field, hitherto regarded as negligible in strength compared with the other fields of particle interaction, seemed to deserve more careful exploration. In the discussion the main points were about the nature of the possible alterna-

tives to prediction and retrodiction as tests of the 'fitness' of hypotheses. What forms could 'diction' take? In what sense were the micro-particles of physics to be regarded as 'ultimate' or 'fundamental'? What exactly was meant by saying that one science or one branch of a science was 'reducible' to another? These were some of the many questions raised and left not wholly answered.

The Vice-Chancellor of the University of Bristol kindly invited the members to a sherry party at Wills Hall on the Saturday evening. Thereafter, small informal groups, oblivious to everything except their own intense discussion, seemed to be generated spontaneously in all the many pleasant corners of Wills Hall and its gardens. At the conclusion of a stimulating week-end, expressions of thanks to the hosts at the University of Bristol, to the staff of Wills Hall and to the organizing secretary were more than mere formalities.

B. C. Brookes

THE NATIONAL RESEARCH COUNCIL OF CANADA

THE forty-third annual report of the National Research Council of Canada, covering the year 1959–60, includes besides the report of the president, Dr. E. W. R. Steacie, of the nine divisions, two regional laboratories and the National Aeronautical Establishment and the financial statement, the annual report of Canadian Patents and Development, Ltd.*.

During the year the Council provided 8·7 million dollars in support of pure research in the universities, compared with 6·3 million dollars in 1958–59, of which 84 per cent was for 875 research grants and the remainder for 425 postgraduate scholarships, fellowships and associateships. The Council's scientific research staff of 658 included 137 postdoctorate Fellows, and in addition 916 technical personnel and 866 general service and administrative staff were employed. Claiming that neither the United States nor the United Kingdom possesses the clear but flexible delineation of administrative authority for science that exists in Canada, Dr. Steacie suggests that in Canada the responsibilities of the Minister for Science are constitutionally exercised by the chairman of the Privy Council Committee on Scientific and Industrial Research, and that in this respect Canada is forty years ahead of the United Kingdom. The problem in Canada is to ensure that scientific activities are so organized as to encourage the full development of the scientific and technical resources of the country. The first responsibility of a national science policy must be support of research in the universities, and the problem is how to maintain the strength and depth of the university science departments and, at the same time, satisfy the requirements of defence, industry and development of national resources with the vigour and competence demanded by international competition, without over-emphasizing technology at the expense of other activities. Dr. Steacie, noting that the Research Council has proved in the past to be an effective channel for supporting science in the universities, urges the need for a continual review of the support of science in the universities to ensure that procedures continue to evolve with the growth of science and changes in administrative practice. Further, while in Canada those departments of Government with administrative responsibilities for natural resources are responsible for the basic research to support their programmes, the Research Council has the function of ensuring the general adequacy of all remaining basic research, but Dr. Steacie stresses the importance of backing Canadian industry by an industrial research effort as great as the scientific resources of the country can support.

Of the work of the Division of Applied Biology, the report notes a co-operative project with the Department of Agriculture on the design and performance of jacketed cold-storage rooms requiring fundamental knowledge of the factors determining low-velocity airflow through shallow ducts, and a study by the Biometrics Section of agricultural meteorology as an extension of the statistical study of protein variability in wheat and wheat exports. Preparations were begun, including design of equipment, for an international expedition to study adaptation to cold by Eskimos. The work of the Division of Applied Chemistry on metals has gradually expanded during recent years, and now includes investigations of the effect of composition and structure on the optical and magnetic properties of a wide variety of alloys. A new technique, developed by the Division about eight years ago for the contacting of fluids and solids, has now been put into commercial operation in grain drying. The Division of Pure Chemistry has shown that ionization potentials of radicals prepared by pyrolytic reactions can be measured by electron impact in the mass spectrometer, and a study of the diffusion of chloride ions in single crystals of sodium chloride and of potassium chloride has shown that the diffusion is very sensitive to the presence of gross imperfections such as dislocations and grain boundaries in the crystals, while attempts to correlate the accumulated observations in the photo-oxidation of ketones have led to the conclusion that not only the rate but also the nature of the products of the reactions of methyl radicals with oxygen depend on the total pressure in the system as well as the presence of molecules containing easily abstractable hydrogen.

In the Division of Applied Physics a new group has been established for plasma research, work was completed in the interferometry laboratory which contributed to an international agreement to base the unit of length, the international metre, on a particular wave-length of the spectrum of an isotope of krypton, and the experiment to determine g, the acceleration due to gravity, by direct observations on a falling body was completed. The group in the Division of Pure Physics concerned with cosmic ray work is still devoting much of its efforts to international co-operation of the type started during the International Geophysical Year, and the development of a space research programme in Canada has permitted cosmic ray measurements with rockets flown to high altitudes. In the X-ray diffraction laboratory

* Forty-third Annual Report of the National Research Council of Canada, 1959–60, including the Annual Report of Canadian Patents and Development, Limited. (N.R.C. No. 5665.) Pp. 40. (Ottawa: Queen's Printer, 1960.)

important results are being obtained in the crystal chemistry of vanadium minerals and the stereochemistry and absolute configuration are being established for certain narcotics the structural formulæ of which have long been in dispute.

The Division of Mechanical Engineering records increasing emphasis on longer term investigations in thermodynamics and engine evolution, and many new propulsion problems in air transport are also being studied, especially those arising from vertical take-off and landing, while certain fluid mechanical aspects of nuclear reactors are being examined. At the National Aeronautical Establishment a substantial research effort has been redirected to problems of high-speed and very high-speed flight, and in particular an increasing effort is being applied to problems arising from very high temperatures. Much of the work of the Radio and Electrical Engineering Division was concerned with defence projects, but the remainder of the programme was concerned with fundamental problems in electrical engineering and electronics, and a pressure gauge capable of measuring the atmospheric pressure at satellite altitudes was developed.

Work at the Prairie Regional Laboratory, Saskatoon, is devoted to a more thorough understanding of the plants and micro-organisms growing on the prairies; but to promote the development of oil-seed crops as alternatives to cereal crops an intensive study of the chemical structure of glycerides was undertaken. At the Atlantic Regional Laboratory, Halifax, where the most efficient way of drying the commercially important plant materials of the region has been studied, a semi-commercial scale batch dryer was developed and a continuous dryer is now being designed and constructed in co-operation with industry.

SAFETY OF YOUNG PEOPLE IN FACTORIES

PROBABLY the most important chapter in the annual report of the Chief Inspector of Factories for 1959* is one of two chapters dealing with subjects of interest without being necessarily restricted to the events of the year—that dealing with the prevention of accidents to young persons. While the consistent downward trend in the number of fatal accidents continued in 1959, there was an increase in the number of reported accidents, and the Chief Inspector is disturbed at the increase in the number of accidents to young persons, from 9,838 in 1958 to 11,001 in 1959. This rise is not due just to an increase in the numbers employed, and indicates clearly that redoubled efforts will be necessary to hold the rate of accidents to young people in check, as increasing numbers of school-leavers enter industry in the coming years. The present drive to train young persons in safe working must be intensified, he writes, not only by industry but also by secondary and technical schools and colleges.

The Chief Inspector, in his letter of presentation, points out that it is evident from the large number of accidents to the head and neck, to the feet and ankles and to the hands, that much more could be done to reduce such accidents by the wearing of suitable clothing, such as safety helmets, goggles, adequate footwear and gloves, and that careful attention would reduce dramatically the grand total of all reported industrial accidents. Young persons, particularly during the first year of employment, tend not to take adequate safety precautions and are more liable to run the risk of suffering injury than older workers. Ignorance of factory conditions and hazards, inexperience and natural curiosity, the desire to prove oneself, contempt for 'safety first' principles, liability to fatigue, and boredom leading to 'skylarking', can all be contributory factors, and there are many examples in the records of the factory inspectorate of the kind of accident in which youngsters are concerned for such reasons.

Young persons, it is clear, enter employment with a handicap, and it is the responsibility of their employers to help them overcome it by providing sound training and careful supervision and by insisting on high standards of obedience to safety rules. Many of the large firms have, in fact, built up excellent organizations for this purpose, and in his annual report for 1951 the Chief Inspector, Sir George Barnett, attributed the considerable reduction in the post-war accident-rate mainly to this factor. Many managements, however, did not trouble to make allowances, and since then the rate of decrease of accidents to young persons has slowed down, and the decrease in the number of accidents to young persons is, moreover, proportionately less than the corresponding decrease for all employed persons.

While there have been several important pieces of legislation since 1937 affecting young persons employed in factories, such as prohibition or restriction of employment in certain dangerous or unhealthy trades, prohibition of employment on certain types of dangerous machinery or in carrying or lifting excessive weights, limitation of the number of hours a young person may work and the provision of medical supervision, the legal contribution must be supplemented by effective training and supervision, beginning in schools and colleges and continuing in industry. There are few places where the young can be prepared for work in the factory so well as in secondary school and college workshops and housecraft rooms. Classes there provide an excellent opportunity for showing how tools should be maintained and used, and machines properly guarded. The teacher, too, can inculcate a degree of safety consciousness and an acceptance of discipline in the correct use of machines and tools which is invaluable in factory life. As the Chief Inspector observed in addressing a conference on "Accident Prevention in Technical Colleges" at Blackpool in June 1958, arranged by the North West Regional Advisory Council for Further Education, his teachers are the best people to give the neophyte entering the factory the confidence that he requires.

The Chief Inspector did not suggest that safety should be taught as a subject *per se*, but rather that safety teaching should go hand in hand with the various subjects, and in the present report the Chief

* Ministry of Labour. Annual Report of the Chief Inspector of Factories on Industrial Health, 1959. Pp. iii+60. (Cmnd. 1137) (London. H.M. Stationery Office.) 3*s*. 6*d*. net.

Inspector refers to encouraging developments as a result of the initiative of the North West Regional Council. The Council itself set up an Industrial Hazards Sub-committee, which organized three courses in accident prevention at Liverpool, Manchester and Preston, and afterwards the Cheshire County Education Authority established a permanent committee to deal with safety training in colleges in Cheshire, on which both industry and college staffs are represented. The general problem has also been discussed at a conference held recently in Glasgow, attended by a number of principals, heads of departments and teachers from technical colleges in Scotland, and addressed by senior members of the factory inspectorate.

Among the suggestions which found favour with the conference were publication of a safety code for each college; appointment of a member of the teaching staff to be specially responsible for safety matters; inclusion in examination papers of questions relating to safety; and close liaison between the technical colleges and inspectors of factories, who can give occasional lectures and advise on safety precautions. A pamphlet, comprising mainly speeches delivered at the Blackpool conference, has already been distributed to technical college teachers in the north-west region and received a wide circulation in other parts of Britain, but these efforts are only a beginning and, as the Chief Inspector now emphasizes, much more remains to be done if young people are to come into industry adequately prepared and the transition from school to industry is to be as smooth as possible. He urges that it is important for the success of this work that education authorities and individual principals and heads of departments at technical colleges should recognize the seriousness of the problem and the need to take steps to deal with it.

It might be added that this is a matter that could well be recognized as a professional responsibility by scientists and technologists, not simply when their own work as teachers or in industry brings them in direct contact with it, but through their professional organizations. Their co-operation and guidance can sometimes make the decisive difference between success and failure, and this is no less true in respect of some of the suggestions for action by employers which are made in this special chapter of the Chief Inspector's report. Apart from care in picking young people for the work they are going to do, training schemes should include six particular points. The young worker should be taken around those parts of the factory where he will work and should be shown what the principal dangers are, how they arise and how to avoid them. A fully competent adult worker should directly supervise the young person's work during the initial period of training and the proper method of working any machine on which the youngster is to be employed should be illustrated in detail and the dangers associated with other undesirable methods explained. Departmental managers and other supervisory grades should be given clear instructions on accident prevention and on the need for keeping close control over the work of the young persons under their charge, and strict discipline should be enforced in the adoption of safe methods. Special safety propaganda should hammer home the important points and make young workers aware of the importance which is attached by the employer, and all in supervisory positions, to the principles of accident prevention.

Clearly not all these points concern either the scientist or technologist as such, but in many of them his interest and co-operation can be decisive factors. Moreover, as the report concludes, it is not only firms with large numbers of youngsters and great financial resources that can achieve substantial results. It is well within the capacity of managers and supervisory staffs in smaller firms to make the effort to see that their young recruits have a good and safe start in their chosen career, and many such managers and members of supervisory staffs, as well as teachers and departmental heads in technical colleges, are themselves likely to possess scientific or technological qualifications.

THE COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION IN AUSTRALIA

THE eleventh annual report of the Commonwealth Scientific and Industrial Research Organization in Australia, covering the year 1958–59*, notes a number of changes in organization.

The Division of Industrial Chemistry has become the Chemical Research Laboratories, with three Divisions, Chemical Physics, Mineral Chemistry and Physical Chemistry, and three independent Sections, namely, Cement and Ceramics, Chemical Engineering and Organic Chemistry. Similarly, the Wool Textile Research Laboratories have been renamed the Wool Research Laboratories, with Divisions of Protein Chemistry, Textile Physics and Textile Industry. The Soil Mechanics Section of the Division of Soils has become an independent section of the Organization and the unit of the Division of Plant Industry and Plant and Soil Laboratory, Brisbane, becomes an independent Division of Tropical Pastures, while the former Radio Research Board Laboratory, Camden, New South Wales, has become an independent Upper Atmosphere Section. Collaboration with the universities has been further extended by the establishment with the University of Melbourne of a joint laboratory for research and soil mechanics at Syndal, Victoria, and of a Meat Research and Teaching Centre at the University of Sydney Animal Husbandry Farms, Camden, New South Wales. A Rice Research Station is being established on the coastal plains near Darwin, where studies will be made of nutrition and water requirements of rice and of possibilities for developing varieties well adapted to that environment. Two frigates, specially equipped for oceanographic survey work, are being made available to the Organization for periods of about 12 weeks a year, and this assistance will facilitate the more comprehensive and regular programme of observations which must be undertaken before a clear picture of the oceanography of the waters surrounding Australia can be developed.

* Eleventh Annual Report of the Commonwealth Scientific and Industrial Research Organization for year 1958–59. Pp. 181. (Canberra: Commonwealth Government Printer, 1960.)

In co-operative industrial research support of the Australian Leather Research Association, the Bread Research Institute of Australia, the Wine Research Institute and the Australian Coal Association (Research), Ltd., continued. New research projects sponsored by industry commenced during the year included investigation of solid lubricating materials derived from Australian beach sand minerals; development of methods for determining the oxygen content of cyanide solutions used in extracting gold from its ores; research on the colorimetric properties of pigmented materials; and the study of changes in shell egg quality during marketing. The design study for the proposed giant radio-telescope for the Division of Radiophysics has been completed, and the radio telescope is scheduled for completion early in 1961.

During the year 24 junior and 26 senior postgraduate studentships were awarded as well as 14 overseas research studentships. Of the Organization's income of £8,060,831 in 1958–59, £6,297,597 was from Treasury appropriation and £1,322,576 from the Wool Research Trust Fund Account. Of the expenditure of £7,538,477 on research activities, £776,186 was on animal health and production, £831,237 on the plant industry, £263,480 on food preservation and transport, £336,868 on forest products, £678,571 on chemical research, £198,144 on fisheries and oceanography, £657,310 on the National Standards Laboratory, £157,049 on building research, £403,453 on radiophysics, £446,402 on wool research, £203,276 on fuel research, £125,962 on wildlife survey, and £202,226 on land research and regional survey. Besides summarizing the work of the Organization during the year in nearly thirty different fields, the report includes details of the membership of the Council and its committees and of the professional staff of the Organization as well as a list of papers published during the year.

THE INSTITUTE OF PHYSICS AND THE PHYSICAL SOCIETY

The Physical Society

At the extraordinary general meeting of the Physical Society held on July 5, in London, the reports of the council and the accounts for the year ended December 31, 1959, were presented and adopted and the special resolutions for the voluntary winding up and the transfer of the assets of the Society to the newly amalgamated body, the Institute of Physics and the Physical Society, were unanimously carried.

The year under review in the annual report is stated to have been very satisfactory from the financial point of view, with an overall excess of income over expenditure of £3,796. The Exhibition Contingency Fund was increased by £4,000 to £12,000, but the exhibition account still showed a profit of £1,966. The 1959 exhibition of scientific instruments and apparatus was held earlier in the year, January instead of March, but there was no falling off in the keenness of exhibitors to obtain space or in the attendance of visitors to the exhibition.

The "Handbook of Scientific Instruments and Apparatus", the catalogue of the exhibition, was in great demand and sold well. The flow of manuscripts for publication in the Society's *Proceedings* remained steady during 1959, but because of the printers' strike the volume of material published was less than in former years. 174 papers, 72 research notes and 25 letters to the editor were published, and 54 out of a total of 302 manuscripts received were rejected. Volume 22 of the "Reports on Progress in Physics", which was published during the autumn, was the largest for some years and contained fourteen articles. The sale of past issues of both *Proceedings* and the "Reports", as well as of reprints of individual articles in the "Reports", showed a marked increase. A list of the various lectureships, prizes and medals awarded by the Society during 1959 and their recipients is given in the annual report.

The lectures and the presidential address are published in the "1959 Year Book of the Physical Society". Brief reference is also made in the report to the activities of the Society during the year and in particular to the conferences lasting two or three days which were held on various subjects in Birmingham, Durham, Edinburgh, London and Oxford. The attendances were usually between 100 and 300, with members of the Society forming the majority.

The Institute of Physics

An extraordinary general meeting of the Institute of Physics was held on July 5, 1960, in the Institute's House, 47 Belgrave Square, London, with the president, Sir George Thomson, in the chair. The first part of the meeting took the form of the annual general meeting and the fortieth annual report of the Board of the Institute of Physics was presented and adopted*. The meeting then considered three special resolutions concerned with the winding up of the Institute and the handing over of its property and its funds to the amalgamated body, the Institute of Physics and the Physical Society. The resolutions were carried unanimously.

The report records the continued growth of the Institute, both in the number of its members and in its activities in many fields, including education, scientific publications and conferences, symposia and meetings arranged by its branches and specialist groups. During the year, 933 applications for election or transfer to the various grades of membership were received, and the total membership increased by 445 to 6,754. Five technical colleges applied for recognition by the Institute as institutions having courses of work approved for the purpose of the membership regulations and all five were accepted.

Thirty-nine of the 119 candidates who presented themselves for the examination for the graduateship grade of membership were successful; 13 possessed university degrees and 26 the Higher National Certificate in applied physics. The fifteen question papers, together with the examiners' comments, were published in the September issue of the *Bulletin* of the Institute, and afterwards also as a pamphlet.

* Institute of Physics. Fortieth Annual Report of the Board of the Institute of Physics for the year 1959. Pp. 19. (London: Institute of Physics.)

New regulations and syllabuses for the graduateship examination, which will be in two parts, are to come into operation in 1962. There were 820 candidates from 46 technical colleges for the Ordinary National Certificate in applied physics and 296 from 23 colleges for the Higher Certificate.

A new edition of the booklet "The Scientific Education of Physicists", which gives guidance on training and a summary of information about the physics departments of all universities and recognized technical colleges in Great Britain, was published during the year. A symposium on "Current Developments in the Production of High Vacua" was held in London on April 17, and a two-day conference on "Some Aspects of Magnetism" in the University of Sheffield during September 22–24. Summarized accounts of the proceedings of the symposium and of the conference have been published in the *British Journal of Applied Physics*. Books published for the Institute included reprints of the first five monographs in the "Monographs for Students" series, and a new volume, "Mechanical Design of Laboratory Apparatus", by H. J. J. Braddick; "The Design of Physics Research Laboratories", the proceedings of a symposium arranged by the London and Home Counties Branch of the Institute; and a second edition of "Physics as a Career".

Details are given in the annual report of the amount of material submitted and published during the year in the Institute's two monthly journals, the *British Journal of Applied Physics* and the *Journal of Scientific Instruments*. The Journals Advisory Committee at its meeting, held during May, agreed that the scope of the *British Journal of Applied Physics* should not be limited despite the appearance of several new journals devoted to particular branches of applied physics. The circulation of the *Journal* continued to increase, but that of the *Journal of Scientific Instruments* showed a slight decrease for the first time for many years. The page size of the *Bulletin* was increased to conform with that of the two *Journals*, and the 324 pages of text, which contained about 22 per cent more material than the 336 pages of the 1958 volume, included twenty-five articles and 114 book reviews, in addition to Institute news.

The activities of the Australian, Malayan and the nine Great Britain branches, together with those of the specialist groups of the Institute, are outlined separately in the report. Two conferences were held by the Australian branch in Melbourne, the second "Conference on Contemporary Optics" during February 25–27, and the "Solid State Physics Conference" during August 17–21. A new division was formed in the Australian Capital Territory. The Applied Spectroscopy Group held an all-day symposium on "Reviews of Recent Developments in Spectroscopy" in May; the Education Group an Easter conference on the teaching of science to children up to the age of fifteen; the Electronics Group a two-day meeting in October on the subject of noise in electronic devices; and the Non-destructive Testing Group the first joint conference with the Société Française de Métallurgie in Paris. The Stress Analysis Group undertook a new venture in April when it arranged a three-day international conference on stress analysis in Delft, Holland. Fifty-one papers covering a wide range of topics were presented, and a selection of the papers is to be published in book form.

The annual dinner of the Institute was held on May 5, at the Park Lane Hotel, London, when 265 members and guests were present. The speakers were the president, Sir George Thomson, Sir Keith Murray, Sir Harry Melville and Mr. O. W. Humphreys. The alterations to the Institute's House, which had to be postponed for reasons of economy, were completed during 1959, and the senior staff dining room which had been used temporarily as an office was converted into a committee/dining room. The furnishings and décor were provided for by friends of the Institute and from the bequest of Mrs. W. Phillips. The Institute's accounts show a substantial increase in members' fees and on the publication business. £3,450 was transferred from the Institute's accounts to the Endowment Trust Fund account, but this was only just sufficient to cover the cost of the scientific and educational activities carried out by the Fund for the Institute. The Benevolent Fund continues to be well supported by members, and a further donation of £A.200 received from the Australian Branch's Special Fund and an additional payment of £258 in respect of tax recovered on payments made by the Trust set up under the will of the late Mrs. W. Phillips were very welcome. During the year £936 was paid out in assistance to ten cases.

FERAL MUNTJAC DEER (*MUNTIACUS* SPP.) IN THE WEST MIDLANDS

TWO species of muntjac deer, the Chinese (*Muntiacus reevesi*) and the Indian (*M. muntjac*), were introduced into England at Woburn Park, Bedfordshire, about the beginning of this century. Later they were kept at Whipsnade and at least two private zoos (Crowland Abbey, near Wellingborough, and at Broxbourne, Herts). During the past half-century, muntjac have been reported in Bedfordshire, Northants, Warwickshire, Bucks, Herts, Berks, Cambridgeshire, Huntingdonshire, Essex, Leicestershire, Middlesex, Norfolk, Oxon., Staffordshire and Suffolk. Only in the last five counties can it be stated as certain that the deer are established as a regularly breeding species at the present time.

The successful colonization by the muntjac of a wide area of Britain has taken place very largely without the knowledge of its human inhabitants. T. J. Pickvance and J. S. R. Chard have prepared an article directing the attention of naturalists and others to the presence of this small deer and indicating some of the problems involved in recording the distribution and habits of the muntjac (*Proceedings of the Birmingham Natural History and Philosophical Society*, 19, Part 1; 1960).

The muntjac is unlikely to become the object of measures of extermination. Unlike the larger species of deer, it does no harm to trees, and from places where it sometimes becomes a nuisance, such as market

gardens and allotments, it can be excluded by wire netting. Control will not prove difficult as it is easily caught, and, being a creature of habit in its movements, is not difficult to shoot. Its small size and retiring habits aid its unobtrusive spread. Thus, an increasing number of naturalists will be able to study this species which has an interesting form of territorial behaviour.

The main part of the article deals with records of the colonization by the muntjac of Warwickshire. These are typical of those gathered during surveys made with the view of determining not only the present distribution of the animal but also the rate and direction of colonization and the past history of the movements which have taken place.

NOMENCLATURE OF THE NICOTINAMIDE NUCLEOTIDE COENZYMES

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THE nomenclature of the nicotinamide nucleotide coenzymes has been a subject of long-standing disagreement, and unanimity has not yet been reached. Several different systems are in use to varying extents.

Included with other subjects in the terms of reference of the Enzyme Commission of the International Union of Biochemistry[1] is the nomenclature of enzymes and of coenzymes, and during the past three years the Commission has been giving careful and detailed consideration to the question of coenzyme nomenclature in an effort to reach a generally acceptable solution. The question has also been considered by the Biological Chemistry Nomenclature Commission of the International Union of Pure and Applied Chemistry. A summary of the points involved and the reasons for the recommendations of the Commissions may be of interest.

Present Position

The situation that has to be faced is that, except perhaps in the United States, there is no unanimity about the naming of the two coenzymes. Four different systems are in use, although to very different extents, and the special difficulty of the position arises from the fact that the system that is most used is that which has the strongest objections from the chemical point of view. The four systems are: (*a*) cozymase and phospho-cozymase; (*b*) codehydrogenase I and codehydrogenase II (or codehydrase I and codehydrase II by some Continental writers); (*c*) coenzyme I and coenzyme II (abbreviated to CoI and CoII); (*d*) diphosphopyridine nucleotide (DPN) and triphosphopyridine nucleotide (TPN). The first system is probably the least, and the fourth the most, used at the present time. None of these systems is satisfactory, the first three because they are uninformative, the last because it is incorrect, as a number of reviewers have pointed out[2-5].

There is rather more consistency among the journals than there is among authors of books and reviews. The *Journal of Biological Chemistry*, which had previously used both cozymase and coenzyme I, first used diphosphopyridine nucleotide in about 1940; and it has continued to do so, along with cozymase and coenzyme I, until about 1950, and as the sole form after that date The *Biochemical Journal* used cozymase and coenzyme I, and did not permit diphosphopyridine nucleotide, until as recently as 1953, but since then has used the last name almost entirely. The index of *Chemical Abstracts*, however, still uses codehydrogenase I rather than DPN.

Di- and Tri-phosphopyridine Nucleotide

There would be no objection whatever to the use of the names diphosphopyridine nucleotide and triphosphopyridine nucleotide if they did not indicate chemical structures, but the main objection is, in brief, that not only do they fail to give the structure of the coenzymes properly but also that they are the chemical names of other compounds. It is somewhat like using the name 'methyl acetate' for pyruvate; the name indicates a structure, but it is the wrong structure.

The names are derived from, though not the same as, names introduced by Warburg[6] in 1936 as convenient descriptions. The term 'pyridine nucleotide' was used, quite legitimately, to distinguish this class of compounds from purine nucleotides such as the adenine nucleotides. To distinguish the coenzymes from each other they were described as 'the diphospho-' and 'the triphospho-pyridine-nucleotide', at first with the definite article, although this was almost immediately dropped and the terms thereafter used as names in the German forms 'Diphospho-Pyridinnucleotid' and 'Triphospho-Pyridinnucleotid'.

'*Diphospho-*'. In 1939, F. G. Fischer[2], in his review on the subject, pointed out that these names, though concise, were incorrect. According to chemical terminology, 'phospho-*X*' denotes *X* combined with an additional phosphate group; but the word 'nucleotide' already includes a phosphate group, thus a 'diphospho-(di)nucleotide' would contain four phosphate groups, and not two as does the coenzyme. Fischer suggested that, especially in relation to the accepted names of the analogous flavin nucleotides, the names 'Pyridine-Adenine-Dinucleotide' and 'Phospho-Pyridine-Adenine-Dinucleotide' would be clearer. They would have the advantage of showing that the compounds are dinucleotides containing adenine, which was not indicated by the earlier names. Probably because of the outbreak of war in the same year, these suggestions did not receive the attention they deserved.

'*Triphospho-*'. It was at first believed that the three phosphate groups of triphosphopyridine nucleotide were joined in line, as in adenosine triphosphate, so that the relationship between the two coenzymes would be analogous to that between adenosine diphosphate and adenosine triphosphate. When the true structure of triphosphopyridine nucleotide was determined by 1950 by Kornberg and Pricer[7], it was found to be a monophospho-dinucleotide, so that the prefix 'triphospho-' became less appropriate.

'*Diphosphopyridine-*'. Perhaps the most serious objection arose when the names became anglicized,

Nicotinamide mononucleotide (NMN)	Nicotinamide—D-ribose—phosphate
Coenzymase Coenzyme I (CoI) Diphosphopyridine nucleotide (DPN) Nicotinamide-adenine dinucleotide (NAD)	Adenine—D-ribose——phosphate Nicotinamide—D-ribose—phosphate
Flavin mononucleotide (FMN)	*iso*Alloxazine—ribitol—phosphate flavin
Flavin-adenine dinucleotide (FAD)	Adenine—D-ribose——phosphate *iso*Alloxazine—ribitol—phosphate
Phospho-coxymase Coenzyme II (CoII) Triphosphopyridine nucleotide (TPN) Nicotinamide-adenine dinucleotide phosphate (NADP)	Phosphate Adenine——D-ribose——phosphate Nicotinamide—D-ribose—phosphate

Fig. 1 Structures of nicotinamide and flavin nucleotides

first I believe in about 1940 in the United States. The form used by Warburg, namely, 'Diphospho-Pyridinnucleotid', was clearly intended to be taken in the sense of diphospho(pyridinenucleotide), as shown by the hyphen and the capital P. The introduction of a space before 'nucleotide' gave a form with quite a different meaning. The name 'diphosphopyridine nucleotide' means quite unambiguously a nucleotide of diphosphopyridine, that is, a substance of the structure diphosphopyridine—D-ribose—phosphate, and it is not surprising that the biochemists have often been criticized by the organic chemists for using such names.

'*Dihydrodiphospho-*'. For the reduced or dihydro-forms, diphosphopyridine nucleotide and triphosphopyridine nucleotide yield names beginning with the undesirable prefix 'dihydrodiphospho-', which is a further objection.

'*Pyridine-*'. One may properly use the term 'purine nucleotides' for the whole class, but in referring to a particular nucleotide the name of the particular purine is used One says 'flavin-adenine dinucleotide' and not 'flavin-purine dinucleotide'. Correspondingly the word 'pyridine' ought not to be used for the names of particular nucleotides, unless they are in fact nucleotides of pyridine itself. 'Pyridine' should not be used when 'nicotinamide' is meant. The coenzymes are nicotinamide compounds, and the corresponding pyridine compounds are inactive as coenzymes[8]. The diphosphopyridine nucleotide system of nomenclature causes great difficulty in the rapidly expanding work on analogues of the coenzymes. If the nicotinamide nucleotides are called 'pyridine nucleotides', what can one call the pyridine nucleotides ? They surely cannot be called pyridine analogues of the pyridine nucleotides ! The use of diphosphopyridine nucleotide forces the use in current literature of such terms as 'pyridine-DPN' and 'APDPN' (for acetyl-pyridine diphosphopyridine nucleotide), in which the word 'pyridine' occurs twice, although there is only one pyridine ring in the compound. This is a very real difficulty.

'*DNP*'. DNP is the accepted abbreviation for dinitrophenol, a reagent much used in work on the coupling of biological oxidation and phosphorylation. Papers on DNP often contain many references to DPN, and the similarity makes them confusing and difficult to read.

'*FMN, FAD, NMN,* — ?'. Finally, the name diphosphopyridine nucleotide obscures the close and important analogy with the corresponding flavin compounds, shown in Fig. 1. Flavin-adenine dinucleotide (FAD) is the same substance with the nicotinamide end changed into the flavin structure. Flavin mononucleotide (FMN) is the same without the adenylic acid half of the molecule. Nicotinamide mononucleotide (NMN) is the coenzyme without the adenylic acid. These three names and the corresponding abbreviations are quite generally accepted, and there is no suggestion that they should be changed. To complete the scheme we should expect NAD for nicotinamide-adenine dinucleotide, thus :

FMN	NMN
FAD	NAD

The use of DPN instead of NAD breaks the logic of the nomenclature.

Summary of Objections

To recapitulate, the main objections to the name diphosphopyridine nucleotide are : (*a*) the coenzyme is not a nucleotide of diphosphopyridine as the name indicates ; (*b*) the name indicates the presence of four phosphate groups instead of two ; (*c*) it does not indicate that the coenzyme is a dinucleotide or that it contains adenine ; (*d*) the coenzyme is not a nucleotide of pyridine but of nicotinamide ; (*e*) the pyridine nucleotides, to which the name properly applies, are inactive as coenzymes ; (*f*) the use of the name for the nicotinamide compound makes it impossible to name the pyridine analogues satisfactorily ; (*g*) the combination 'dihydrodiphospho-' in the name of the reduced form is undesirable ; (*h*) the name is out of line with the FMN FAD NMN sequence and obscures the close chemical analogy with the flavin compounds ; (*i*) the corresponding name triphosphopyridine nucleotide suggests a triphosphate structure rather than the actual monophospho-dinucleotide structure.

In view of the strong chemical objections, the Enzyme Commission felt itself unable to recommend the continued use of the DPN system of nomenclature, particularly as a satisfactory alternative was available. The difficulty is not a chemical one, for there is no doubt about what the substance is : it is nicotinamide-adenine dinucleotide. It is the psychological difficulty of bringing the correct name into use, when an incorrect name has become well established. The Commission fully realizes that it is taking a serious step in recommending a change, and that there is likely to be some opposition, perhaps especially in America, as there was in Britain when DPN replaced Co I. However, this moment, when a real effort is being made to bring the terminology of enzymology into order, is the right one to put the coenzyme nomenclature right also. It is probably the last opportunity there will be of doing so ; if it is not done now, there is not likely to be another chance.

Some workers feel that the whole matter should be left optional, so that authors should be free to use any system they wish. The difficulty facing the Commission, however, was that, apart from the fact that it was given the task of dealing with coenzyme nomenclature, it also had to deal with the nomenclature of enzymes, and the names of a large number of enzymes depend on those of the coenzymes. It was therefore obliged to make a choice, in order to avoid the necessity for more than one systematic name for each of these enzymes.

Nicotinamide-adenine Dinucleotide

It has therefore decided to recommend that both Co I and DPN should be dropped, and that the

coenzyme should be known by its actual chemical name, nicotinamide-adenine dinucleotide, which may be abbreviated to NAD. It will be seen that this name avoids all the objections mentioned above, it indicates the structure of the compound, it brings out the analogy with FAD, and it makes it possible to name the analogues satisfactorily. The reduced form would be named dihydronicotinamide-adenine dinucleotide, which indicates correctly the part of the molecule that becomes reduced.

Nicotinamide-adenine Dinucleotide Phosphate

Triphosphopyridine nucleotide (CoII) might be named phospho-nicotinamide-adenine dinucleotide, but this is undesirable, for 'phospho-nicotinamide' is as incorrect as 'diphosphopyridine', and the reduced form would again have the 'dihydrophospho-' prefix. The recommended form 'nicotinamide-adenine dinucleotide phosphate' (NADP) avoids both these objections, and the extra P clearly indicates the formation from NAD by the addition of a phosphate group.

Coenzyme Analogues

Using the NAD system, the naming of the analogues becomes relatively simple and straightforward. For example, the pyridine analogue would be called pyridine-adenine dinucleotide, which might be abbreviated to PAD if desired. The deaminated form is at present called 'desamino-diphosphopyridine nucleotide', but this gives little idea of its nature, since the part of the molecule which is deaminated (the adenine) is not mentioned in the name. The obvious name for it is nicotinamide-hypoxanthine dinucleotide (NHD). The analogue of TPN in which the phosphogroup is attached to the 3′-position instead of the normal 2′-position is at present called '3′-triphosphopyridine nucleotide', which surely cannot be taken as indicating only one phosphate group attached to the 3′-position. The new system would give the natural name nicotinamide-adenine dinucleotide 3′-phosphate, perhaps abbreviated to NAD3P. Other analogues should cause no great difficulty. Abbreviations for the analogues are not being officially suggested; these are merely given as personal suggestions to illustrate the great advantages of the NAD system.

Possible Objections

It remains to consider whether the names now proposed for the coenzymes are in strict accordance with chemical terminology.

'*Nucleotide*'. Can nicotinamide mononucleotide and flavin mononucleotide strictly be termed nucleotides? If the definition of a nucleotide is restricted to substances that can be obtained from nucleic acids (that is, to purine and pyrimidine nucleotides), they cannot, because of the different bases present. Probably, however, nobody would wish to narrow the definition in this way, and it is much more reasonable to use the term to denote the chemical structure: base—pentose—phosphate. Clearly nicotinamide mononucleotide qualifies as a nucleotide.

The case of flavin mononucleotide is not so clear, for two reasons. In the first place, it contains not ribose but ribitol, so that the —CHOH— group in position 1 of the ribose is represented by a $—CH_2—$ group in the flavin. However, the term nucleotide is also applied to the deoxyribonucleotides, in which the —CHOH— group in position 2 of the ribose is replaced by a $—CH_2—$ group. It is not unreasonable, therefore, to make the term cover both modifications, although the change in the 1-position is the more important, since it prevents ring formation. In actual fact, the flavin compounds have been universally called nucleotides for well over twenty years, and there is no suggestion that their nomenclature should be changed.

In the second place, the term 'flavin' includes not only the base but also the ribitol. Therefore the term 'flavin nucleotide' must be understood as a nucleotide containing flavin, rather than a nucleotide 'of' flavin in the sense in which NMN is a nucleotide of nicotinamide.

'*Dinucleotide*'. Finally, can nicotinamide-adenine dinucleotide and flavin-adenine nucleotide be strictly termed dinucleotides? A purist might hold that the term implies that the two mononucleotides are linked in the same way as are the nucleotides in nucleic acid, by a 3′-5′-linked phosphate group. However, it would seem reasonable to consider a compound formed by the simple union of two mononucleotides to be a dinucleotide, particularly as the two classes of dinucleotides only differ in the point of attachment of a single bond.

'Dipeptide' has been quoted as an analogy where the term implies a definite point of linkage, but the analogy is not a valid one. A dipeptide is not formed by the union of two monopeptides, and the name is clearly based on different principles. A truer analogy would be 'disaccharide', which is used for a compound formed by joining two monosaccharides, without respect to the point of attachment.

Substances of the flavin-adenine nucleotide type have been called dinucleotides ever since their first discovery, and it is the only name available. It has probably appeared far more often in the literature in this sense than in the sense of the 3′-5′-linked compounds, and it would be unreasonable now to restrict its use to the latter type.

Conclusion

Such are the reasons which have led the Enzyme Commission of the International Union of Biochemistry to recommend the use of NAD and NADP. The Biological Chemistry Nomenclature Commission of the International Union of Pure and Applied Chemistry has also decided, after considering the possible alternatives, to recommend these names in place of the existing systems. Preliminary experience has shown that, even by those whose first reaction is to express a preference for the retention of DPN, the new names are very quickly found to be attractive and satisfactory. It is hoped that when they become the official recommendations of both International Unions the journals will give a lead in their adoption.

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STABILIZATION OF SEDIMENTARY COASTLINES

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THE major problems in coastal engineering originate from the mobility of sediment on the ocean floor in the vicinity of coastlines. Recent attempts at tracing this movement have involved the use of radioactive isotopes. These are costly, can be a hazard to health and generally suffer from a short life for tracking purposes. Unless material can be identified for at least twelve months, the net motion cannot be accurately ascertained.

Another approach appears simpler and more rewarding. It is based on the premise that the major features of a coastline emanate from centuries of interaction between geological and climatic factors. Of the former, wave action is the most important, particularly the action of swell, although storm sequences play their part by putting the sediment continually back into circulation. But in the end the predominant swell will give the coastline its particular outline, the recognition of which can help define the direction of the net sediment movement.

Model Tests

Tests have been carried out at the University of Western Australia to determine this equilibrium shape for some persistent swell direction. In a scaled model of a typical coastline, waves were generated at an angle of 45° towards a straight length of sandy beach in which were included three concrete sections resembling rocky headlands. Up-coast of the two beach units so formed, no sand replenishment occurred, and the coast was allowed to erode. Material was removed beyond the down-coast rock outcrop so as not to interfere with the natural shaping of the coastline.

The depth of the water in the model was constant at 7 in. and the beach was built up flat 3 in. above this level, with 20 ft. distance between headlands. No scale can be attached to the study as no prototype conditions existed for it; but if an undistorted scale of 1 : 60 were to be placed on the previous dimensions, the waves generated would have represented prototype waves of 10-sec. period and 5-ft. height approximately.

The waves were generated for intervals of several hours, after which a survey was made of the water-line and the underwater depths. This was continued until a quasi-permanent shape resulted in the up-coast unit, which occurred when any wave broke simultaneously around the length of the bay so formed. Fig. 1 shows the progressive stages in the beach-line of the two tests carried out. Fig. 2 shows the underwater contours at the end of each test.

The conclusions that may be drawn from these figures are:

(*a*) The equilibrium shape for a sedimentary coastline with oblique swell is that of a half-heart with the curved portion up-coast and the tangent section down-coast of the bay unit. Although the final shapes obtained in the up-coast bays of the model tests only approximated to this, it can be reasoned that with intermittent storm waves and slight alterations in wave directions the beach-lines would have been smoothed out. (It is intended to conduct such tests in the future.) The straight section should be almost parallel to the crests of the waves in deep water as they are refracted very little, whereas the curved portion of the bay is sculptured by the waves which are diffracted around the up-coast headland and refracted inside the bay.

(*b*) The shape of the down-coast bay at any time is dictated by sediment passing to it from the up-coast bay. In Fig. 1 the former is more eroded in Test No. 1 than Test No. 2 because less material has been removed from the up-coast unit. It can be seen how the supply of sediment to the down-coast bay will vary continuously throughout the full development of the up-coast bay.

(*c*) From the underwater contours of Fig. 2, it is seen that a circular current has developed which has caused a shoal near the tangent point. In Nature this is not likely to be so pronounced because of the intermittent nature of the wave occurrence and the influence of storm sequences. It is this circulation that has helped cause the irregular shape of the model coastlines, because the bottom contours influence the refraction pattern of the waves.

But the principal deduction is that, given a persistent swell from an oblique direction moving sediment down-coast, an erosive situation will cause bays of the half-heart shape to be fashioned between the headlands. Equally, the occurrence of such bays will indicate the net movement of sediment and the direction of the persistent swell.

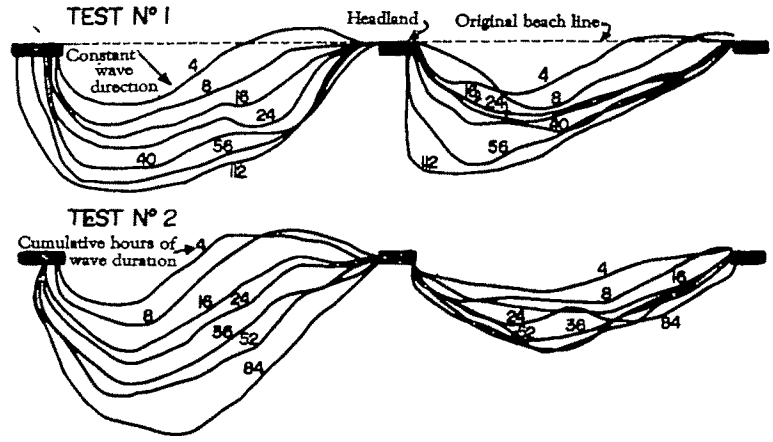

Fig. 1. The model beach-line after specified hours of wave duration from a constant direction

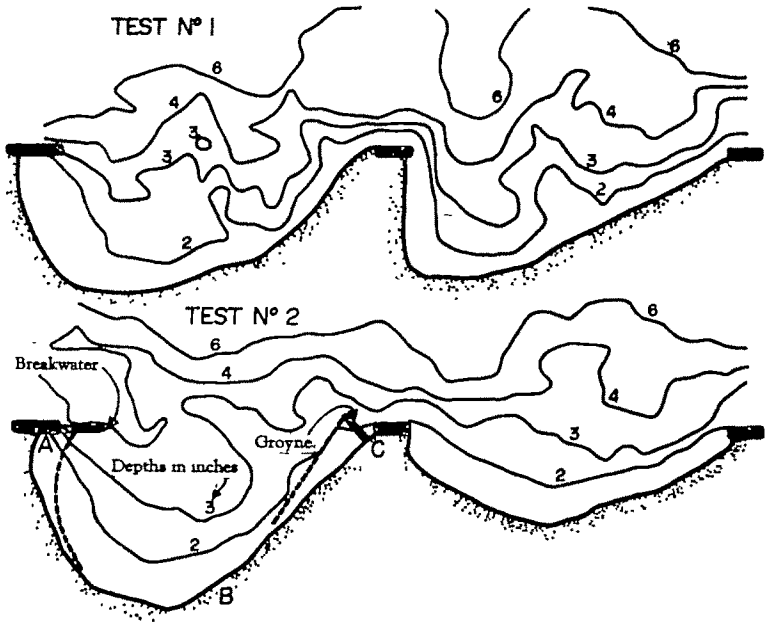

Fig. 2. Underwater contours in the model when the up-coast bay was in quasi-equilibrium. Accreting effect of the groyne and breakwater is shown dotted

Equilibrium Shape In Nature

To check the validity of this contention in Nature, a section of the South African coast has been chosen where a predominant wave direction is known to exist[1,2]. An outline of the coast is sketched in Fig. 3. As indicated, the persistent swell is from the south-west, and the bays have taken the half-heart form of which the tangent section tends to be normal to the wave direction. The shape of the continent would preclude much movement of sediment eastward around Cape Agulhas, and hence erosion has occurred along this section of coast over the centuries and is probably still doing so. Notwithstanding any seasonal or other reversals, the net or long-term movement of sediment is towards the east.

With the acceptance of conditions producing the equilibrium shapes of coastline, it is possible to produce a map showing the net sediment transport around the coastlines of the world. I am at present undertaking this, checking areas with less-pronounced features by referring to any ocean-swell charts which are available.

Stabilization of a Coast

Although reversals of drift can cause problems of erosion and silting in man-made coastal structures, the major difficulties arise from the long-term movement in one direction. Attempts at reducing or prohibiting this motion of sediment, generally by means of groynes, have met with varied success.

Referring to Fig. 2, it is apparent that if groynes are constructed between B and C they are equivalent to extending the headland out to sea and, assuming that there is still some longshore movement, the shoreline will advance by accretion to the new line shown dotted. The groyne here has accomplished its purpose. On the other hand, groynes built in an area AB, if it is still subject to erosion, will be ineffective. Should the bay be almost stable, groynes built there might sustain the coastline against seasonal fluctuations, although it has been shown elsewhere how groynes can accelerate erosion[3]. A more effective means of building up the coast between A and B is to extend the headland at A by means of a breakwater or other structure. The waves then have a new centre of diffraction and will effect a new shape as indicated.

On a coastline where there is substantial net movement of sediment, the best means of reducing it, or preventing it altogether, is to construct headlands about which the stable half-heart bays may form. The distances between these headlands should be of the order of miles, so that a wide expanse of

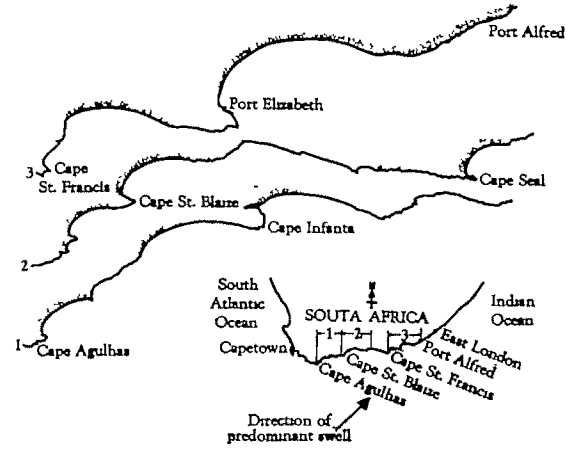

Fig. 3. Section of the South African coast where a south-westerly swell is predominant. Areas dotted indicate sandy shorelines as recorded in Admiralty Charts Nos 2083, 4 and 5

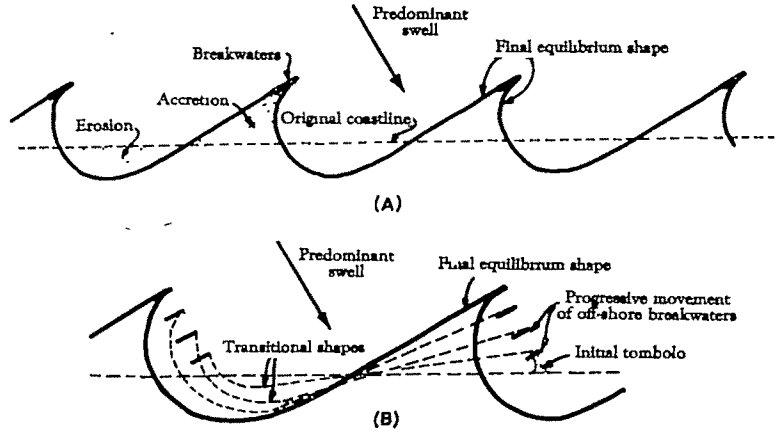

Fig. 4. (A) A method of preventing long-term movement of sediment along the coast, showing allowances for erosion and accretion. (B) A step method of approaching the stable half-heart shape by means of a movable offshore breakwater

ocean floor is affected. Allowance will therefore have to be made for erosion of some coastal areas and accretion in others is illustrated in Fig. 4*A*.

Because of the magnitude of structures required (to be effective in the first instance at the initially large distances offshore), a step procedure seems advisable. For example, a floating offshore breakwater sunk near the coast would cause a tombolo to form, after which a certain quantity of sand would accumulate. The breakwater could then be refloated and moved seawards. This process would need to be continued until the equilibrium shape was obtained as shown in Fig. 4*B*.

With such stable bays no sea defence works would be necessary, because a sedimentary coast can provide a defence which is far superior to any sea walls or revetments devised by man. But to allow for storm-cycles and the short-term reversals of drift, a sufficient width of beach should be allowed as working capital on which the sea can operate. Once the coast has been stabilized, by preventing the net movement of sediment, no long-term erosion need be anticipated and the 'active' beach width can be minimized.

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RADIATION-INDUCED IONIC REACTIONS: THE RETARDATION OF THE HOMOPOLYMERIZATIONS OF α-METHYL STYRENE AND β-PINENE BY WATER

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EVIDENCE has been presented[1,2] that the polymerization of *iso*butene initiated by ionizing radiation is a liquid-phase ionic reaction. It is also stated[1] that high polymer is formed by irradiation of α-methyl styrene at low temperatures, although no experimental results are quoted. As both *iso*butene and α-methyl styrene are examples of monomers that do not readily polymerize by radical mechanisms[2], it is to be expected that their facile homopolymerization would be favoured by an ionic mechanism. Nevertheless some recent communications[3,4] describe the γ-ray polymerization of α-methyl styrene as a radical process, and since the reported inhibitory effects of oxygen and benzoquinone on the radiation-induced polymerization of *iso*butene are equivocal with respect to either radical or ionic mechanisms, we wish to report new evidence in favour of the ionic polymerization of α-methyl styrene and β-pinene carried out *in vacuo* at the ambient temperature, about 30° C., of a cobalt-60 γ-ray source. Both these latter monomers were found to undergo a high degree of conversion to polymer without the marked reduction in rate as a function of amount of conversion that was previously observed for *iso*butene[1]. Again, in contrast to *iso*butene where the isolated polymer had an $\overline{M}_n$ exceeding 100,000 for less than 20 per cent conversion[1], the $\overline{M}_n$ values obtained for α-methyl styrene and β-pinene polymers in this investigation only correspond to about 15 monomer units in each case.

Our earliest experiments on β-pinene[5] established that the polymer yield was sensitive to the pre-treatment of the monomer and particularly to the drying agent employed. Thus it was found that the drying of freshly distilled monomer over sodium, magnesium perchlorate, phosphorus pentoxide and calcium hydride in a large number of separate experiments all gave initial values for *G*(-monomer) of less than 50, whereas passage of the β-pinene over activated alumina and silica gel gave corresponding polymer yields of 370 and 1,055 respectively. Further, the use of silica gel for drying the liquid within the vacuum apparatus gave the highest yields hitherto recorded for β-pinene, *G*(-monomer) exceeding 3,000 in some runs. The use of molecular sieve 4*A* (aluminium sodium silicate) as a drying agent for the vapour *in vacuo* gave corresponding *G* values around 400; but by this procedure the monomer suffered partial isomerization to α-pinene and camphene before irradiation. A confirmation that the polymer yield is affected by the efficacy of the drying agent and not by the removal of other impurities is provided by the effect of deliberately added water to β-pinene; in this instance a sample of water-saturated monomer gave polymer with only a *G*(-monomer) of 6·8.

A similar conclusion that water exerts a powerful retarding effect on the radiation-induced polymerization of α-methyl styrene is afforded by a comparison of yields obtained with monomer samples which had been first passed down silica gel and then either sealed *in vacuo* or else equilibrated with excess water in a vacuum line prior to seal-off. In the former case the *G*(-monomer) values measured with a dilatometer were of the order of 10,000 whereas the latter conditions gave an initial *G* value of about 10. Additional experiments in which concentrations of water below 0·02 weight per cent were added to samples during the course of polymerization showed a marked suppression of the original high rate.

The important role of water in these systems as a polymerization inhibitor cannot readily be explained in terms of the radical reactions (1) and (2):

$$R\cdot + H_2O = RH + OH \qquad (1)$$

$$R\cdot + H_2O = ROH + H \qquad (2)$$

Both these processes are endothermic in the forward direction, and the reverse of (1) is a facile reaction of OH radicals with organic compounds. In any event, these reactions would lead to chain transfer rather than the marked retardation which is observed.

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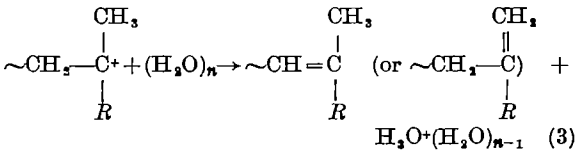
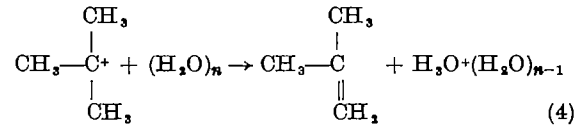
There is no evidence that water acts as a chain transfer agent in radical polymerization in aqueous systems[6]. However, in terms of an ionic polymerization mechanism, it is apt to consider the possibility that reaction (3) represents the interaction of water with a propagating cationic centre.



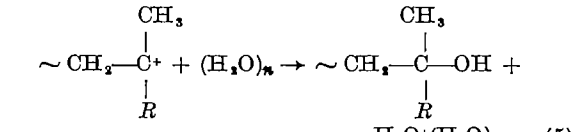
$$\sim CH_2-\underset{\underset{R}{|}}{\overset{\overset{CH_3}{|}}{C}}{}^{+} + (H_2O)_n \rightarrow \sim CH=\underset{\underset{R}{|}}{\overset{\overset{CH_3}{|}}{C}} \quad (\text{or} \sim CH_2-\underset{\underset{R}{|}}{\overset{\overset{CH_2}{\|}}{C}}) + H_3O^+(H_2O)_{n-1} \quad (3)$$

For the comparable reaction represented by (4):



$$CH_3-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}{}^{+} + (H_2O)_n \rightarrow CH_3-\underset{\underset{CH_2}{\|}}{\overset{\overset{CH_3}{|}}{C}} + H_3O^+(H_2O)_{n-1} \quad (4)$$

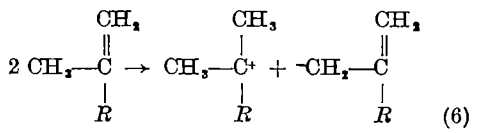
it can be calculated that in the gas phase ($n = 1$) it represents an endothermic process by 27 k.cal./mole. Nevertheless, if the hydronium ion H_3O^+ is fully solvated by surrounding water molecules, reaction (4) becomes exothermic by virtue of the heat of solution of H_3O^+, which amounts[7] to more than 100 k.cal./mole. Franklin[8] has calculated that the forward reaction (4) is 21 k.cal./mole exothermic when all the reacting species are solvated in dilute aqueous solution; by consideration of both heat and entropy changes it was also deduced[8] that the ratio of rate constants for the forward to the reverse reaction (4), at 25° C., is $1 \cdot 1 \times 10^{15}$. Also Evans and Halpern[9] have measured a similar activation energy of 22·6 k.cal./mole for the acid-catalysed addition of methanol to α-methyl styrene which involves a rate-determining step analogous to the reverse of (4) except for the replacement of water by methanol in the reaction. Thus this evidence suggests that the acid-base equilibrium in reactions akin to (3) and (4) in hydroxylic media lies well over to the right-hand side of the equation. Another exothermic process representing the interaction of a carbonium ion with water[8] is illustrated by (5) and represents the familiar fast solvolysis reaction of carbonium ions in aqueous media:



$$\sim CH_2-\underset{\underset{R}{|}}{\overset{\overset{CH_3}{|}}{C}}{}^{+} + (H_2O)_n \rightarrow \sim CH_2-\underset{\underset{R}{|}}{\overset{\overset{CH_3}{|}}{C}}-OH + H_3O^+(H_2O)_{n-1} \quad (5)$$

Similar calculations to those for (4) show[8] that reaction (5) is again highly favoured in the forward direction. We therefore surmise that the theoretical validity of reactions (3) and (5) for the removal of carbonium ions rests on the degree of solvation of the hydronium ion formed.

In a solvent of low dielectric constant it is likely that ions only maintain their existence as ion-pairs. The overall act of radiolysis to form a suitable ion-pair can be represented by (6) where the products consist of a carbonium ion and an allylic carbanion:



$$2\,CH_2-\underset{\underset{R}{|}}{\overset{\overset{CH_2}{\|}}{C}} \rightarrow CH_3-\underset{\underset{R}{|}}{\overset{\overset{CH_3}{|}}{C}}{}^{+} + {}^{-}CH_2-\underset{\underset{R}{|}}{\overset{\overset{CH_2}{\|}}{C}} \quad (6)$$

In the case of β-pinene the carbonium and carbanion centres may be located in a rearranged molecule[5]. The path of formation of the ions in (6) could involve the reaction of the parent ion with an olefin molecule to form the carbonium ion and an allylic radical[10,11], followed by electron capture by the latter.

According to this postulate, polymerization proceeds because of stabilized ion-pairs which allow the positive ion a sufficient lifetime to engage in many addition and transfer (to monomer) steps before eventual neutralization by the counter-ion. The presence of water in such a non-polar medium would lead to strong dipole association, whereby dispersed water molecules would be rapidly attracted by electrostatic forces to the vicinity of an ion-pair in a time which has been estimated by Ingold[12] to be less than 10^{-6} sec.; this period is of the same order as the estimated interval between successive propagation steps in the cationic polymerization of *iso*butene[3]. When sufficient water molecules are present in the solvation sheath of the ion-pair, reactions (3) and (5) provide a path for the removal of the positive propagating ion and its replacement by a solvated hydronium ion, thus quenching the polymerization.

In conventional ionic polymerization induced by Friedel-Crafts catalysts, traces of water often function as a necessary co-catalyst to form the initiating complex[13], but there is evidence that further increase in water concentration can lead to a reduction in polymerization-rate[14].

The practical importance of this effect of water in the radiation chemistry of olefins is that latent processes may not be fully realized unless the most rigorous drying of solvents is employed. Divergent yields have been reported by different workers[1,2] for the polymerization of *iso*butene at − 78° C.; since enhanced yields were obtained in this system[15] by the addition of solid powders such as silica gel and zinc oxide, these latter results may well be attributable to the dehydrating effect of such additives. In other work on the homopolymerization of α-methyl styrene, the recorded rates of polymer formation per 10^6 rads have ranged from 0·01 per cent conversion[3] to values between 0·7 and 5·0 per cent[4]. At the same temperature (30° C.) and with comparable dose-rates we have observed considerably greater yields amounting to more than 10 per cent conversion per 10^5 rads; even such yields may in truth be only limiting values, since a finite concentration of water must persist under the driest conditions hitherto employed.

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A PROBABLE FREE-RADICAL MECHANISM FOR SYMBIOTIC NITROGEN FIXATION

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SOME recent very significant experimental data on the evolution and isotopic exchange of hydrogen from nitrogen-fixing root nodules, obtained by Hoch, Schneider and Burris[1], serve to illuminate various possible reaction mechanisms of biological nitrogen fixation. Recent theoretical work[2] on the properties of aqueous nitrogen and current experimental work[3–5] on the physical-chemical properties of certain hæm proteins ('legoglobins'[4], *Lb*, rather than 'leghæmoglobin') associated[6–8] with symbiotic nitrogen fixation, when combined with the information provided by Hoch, Schneider and Burris, has brought to mind a new relatively simple set of hypotheses concerning the first several steps of symbiotic nitrogen fixation. Many of the previous ideas on this subject have been discussed and developed by Roberts[9]. The central hypothesis in the present quite different approach involves formation of the as yet unobserved but thermodynamically predicted[2] free radical N_2H. In conjunction with ideas and facts[3] about the affinity of legoglobins for nitrogen and other simple gases, and knowing[4] that the oxidation potential of iron in ferrolegoglobin is extraordinarily great, the hypothesis of N_2H formation accounts for a diversity of phenomena which is otherwise not understandable at present, as shown below.

Since about 1 per cent of the secondary[3,4] (. . .) hæm sites on hydrated ferrolegoglobin, $Lb\mathrm{Fe}^{+2}\underset{\mathrm{H}}{\mathrm{OH}}\ldots$ (or on oxygenated $Lb\mathrm{Fe}^{+2}\mathrm{O}_2\ldots$), are known[3] to be occupied by nitrogen at 293° K. and 1 atm., it is probable that the first step is :

$$\mathrm{N}_2 + Lb\mathrm{Fe}^{+2}\underset{\mathrm{H}}{\mathrm{OH}}\ldots \rightleftarrows Lb\mathrm{Fe}^{+2}\underset{\mathrm{H}}{\mathrm{OH}}.\mathrm{N}_2 \qquad (1a)$$

or, in aerobic regions of the nodule :

$$\mathrm{N}_2 + Lb\mathrm{Fe}^{+2}\mathrm{O}_2\ldots \rightleftarrows Lb\mathrm{Fe}^{+2}\mathrm{O}_2.\mathrm{N}_2 \qquad (1b)$$

or, on some 'hydroperoxyl sites' produced through the electron affinity of oxygen and subsequent reactions :

$$\mathrm{N}_2 + Lb\mathrm{Fe}^{+2}\mathrm{O}_2\mathrm{H}\ldots \rightleftarrows Lb\mathrm{Fe}^{+2}\mathrm{O}_2\mathrm{H}.\mathrm{N}_2 \qquad (1c)$$

An initial step (1*d*) like (1c) except with Fe^{+3} instead of Fe^{+2} is also possible. Because of the noble-gas character of nitrogen, no other possibilities for 'sorption' of nitrogen at room temperature and pressure than reactions of type (1*a*–1*d*) are presently evident ; and it will be shown below that nitrogen must be bound to some other molecule in order that certain fixation reactions can occur. The standard free energy changes for (1*a*–1*d*) are about + 2·4 k.cal./mole[3]. Considering the high concentration of *Lb* in nodules[4,7], this allows a relatively great molar concentration of sites occupied by nitrogen, compared with many enzyme-substrate systems, in spite of the fact that the sites are far from saturated.

A thermodynamically feasible second step is the production of atomic hydrogen, or the somewhat equivalent hydroperoxyl radical water, at the site of nitrogen attachment. This follows from knowing[5] that, at least for one *Lb* species, the oxidation potential for $Lb\mathrm{Fe}^{+2} \rightarrow Ln\mathrm{Fe}^{+3} + e^-$ at *p*H 5·7 is + 30 mV. relative to the standard hydrogen electrode and that this potential has the very large *p*H dependence $\mathrm{d}E^{0\prime}{}_{\mathrm{ox}}/\mathrm{d}(p\mathrm{H}) = +\ 126$ mV./*p*H. That is, in a certain range of low *p*H, ferrolegoglobin itself without any other substrate than the usual hydronium ions in the environment of the protein must be able to liberate appreciable concentrations of hydrogen. For example, at $p\mathrm{H}_{Lb} = 5{\cdot}7$ the free energy change for $Lb\mathrm{Fe}^{+2} + \mathrm{H}^+ \rightarrow Lb\mathrm{Fe}^{+3} + 1/2\mathrm{H}_2$ is − 690 cal./mole when (H^+) and (H_2) are at unit activity ; at $p\mathrm{H}_{Lb} = 5{\cdot}0$ but likewise with $a_{\mathrm{H}^+} = 1$, $a_{\mathrm{H}_2} = 1$, the corresponding free-energy change is − 2720 cal./mole. This means that at equilibrium, $P_{\mathrm{H}_2} = 4{\cdot}4 \times 10^{-7}$ atm. for *p*H = 5·7, and $P_{\mathrm{H}_2} = 1{\cdot}15 \times 10^{-2}$ atm. for *p*H = 5·0, when the activity ratio $\rho = (Lb\mathrm{Fe}^{+2})/(Lb\mathrm{Fe}^{+3})$ is assumed to be $1{\cdot}0 \times 10^{-2}$. If all but 0·5 per cent of the *Lb* is maintained in the reduced state by reactions in the nodule ($\rho = 5 \times 10^{-3}$) then for *p*H = 5·0 the P_{H_2} can reach the relatively high value of $0{\cdot}04_6$ atm., comparable to what was found by Hoch, Schneider and Burris some 300 min. after nodule excision. This range of *p*H values is about one unit lower than the gross average values found[5] in soybean roots and nodules ; but lower values in *Lb*-containing micro-regions of the nodule would be consistent with the strongly acid groups that are associated with the quite low isoelectric point of legoglobins (*p*H 4·4–4·7)[10]. It should be recalled[4,7] that *Lb* exists in rather high concentrations in root nodules.

Not only does the above analysis account for the observed hydrogen production so far as equilibrium may be concerned ; but it also implies the intermediate production of H radicals or their equivalent, in harmony with current ideas about the mechanism of hydrogen liberation from electrodes or polyelectrodes. Thus we expect :

$$Lb\mathrm{Fe}^{+2}\underset{\mathrm{H}}{\mathrm{OH}}\ldots + \mathrm{H}^+_{\mathrm{aq.}} \rightleftarrows Lb\mathrm{Fe}^{+3}\underset{\mathrm{H}}{\mathrm{OH}}\ldots + \mathrm{H} \qquad (2a)$$

or, in aerobic regions :

$$Lb\mathrm{Fe}^{+2}\mathrm{O}_2\ldots + \mathrm{H}^+_{\mathrm{aq.}} \rightleftarrows Lb\mathrm{Fe}^{+3}\mathrm{O}_2\mathrm{H}\ldots \rightleftarrows Lb\mathrm{Fe}^{+3}\underset{\mathrm{H}}{\mathrm{OH}}\ldots + \mathrm{HO}_2 \qquad (2b)$$

Note that hydrogen atoms would be produced at the same site that promotes nitrogen attachment, a situation very favourable kinetically for a reaction between nitrogen and hydrogen atoms, even though at equilibrium the hydrogen atom concentration must be very small relative to hydrogen. Furthermore, even in the presence of some oxygen a high reductive potential can be maintained by *Lb*, accord-

ing to the results of George and Stratmann[11] for the quite similar myoglobin.

The third step would then be a direct or indirect combination of nitrogen and hydrogen atom, the simplest being:

$$Lb.N_2 + H \rightarrow Lb.N_2H \qquad (3)$$

In equation (3) $Lb.N_2$ represents any one of the three complexes produced in (1*a*), (1*b*) or (1*c*). The reason for emphasizing the existence of a complex in equation (3) is to bring out the fact that a free radical and a molecule may not combine without some means of dissipating the binding energy; in this case the known forces[3] exerted by the hæm protein on nitrogen ('secondary gasation') can serve such an essential purpose. It has already been shown[2] that the standard reaction for $N_2 + H_2 \rightarrow N_2H$ would be spontaneous; and that a standard free energy investment of 32 k.cal./mole would be required to break the N_2. H bond. Furthermore, as reaction (3) proceeds it would have to shift equilibrium (2*a*) and lead to the appearance of (oxidized) ferrilegoglobin, which is what Hamilton, Shug and Wilson[12] found in reduced nodule extracts when helium was replaced by nitrogen. However, equilibrium (2*a*) must be maintained with a preponderance of *Lb* in the ferrous form for an appreciable yield of hydrogen. This is in harmony with the observations of Keilin and Smith[7] that at all stages of nodule development no ferrihæm proteins were observed ($\rho \gtrsim 10^{-2}$). In order to maintain such a favourable reduction potential at the iron site, some coupling of legoglobin with an electron transport system is required; and such a coupling is likely according to Falk, Appleby and Porra[13]. Also, an essential link in such an electron transport system having a one-electron transfer at one end is very probably a molybdoflavoprotein[14], especially since molybdenum is a specific requirement for nitrogen fixation. Nevertheless, a molybdenum reduction site would not be adequate for nitrogen fixation even though its reduction potential for hydrogen atom formation were more favourable than that of an $LbFe^{+2}$ site, because the concentration of molybdenum in the nodule is too small to furnish an adequate number of sorption sites for the weakly bound nitrogen.

Subsequent steps for the successive addition of hydrogen atoms to N_2H_n are obvious and thermodynamically feasible[2], leading to the eventual production of hydrazine, in harmony with the elegant nitrogen-15 tracer experiments of Bach[15]. However, alternative pathways including even oxidative steps[9] may develop at this or even earlier stages owing in part to the possibility[2] of a direct succession of electron, proton captures by N_2H_n. Of course, once N_2H_4 has been formed, the subsequent reduction to $2NH_3$ follows easily through conventional reactions or perhaps through a hydrazine reductase, such as a molybdoflavoprotein. The present view is thus consistent with the idea stressed by P. W. Wilson and R. H. Burris[14] that NH_3 is the "key intermediate" between inorganic and organic nitrogen.

Innumerable side or parallel reactions will undoubtedly develop as soon as N_2H is produced, especially under aerobic conditions. Only two of these need be considered here, to illuminate the possible need[9] for a reinterpretation of the usual Michaelis–Menten constant of the symbiotic nitrogen-fixing process. The back-reactions:

$$2N_2H \rightarrow 2N_2 + H_2 \qquad (4a)$$

or

$$2N_2H \rightarrow N_2 + N_2H_2 \qquad (4b)$$

are thermodynamically feasible[2], and imply rate laws second order with respect to N_2H, meaning that as N_2H production increased, that is, as occupation of active sites by nitrogen increased, a point would be reached where the back reactions would cut down drastically on the increase in net fixation-rate with increasing P_{N_2}, otherwise expected when the reactive sites are not saturated. Thus the apparent fact that the "N_2-fixing complex in nodules is half-saturated at a P_{N_2} of about 0·025 atm.[1]" may actually reflect, in part, the effect of back reactions (4*a*) and (4*b*) going on at a considerable rate. This consideration helps one to understand how the N_2-fixation rate is not appreciably enhanced above $P_{N_2} \approx 0{\cdot}05$ atm., even though only about 1 per cent of the total hæm sites of all kinds are occupied. Further consideration shows, however, that of these the hydroperoxyl site, probably the most active type, must be almost fully saturated at $P_{N_2} = 1$ atm. if the effect of hydrogen, of nitrogen and of the binding of O_2..H.. N_2 are taken into account.

The above hypotheses explain a number of striking facts about symbiotic nitrogen fixation, some of which are discussed briefly below:

(1) *N_2-nitrogen inhibits hydrogen evolution*[1]. The formation of N_2H would divert hydrogen atoms from their normal fate of eventually combining, in association with some third body, for example, protein, to form hydrogen molecules.

(2) *N_2-nitrogen is essential for promoting an appreciable exchange reaction between deuterium and endogenous hydrogen*[1]. The presence of free N_2H would allow the exchange $N_2H + D_2 \rightarrow N_2HD + D$, among others, because the relatively weak binding free energy between nitrogen and hydrogen atoms (32 k.cal./mole) implies that the H in N_2H is relatively free to act as a kind of quasi H-atom; and $H + D_2 \rightarrow HD + D$ is known[16] to occur readily even in the low-temperature range of + 10° to 100° C.

(3) *H_2-hydrogen inhibits the evolution of hydrogen, itself.* From the present point of view, the evolution of hydrogen would probably depend on two slow processes in series: (*A*) Production of hydrogen atoms from $LbFe^{+2}$; and (*B*) conversion of the hydrogen atom to the molecule, either by (*a*) a very slow process of two hydrogen atom migrations or attachments to the same third-body site, analogous to the probable mechanism giving rise to hydrogen over-voltages on electrodes, and/or (*b*) a more rapid process near the reactive site such as $Lb—H_n + H \rightarrow Lb—H_{n-1} + H_2$, a type common to free radical reactions. Recent preliminary work in this laboratory[5] indicates that nodules treated with hydrogen slowly yield a different, more stable, type of ferrolegoglobin $(LbFe^{+2})_{H_2}$ than that extracted under argon $(LbFe^{+2})_A$ or under air $(LbFe^{+2})_a$. The $(LbFe^{+2})_{H_2}$ had an oxidation potential smaller than that of $(LbFe^{+2})_a$ by about 40 MV.; and at 30° C. the $(LbFe^{+2}O_2)_{H_2}$ auto-oxidized to $(LbFe^{+3})_{H_2}$ only about one-half as fast as fresh $(LbFe^{+2}O_2)_A$. Also, in the potentiometric titration of $LbFe^{+3}$ with phthiocol, several equivalents of hæm-protein side-groups, as well as iron, were easily reducible. Hence I tentatively conclude that hydrogen molecules will convert $LbFe^{+2}$ to a less-reactive form which will at

least slow down step (*A*) above; and possibly alter the rate of step (*B*) as well. This would mean that the intrinsic evolution of hydrogen, itself a possibly unavoidable by-product of the step that produces the essential hydrogen atoms, may eventually lead to a substantial reduction of nodule effectiveness.

(4) *H_2-hydrogen is a specific competitive inhibitor of N_2-fixation.* (*A*) Hydrogen is known[3] to attach itself to legoglobin, with a standard uptake free energy of about + 2·3 k.cal./mole, in a way quite similar to that of nitrogen. If hydroperoxyl sites were the most active type, even though the least abundant, the fixation-rate in the absence of hydrogen would be characteristic of secondary sites nearly saturated with nitrogen because of specific $O_2..H..N_2$ binding forces. In this case the rate would be decreased through displacement of nitrogen by hydrogen. (*B*) The conversion of $LbFe^{+2}$ to a hydrogenated form that produces atomic hydrogen at a lower rate, evidence for which is given in (3), must also result in a decrease in N_2H formation, that is, in rate of nitrogen fixation. (*C*) To some extent molecular hydrogen would also complete for the bound HO_2 radicals, analogous to the competition for OH radicals postulated by Pethica, Roberts and Winter[17], but this must be a second-order effect in view of the slow molecular deuterium exchange-rate in the absence of nitrogen.

(5) *Carbon monoxide inhibits nitrogen fixation but is not primarily a competitive inhibitor.* (*A*) The known attachment of carbon monoxide to legoglobin, forming $LbFe^{+2}CO...$, would not destroy the secondary sites for nitrogen attachment[3,4] except at extreme carbon monoxide pressures, though it would alter (probably lower) the oxidation potential of $LbFe^{+2}$; (*B*) The principal effect of carbon monoxide should be to divert hydrogen atoms away from N_2H formation, according to the known[16] complicated reactions: $H + CO + M \rightarrow HCO$, followed by a set of reactions producing formaldehyde, glyoxal and polymers; and possibly by another parallel set regenerating atomic and molecular hydrogen.

(6) *Carbon monoxide strongly inhibits exchange of endogenous hydrogen with deuterium.* The reactions in (5) (*B*) incorporate hydrogen atoms into compounds much more stable than N_2H, hence are much less likely to furnish exchangeable quasi hydrogen atoms. This implies that those reactions which might regenerate atomic and molecular hydrogen from HCO in the gaseous state are not appreciable under conditions prevailing in the nodule.

(7) *O_2-oxygen is a requirement for symbiotic nitrogen fixation, but there is some inhibition by oxygen at high pressures.* Hydroperoxyl sites on ferrolegoglobin (equation (1c)) are probably the most active though the least abundant type; and also should be nearly saturated by nitrogen at 0·1 atm. This follows from the presence of a loosely bound atomic hydrogen on the hydroperoxyl site adjacent to the secondary site; and from the known affinity between atomic hydrogen and nitrogen. Also, the standard free energy for the change $N_2 + HO_2 \rightarrow N_2H + O_2$ is probably[2] of the order of only a few k.cal./mole but negative. At high values of P_{O_2} the secondary sites could just as well be occupied by oxygen as by nitrogen (that is, by molecules of similar size, shape and polarizability), according to the theory of secondary gasation[3,4]. Of course, the above considerations are not complete or necessarily definitive because of the influence of oxygen on bacterial metabolism.

It must be emphasized that some of the properties of legoglobin referred to in the present discussion may not represent the exact behaviour of the native material within the intact nodule. This is underlined by the fact that legoglobin oxidizes[7] and auto-oxidizes[5] rapidly when extracted aerobically, that it is susceptible to change in the presence of hydrogen and that it is sensitive to dialysis and changes of *p*H and ionic strength[5]. There can be little doubt that the properties of the native legoglobins must be known before the chemical processes in nitrogen-fixing nodules are understood, in accordance with Keilin's early ideas are in harmony with the recent work of Falk, Appleby and Porra[13] showing a correlation between deficiencies of hæm synthesis within the nodule and ineffectiveness of nodules in respect to nitrogen fixation.

It may be concluded that the present set of hypotheses provide a consistent way of viewing most of the central qualitative and semiquantitative aspects of symbiotic nitrogen fixation, excluding for the time being the more difficult questions about the magnitudes of the various rate constants. In view of the complexity of interrelated facts that must be explained, it is difficult at this stage to see an alternative set of hypotheses that could differ radically from the present ones. It would appear worth while to look for the free radical intermediates suggested here, using the powerful high-resolution electron spin resonance techniques now available in some laboratories; but keeping in mind that the free radical spectrum of the expected water, atomic hydrogen, N_2H_n and *Lb* intermediates as a function of time will undoubtedly be most complex. The liberation of molecular hydrogen from aqueous legoglobin and the detection of hydrogen atom radicals in that process would also be an important test of the present hypotheses. Eventually, of course, it should be possible to find conditions for the fixation of nitrogen through the mediation of a protein molecule having properties at least very similar to those of the legoglobins.

I am grateful for support from the Herman Frasch Foundation and the Utah Agricultural Experiment Station in this work.

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INTERACTION ('PERIPOLESIS') OF MACROPHAGES AND LYMPHOCYTES AFTER SKIN HOMOGRAFTING OR CHALLENGE WITH SOLUBLE ANTIGENS

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IN conjunction with an investigation of the lymphoid reactivity to tissue homografts[1], we have recently examined the behaviour of living cells in cultures of lymphoid tissue taken from rabbits which either had received skin homografts or had been challenged with an intravenous soluble antigen.

The explants of lymphoid tissue were set up in a simple culture chamber[2] in plasma clot, with a fluid medium composed of equal parts of human serum and a chemically defined medium[3]. The activity of the cells, and especially of the macrophages and lymphocytes, in the outgrowth from these explants was recorded on 16-mm. film by time-lapse phase-contrast cinemicrography, at 12 pictures per min.

In the initial experiments homografts of skin 2 cm. in diameter were applied to the ventral aspect of the ears, 1–2 cm. from the external auditory meatus, in thirteen young adult male rabbits. Eight to ten days later the first regional (parotid) lymph node draining the area of the graft was removed aseptically. Since it was known that the upper half of the node was more likely to have received lymph from the grafted area and to contain the reactive cortex[1], tissue from this region was taken for culturing. A total of about 120 explants from these lymph nodes were cultured. The effect of a soluble antigen has also been examined by challenging seven rabbits with a single intravenous injection of 5 ml. of horse serum. Three to twelve days later the spleens were removed for culture; a total of about 150 explants were obtained from the seven animals. Control cultures were provided by about 100 explants of spleen from five normal rabbits which had not been exposed to the antigen.

When the cine film of the cultures of the antigenically challenged lymph nodes and spleens was studied, an association was noticed between some of the macrophages and small lymphocytes. The association consisted of the movement of lymphocytes close to the surface of particular macrophages. The cells concerned showed their normal motility during the association, the macrophages moving slowly and at random, while the contiguous lymphocytes continued to move relatively rapidly around the edge and over the upper free surface of the macrophage. This association was seen to persist for prolonged periods; during most of this time the contact between lymphocytes and macrophages appeared to be of a surface-to-surface nature, although the more rapidly moving lymphocytes would at times move away, only to return again to the macrophage.

Prolonged contacts of this nature were not seen in the control cultures of spleen. Though random contacts between macrophages and lymphocytes occurred quite frequently, such contacts never persisted for more than a few minutes.

Figs. 1–4 are enlargements from the original 16-mm. film. In Fig. 1 the arrow indicates a small lymphocyte in close association with the macrophage immediately above, in a culture of lymph node which had drained a homograft of skin. Fig. 2 shows the same two cells, still in contiguity, about 5 hr. later. Figs. 3 and 4 illustrate a similar association between a group of lymphocytes and a macrophage in an explant of spleen which had been challenged intravenously with horse serum. The lymphocytes are so closely packed that they largely obscure the macrophage which is only partially visible. The time-interval between Figs. 3 and 4 is approximately 75 min.

An association between normal small lymphocytes and cells in mitosis, megakaryocytes and malignant cells, has been recorded by Pulvertaft and his colleagues[4,5]. They examined explants of normal and pathological human lymph nodes and bone marrow *in vitro* using time-lapse phase-contrast cinemicro-

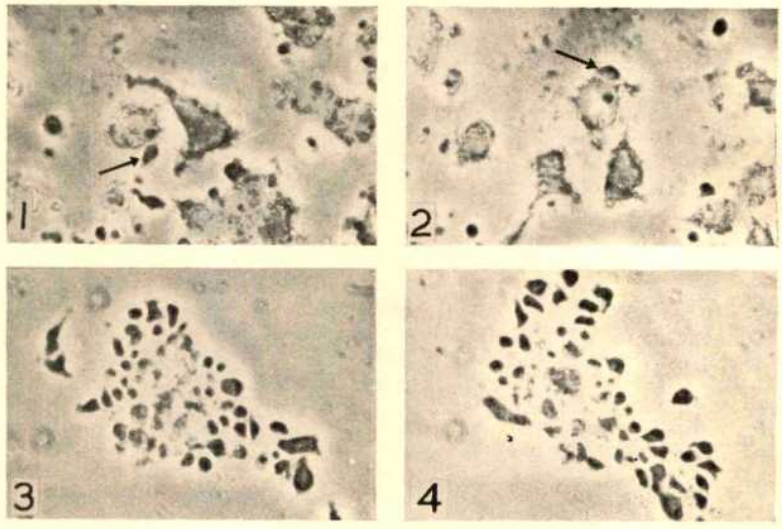

Fig. 1. (1) Cells in the outgrowth from an explant of lymph node which had drained a homograft of skin. Two days *in vitro*. (2) The same cells 5 hr. later. (3) A group of lymphocytes surrounding and partially obscuring a macrophage. Explant of spleen from rabbit injected intravenously with 5 ml. horse serum. Two days *in vitro*. (4) The same field 75 min. later

graphy, and, in many instances, observed the entry of normal small lymphocytes into the cytoplasm of living malignant cells. The cytoplasmic invasion of epithelia, fibroblasts, endothelial cells and ova by small lymphocytes is now firmly established[6]. For these phenomena wherein lymphocytes become adherent to other cells or apparently pass over or into them, Pulvertaft and his colleagues have suggested the name 'emperipolesis' from the Greek 'εμπεριπολησις'—'inside round about wandering'.

The interaction between normal small lymphocytes and macrophages has not been recorded previously, but an association between 'malignant' lymphocytes and macrophages has been shown to occur in tissue obtained from humans with reticuloses[5] and from mice with certain lymphocytic tumours[7].

In our experiments there was no evidence of the entry of small lymphocytes into the cytoplasm of the macrophages. We suggest, therefore, that to this phenomenon of free lymphocytic movement around the perimeter of a cell for hours at a time but without entry into its cytoplasm, the name 'peripolesis' be applied.

The significance of peripolesis is by no means clear. The pattern of our experiments and the results observed would suggest that the phenomenon might be related to the early (radio-sensitive) phase of antibody production. It seems improbable that the foreign human proteins present in the culture medium could be involved in the cellular interaction, as peripolesis was not observed in the control cultures. It might be that the lymphocytes are transferring nutritive substances[8] necessary for antibody production to the macrophages. An antigen-antibody attraction, which might be the explanation of the association which Nossal[9] observed between *Salmonella adelaide* and sensitized plasma cells, cannot be excluded as an explanation of peripolesis. The final possibility exists that the macrophages, having taken up antigen from the extra-cellular fluid *in vivo*[10], are in the process of supplying an antigen-complex to the lymphocytes which then stimulates antibody production.

Though it is now established that the plasma cell series synthesizes antibodies[10,11], other workers have suggested that the stem cell of antibody production may be the macrophage[10,13], primitive reticular (mesenchymal) cell[12] or lymphocyte[13]. Our observations are consistent with those of Roberts *et al.*[13], who showed that subcutaneous or intramuscular injections of cell suspensions containing both macrophages and lymphocytes into X-irradiated immunologically inert rabbits would result in the transformation of these cells, after antigenic challenge, into large pyroninophilic antibody-producing cells.

The suggestion[10] that the macrophages may provide the first link in a chain leading to antibody production would explain the prolongation of skin homograft survival after injection of trypan blue[14], by temporarily impairing the capacity of macrophages to take up antigen derived from the graft.

The phenomenon of peripolesis in antigenically challenged animals is being investigated at the present time and will form the basis of a communication in the near future.

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VISUAL PIGMENT FROM A PURE-CONE RETINA

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ONLY one of the numerous visual pigments that have been extracted to date from the retinæ of vertebrates has any claim to be regarded as a cone pigment[1]. This is iodopsin[2], discovered by Wald in 1937 in the chicken retina. Extracts of chicken retinæ contain a mixture of photosensitive pigments: iodopsin with $\lambda_{max.} = 562$ mμ and a rhodopsin with $\lambda_{max.} =$ about 500 mμ. Since the rhodopsins are known to occur in some pure-rod retinæ, and since the chicken retina is rich in cones as well as rods, it has been assumed that the chicken pigments are not mixed *in vivo* but exist separately, the rhodopsin being in the rods and the iodopsin in the cones.

According to the Duplicity Theory, scotopic vision is mediated by rods, and photopic vision by cones. Consequently, the fact that the scotopic and photopic visual functions of the chicken, as measured by Honigmann[3], roughly correspond to the absorption spectra of chicken rhodopsin and iodopsin also supports the view that these pigments occur in the rod and cones respectively.

These arguments for believing iodopsin to be a cone pigment, though practically compelling, are nevertheless indirect. Until it becomes possible to divide rods from cones and to extract them separately, some doubt remains. Such doubt, which may seem trifling in the case of iodopsin, can be a serious obstacle to interpretation in other instances[4] where extraction of a mixed rod-cone retina likewise yields a mixture of photosensitive pigments but where (unlike the chicken) no sensitivity functions have been measured to provide a guide in allocating the pigments.

In some species of nocturnal animals, the retinæ are of the pure-rod type. In such cases any extractable visual pigment can be confidently assumed to be a rod pigment. Even when a few cones are also present in an otherwise pure-rod retina (for example, rat), this is still held to be a safe assumption, for it is commonly

supposed that the amount of cone pigment is small in comparison with the amount of rod pigment.

Conversely, in those diurnal species which have pure-cone retinæ one could assume that any extracted visual pigment is a cone pigment. Unfortunately, there are not many species which possess such retinæ, and all attempts to obtain visual pigment from them have so far proved unsuccessful[1]. Among the well-authenticated cases of a pure-cone retina is that of the grey squirrel (*Sciurus carolinensis leucotis*)[5]. This article briefly describes a recent successful attempt to extract visual pigment from it.

Extraction of the Squirrel Retinal Pigment

In August 1959, a batch of 40 grey squirrels was received. Between that date and February 1960, several retinal extracts were prepared, the procedures used being varied slightly in order to determine the best conditions for obtaining the visual pigment. The squirrels were fed throughout on standard 41*B* diet with occasional carrot and cabbage. For the first six weeks they also had mixed cereal. The animals thrived on this diet, and the last representatives of the batch weighed about twice as much as when they were first received.

The best extraction procedure found so far is given in the following account of one of the final experiments. Nine squirrels, of total weight 5·9 kgm., were dark-adapted overnight (17 hr.). All subsequent operations were also conducted in the dark room with the aid of a deep red safe-light. The squirrels were first anæsthetized by chloroform. Each animal was then killed by an intraperitoneal injection of nembutal. The eyes were removed and washed in water. Peripheral incisions at about the level of the ora serrata were next made in each eye. The front of the eye, including the lens, could then be lifted away leaving the posterior hemisphere (which contained the retina) full of vitreous humour. The next step was to slide forceps under the retina (which was quite loose) and to grasp it firmly at its junction with the optic nerve. The retina, lying across the limbs of the forceps, was then gently pulled away whole with its vitreous, and placed in McIlvaine's *p*H 7 buffer solution. With gentle shaking, the rather adherent vitreous separated from the retinæ, so that by subsequent centrifuging they were precipitated, leaving blobs of vitreous floating in the supernatant buffer solution. This was removed. Sucrose solution (40 per cent) was then added to the retinæ, and the mixture vigorously shaken. This caused the outer segments of the visual cells (cones) to break away from the retinæ. On centrifuging the mixture, the heavier retinal debris was precipitated to the bottom of the tubes, leaving a slightly cloudy supernatant suspension of visual cells in the sucrose solution[6]. This was pipetted off. A further yield was obtained by shaking the retinal residues a second time with sucrose solution, and repeating the procedure.

The visual cells were precipitated by diluting the suspensions with three volumes of McIlvaine's *p*H 4·6 buffer, and centrifuging them for 35 min. at 4,000 r.p.m. The clear supernatants were then pipetted off, leaving behind compact sediments of visual cells. These were bulked into a single tube with the aid of 4 ml. of *p*H 4·6 buffer (removed after further centrifuging). The combined outer limbs were then extracted with 0·5 ml. of 3 per cent digitonin for 1 hr., after which time the mixture was centrifuged and the clear extract withdrawn and made alkaline by the addition of 0·05 ml. of saturated sodium borate solution (first extract). Further extraction with another 0·5 ml. of the digitonin solution, this time for 25 hr., yielded a second extract which was made alkaline as before. The two extracts were a pale pink colour and faded to pale yellow on exposure to light. The spent cells were pure white. In order to obtain information on the total amount of visual pigment in the squirrel retina (see below), the retinal residues were likewise extracted twice with 0·5 ml. portions of 3 per cent digitonin. These extracts were naturally more contaminated and contained only a trace of visual pigment.

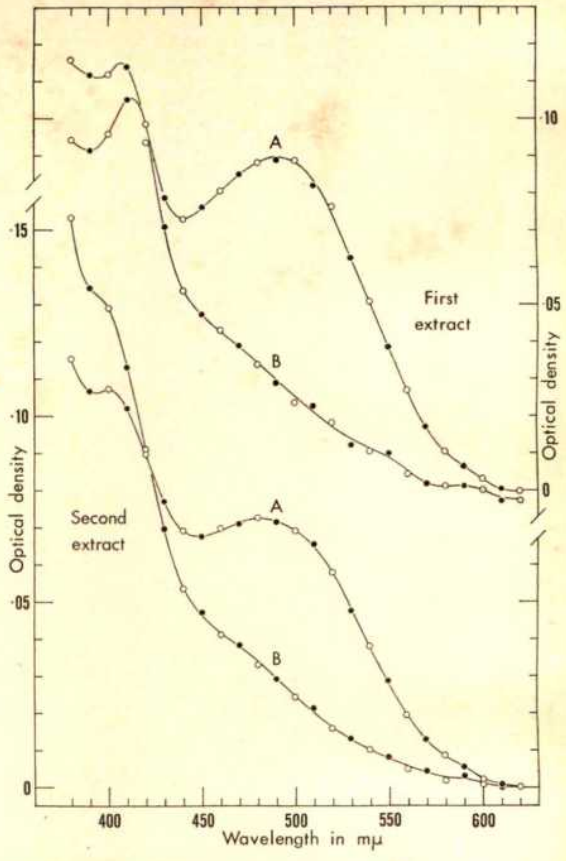

Fig. 1. Density spectra of the first and second extracts of squirrel visual cells before (*A*) and after (*B*) total bleaching. The outward measurements from 380 mμ to 620 mμ are given by the empty circles; the return intervening measurements, by the black circles. Measurements were made at 35·5° C. on the first extract (at lower temperatures the extract became reversibly cloudy), and at 20° C. on the second extract

Nature of the Squirrel Retinal Pigment

The density spectra of the first and second extracts before and after complete bleaching by a 15-W. lamp are given by the curves in Fig. 1. From the shapes of these curves it is clear that, in spite of the washing procedures described above, blood pigment and other impurities were present, in addition to visual pigment. Because of this contamination (relatively less in the first than in the second extract) the maxima for the unbleached extracts—at 490 and 480 mμ respectively—lie at shorter wave-lengths than would otherwise have been the case.

By presenting the results in the form of a difference spectrum (curve for unbleached, minus curve for bleached extract) the contribution of stable impurities

is eliminated. Moreover, a difference spectrum for an alkaline extract normally has its maximum at a wave-length only slightly longer than that for the pure visual pigment. The difference spectrum for the squirrel pigment (second extract) is shown by the circles in Fig. 2. It has $\lambda_{max.} = 504$ mμ, and agrees closely with that found by Bridges[7] under similar conditions for the hamster pigment (crosses). This latter is a 'rhodopsin', that is, a visual pigment based on retinene$_1$. Bridges gives the maximum for the pure hamster pigment at 502 mμ, and we may conclude that the squirrel pigment must be very similar.

None of the extracts prepared in the present investigation was sufficiently dense to allow a useful analysis by the method of partial bleaching[8]; consequently, the homogeneity of the squirrel pigment could not be definitely established. All extracts, however, yielded difference spectra identical within experimental error with that shown in Fig. 2.

The fully bleached extracts showed an unexpectedly high absorption in the 450–550 mμ range (see Fig. 1). This high absorption cannot be ascribed to the Soret band, nor to unbleached visual pigment (since the extracts were exposed to light until no further changes took place). Consequently it must be due to a photoproduct. Some information on this may be obtained as follows. At wave-lengths longer than 500 mμ, the contribution of impurities to the density spectrum of an unbleached extract is small. Consequently, with the aid of the visual pigment nomogram[9] it is possible, from this spectral region, to obtain an estimate of the amount of pure visual pigment present. By subtracting the density spectrum appropriate to this amount from the 'unbleached' curve, a remainder is left which is the contribution of the impurities. If this same contribution is now subtracted from the curve for the bleached extract, we are left with the density spectrum for the pure photoproduct. When this is

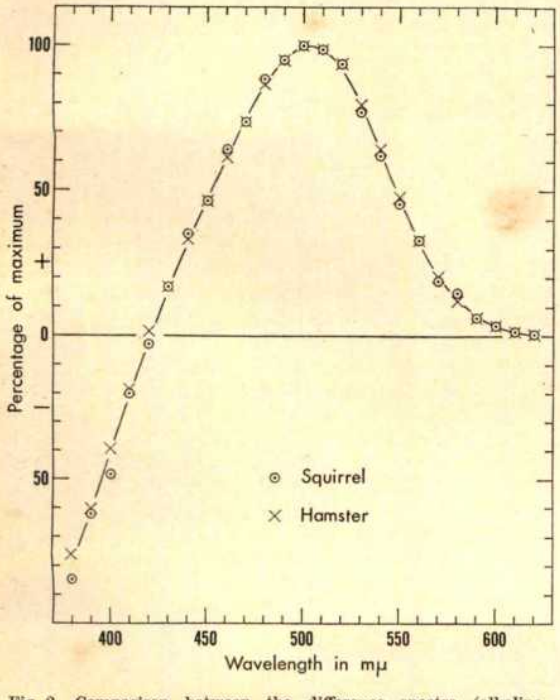

Fig. 2. Comparison between the difference spectra (alkaline conditions) of the squirrel and hamster visual pigments. Squirrel data (20° C.) from second extract; hamster data (25° C.) from Bridges (ref. 7)

done with the curves of Fig. 1, it is found that, in addition to a rising extinction towards the short-wave end of the spectrum, the pure photoproduct has a low maximum at about 480 mμ. Thus the photoproduct of the squirrel pigment includes a 480-mμ pigment as well as the normal retinene$_1$, or retinene$_1$-protein, typical of rhodopsins in solution.

The presence of a 480-mμ pigment in the products of bleaching would tend to displace the difference spectrum towards longer wave-lengths. The amount of 480-mμ pigment was small, however, and the displacement caused must be correspondingly slight. At the least we may say that the true maximum of the squirrel pigment must lie between 490 mμ, the $\lambda_{max.}$ of the least-contaminated extract, and 504 mμ, the $\lambda_{max.}$ of the difference spectrum.

Interpretation of *in vivo* Observations on the Squirrel Retinal Pigment

The retinal pigment of the grey squirrel has been studied by Weale[10] using the method of fundus reflectometry. He measured the fundus reflexion spectrum before and after exposure of the living retina to bright white light. The changes caused by the exposure were interpreted as due to the bleaching of a visual pigment, characterized by a very sharp absorption band with maximum extinction at 530–540 mμ.

How can this result be related to the present finding that extraction of the visual cells of the squirrel retina with digitonin solution yields a typical 'broad-band rhodopsin' with maximum extinction at about 500 mμ?

There are no grounds for supposing that the discrepancy could be due to a gross difference between the light-absorbing properties of the pigment in the *in vivo* and extracted conditions. I have shown that the rhodopsin of the frog (visual pigment 502) has precisely the same absorption in the visual cell as it has after extraction into digitonin solution[1]. This is true also of two other pigments which have been compared in this way, namely, the retinene$_1$ pigment of the conger eel (visual pigment 487) and the retinene$_2$ pigment of the carp (visual pigment 523) (Dartnall, unpublished work).

In any event, Weale (as he was aware) measured the difference spectrum of the squirrel pigment, not its direct absorption. Difference spectra (depending on the conditions under which they are obtained) may, or may not, be useful guides to the absorption spectra of the original visual pigments. In alkaline solution, for example, there is generally little overlap, in the visible, between the absorptions of visual pigments and their photoproducts. The positive portions of difference spectra consequently give good approximations to the original pigment absorptions. When the visual pigment is *in situ*, however, this is not the case. Thus a visual cell preparation of the frog pigment 502 can yield a difference spectrum maximal at 510–515 mμ (ref. 11). This is because a substantial amount of a stable 470-mμ pigment is among the photoproducts formed under these conditions[12]. Similarly, visual cell preparations of the conger pigment 487 and the carp pigment 523 likewise yield 'displaced' difference spectra, with maxima at 502 and 535 mμ respectively (Dartnall, unpublished work).

Reference has been made above to the presence, in bleached squirrel extracts, of a small amount of 480-mμ pigment (in addition to the 'normal' retinene$_1$-protein). It is considered likely that in the water-free

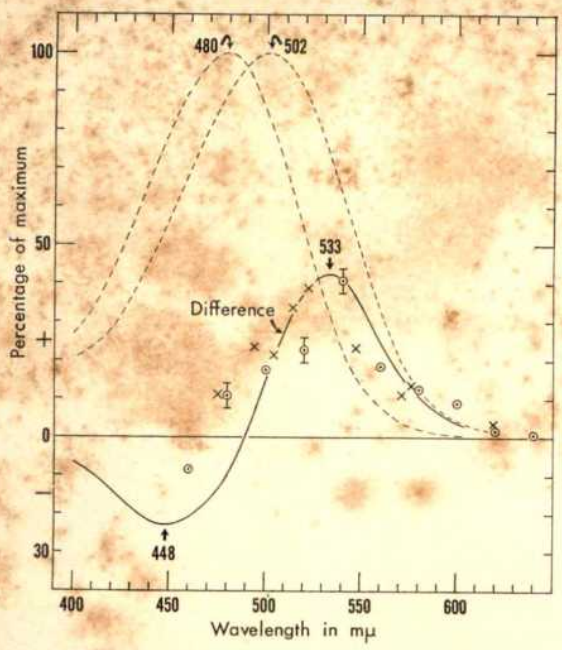

Fig. 3. Interpretation of *in vivo* measurements of the squirrel pigment and of the spectral sensitivity function. Circles (with bars indicating standard deviations) are Weale's results (ref. 10) for the density changes on bleaching the squirrel retina; crosses are Arden and Tansley's mean measurements of spectral sensitivity (equal quantum—intensity spectrum, corrected for lens absorption) (ref. 5). Both sets of results are scaled so that the maxima agree with that of the difference curve, that is, the difference between the 502 and 480 curves

environment of the visual cell this substance may be formed in proportionately greater amount than in solution. If so, then a difference spectrum obtained *in vivo* would bear little resemblance to the spectrum of the original pigment.

In Fig. 3 an attempt has been made to formulate this idea in a semi-quantitative manner. The curves marked '502' and '480' represent the absorption spectra of the squirrel pigment and its 480-mμ photoproduct respectively. The curve marked 'difference' was obtained by subtracting the '480' curve from the '502' curve. It has a positive maximum at 533 mμ and a negative maximum at 448 mμ. Weale's results[10] (shown by the circles in Fig. 3), when suitably scaled, agree tolerably well with this difference curve.

The shape (as distinct from the magnitude) of the difference curve is not markedly affected by the precise spectral location of the pigment and photoproduct curves. (Thus were we to assume a photoproduct at 470 mμ instead of at 480 mμ, the positive and negative maxima of the difference curve would be at 527 and 446 mμ respectively: for a 490-mμ photoproduct they would be at 537 and 452 mμ respectively.) Nor is its shape much affected by quite considerable variations in the relative heights of the pigment and photoproduct curves (arbitrarily shown equal in Fig. 3). We may conclude that the difference spectrum obtained by Weale in his *in vivo* experiments is consistent with that to be expected when a normal broad-band visual pigment having maximum extinction at about 500 mμ bleaches mainly or entirely to a substance having maximum extinction at about 480 mμ.

Amount of Pigment in the Squirrel Retina

At the wave-length of maximum change (*c.* 535 mμ), Weale observed a difference of density of 0·16 between the unbleached and bleached retina. Assuming that the light by which this difference had been measured had passed twice through the pigment layer, he originally[10] supposed the pigment density to be half this figure. One cannot be certain, however, that the measuring light does make such a double transit[13]. Consequently, it is safer to regard the values 0·08 and 0·16 as lower and upper limits respectively.

If the interpretation proposed in Fig. 3 for Weale's results is correct, it is clear that his maximum change amounts only to some 40 per cent of the density of the squirrel pigment. Allowance for this factor raises Weale's estimate from 0·08–0·16 to 0·20–0·40.

It is interesting to compare this value (a measure of the effective absorptivity of the pigment when in the retina) with that for the pigment when extracted. In the most efficient of the present experiments, nine squirrels were used, the isolated visual cells being twice extracted with digitonin solution (first and second extracts of Fig. 1). The residual retinæ were likewise extracted twice. Adding the density results for all four extracts gives the total pigment yield as 0·55 ml. of extract of density 0·182 (per 0·5 cm.). Assuming the retinæ to be hemispheres of 1·15 cm. diameter, it is calculated that such a quantity of pigment would, if spread uniformly over the whole retinal area, cover it to an optical density of 0·0054.

The two values disagree grossly. Even after discounting a possible 3/2 factor[14] for increased absorptive efficiency due to orientation of the pigment molecules in the cones, the *in situ* estimate is still 25–50 times as great as that from extraction results.

Estimates of *rod* pigments *in situ* and after extraction normally agree fairly well when allowance for orientation and for the fraction of retinal area occupied by the rods[14] is made. The present discrepancy with the squirrel *cone* pigment shows that the effective absorptivity of the pigment is greatly enhanced *in situ*, for example, by a mechanism which concentrates all the light incident on the inner segment of a cone into the smaller, pigment-containing area of the outer segment[15].

Interpretation of the Squirrel Spectral Sensitivity Curve

Arden and Tansley[5] have determined the spectral sensitivity of the grey squirrel from measurements of electroretinograms taken from animals under light nembutal anæsthesia. Their mean values (from two dark- and two light-adapted squirrels) are shown by the crosses in Fig. 3, and are seen to be in tolerable agreement with the difference curve.

This agreement suggests that the spectral sensitivity function may be mediated by a mechanism depending on the difference between the light absorbed by visual pigment chromophores and that absorbed by '480-' chromophores. The precise way in which this could occur is a matter for conjecture at present. One possibility, which has the merit of suggesting crucial electroretinogram experiments, is outlined below.

Hubbard and Kropf[16] have suggested that when rhodopsin (in a dry film or at low temperature) is irradiated, "steady state mixtures of chromoproteins including photoregenerated rhodopsin and iso-rhodopsin" are formed. We shall postulate that in the water-free environment of the cone a similar situation arises, and that continuous irradiation results in a steady-state mixture of the 480-mμ pigment and photoregenerated squirrel rhodopsin. In other words, we postulate that the 480-mμ pigment formed when

squirrel rhodopsin bleaches is similarly photosensitive in the cone, and reverts totally or partially to the original pigment on absorption of light quanta.

Consider a cone which (as a consequence of its past history of exposure to light) contains approximately equal densities of 480- and 502-mμ pigments. If, now, this cone is exposed to light of wave-length about 490 mμ (which both pigments absorb equally, see Fig. 3) then the net changes in the pigment composition of the cone will be nil, for, on average, just as many 502-chromophores will be lost through bleaching as will be gained by photo-regeneration. Exposure of such a cone to any wave-length longer than 490 mμ will result in a net increase in 480-chromophores. Conversely, exposure to any wave-length shorter than 490 mμ will cause a net increase in 502-chromophores.

If we suppose that it is the change in chromophore constitution of the cone which ultimately provides the stimulus, then the sensitivity would be given by the *modulus* of the difference curve in Fig. 3. This modulus is a double-humped curve with maxima at 448 and 533 mμ and with a deep depression between, touching zero at about 490 mμ. Unfortunately, Arden and Tansley's observations were not extended far enough into the short wave-lengths to ascertain whether there is a second maximum of activity at about 450 mμ.

It has already been noted that the shape of the difference curve is not markedly affected by quite large variations in the relative heights of the 502- and 480-curves. Thus the form of the spectral sensitivity curve for the mechanism proposed here would not change greatly over a wide range of cone compositions. One would expect, however, that a true threshold sensitivity function would reproduce the 502-curve alone. Conversely, if the cones contained virtually only the 480-mμ pigment (for example, after prolonged pre-adaptation to light of long wave-length) one would expect the spectral sensitivity to follow the form of the broad-band 480-curve.

I gratefully record my thanks to Mrs. M. R. Bright for assistance with the experiments and to Miss C. Kerr for tending the squirrels.

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HOST SPECIFICITY OF TWO *XANTHOMONAS* SPECIES

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DYE[1] has stated that he was able to adapt cultures of twenty species of *Xanthomonas*, after four successive passages through the leaves of young dwarf bean plants, to produce infection symptoms on bean leaves that could not invariably be distinguished from those caused by *X. phaseoli* (Smith) Dowson. This finding suggests that the host specificity of the xanthomonads may not be a stable character.

An attempt was made to adapt *X. malvacearum* to produce infection symptoms on the leaves of *P. vulgaris* var. Banja, similar to those produced by *X. phaseoli* var. *fuscans* (*X. phaseoli* and *X. phaseoli* var. *fuscans* cause similar disease symptoms on *P. vulgaris* leaves). In the first experiment the plants were grown in the greenhouse until the first trifoliate leaf was half-developed. They were then placed in a humidity chamber maintained above 70 per cent relative humidity and between 22° and 30° C. for 24 hr. and afterwards inoculated by needle with pure bacterial slime taken from 48-hr. old cultures grown at 27° C. on potato–sucrose–agar plus chalk. The plants were covered for 24 hr. with a transparent polythene bag. No difficulty was experienced in re-isolating *X. malvacearum* from the vein tissue immediately adjacent to the points of needle puncture, 7–9 days after inoculation. Six single colonies were mixed to provide inoculum for re-inoculation. The process of inoculation, isolation and re-inoculation was repeated six times. On the 6th inoculation, leaves were also spray-inoculated by an atomizer with an aqueous suspension of the 'trained' bacterium from the 5th re-isolation until the leaves became water-soaked. As a control the leaves of another set of bean plants were sprayed with the original culture at approximately equal concentration (5×10^7 bacteria per ml.). The symptoms produced by the two cultures were similar, indicating that the successive transfers into bean tissue had not resulted in any alteration in its pathogenicity. Both bacterial cultures appeared to be capable of multiplying in bean tissue as the tissue of the sprayed leaves became slightly water-soaked in appearance 48 hr. after inoculation. After that time the tissue dried rapidly, forming light-brown necrotic areas. Both bacterial cultures caused, to the same degree, typical disease symptoms (angular leaf spot) when sprayed on to cotton leaves.

If the acquisition of new virulent characteristics is possible this must be engendered by some property or reaction of the new host plant and thus isolation and multiplication of the bacterium in pure culture is an unnecessary complication. In the second experiment bean leaves were used as the sole medium for multiplication of *X. malvacearum*. The technique was as follows: An aqueous suspension of *X. malvacearum* was prepared (approximately 5×10^7 bacteria per ml.) and sprayed by an atomizer on to the first and second trifoliate leaves (the second trifoliates were one-third fully developed) of 10 bean plants grown in the green-

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house. One half of each leaflet was sprayed until the tissue became water-soaked. Two to three days after inoculation disease symptoms became apparent as diffuse water-soaked areas. These did not increase in size and dried to form sunken, light-brown, necrotic areas (Fig. 1). One week after inoculation the necrotic areas from about 60 leaflets were cut out from the surrounding unaffected tissue and macerated in 150 ml. of distilled water. After standing for 3 hr. to allow the bacteria to diffuse out of the tissue, the suspension was filtered through muslin. The filtrate was used to spray the first and second trifoliate leaves of a second batch of bean plants. Some of the bacteria were lost by run-off during spraying, but a high proportion of the bacteria that had multiplied in bean tissue were re-inoculated into fresh tissue. The process was repeated seven times. The 'trained' bacterium was isolated, on solid media, from several necrotic areas which resulted from the seventh spray. Several single colonies were mixed together in distilled water to form a suspension (concentration of about 5×10^7 bacteria per ml.). An aqueous suspension of the original culture of approximately equal concentration was also prepared. The two were sprayed on to leaves of bean and on to leaves of resistant and susceptible varieties of cotton. Although the infection symptoms produced differed according to the host plant, the reactions of any particular host to the suspensions of 'trained' and 'untrained' bacteria were identical.

In an attempt to adapt *X. malvacearum* to breakdown the resistance of the cotton variety *BAR* 12/15 (carrying the bacterial blight resistance genes B_2 and B_{6m}), the same 'training' procedure was employed as that described for the second experiment. The process of inoculation and re-inoculation of an aqueous suspension of the bacterium into *BAR* 12/15 leaf tissue was repeated 15 times. During the 'training' period there was no suggestion of any change in the pathogenicity of the bacterium to *BAR* 12/15 leaf tissue. This was confirmed by spraying both 'trained' and 'untrained' bacteria in aqueous suspension of approximately equal concentrations on to the leaves of two resistant and two susceptible varieties of cotton, when again no differences were apparent.

It was also found that there was no change in the virulence of *X. phaseoli* var. *fuscans* in response to a 'training' period in cotton leaf tissue involving 4 re-inoculations carried out as described in the second experiment. The 'trained' bacterium also retained its pathogenicity to *P. vulgaris*.

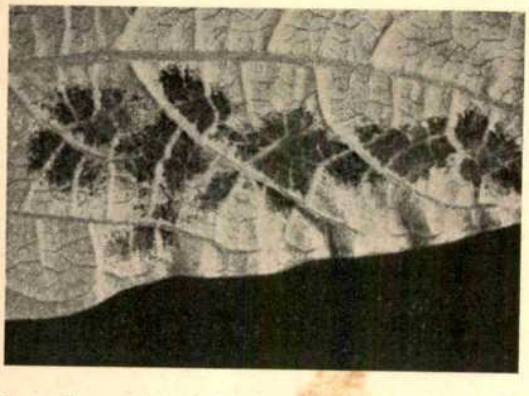

Fig. 1. The reaction of the bean leaf to either 'trained' or 'untrained' *Xanthomonas malvacearum* showing ill-defined, diffuse necrotic areas. (×2, lower surface)

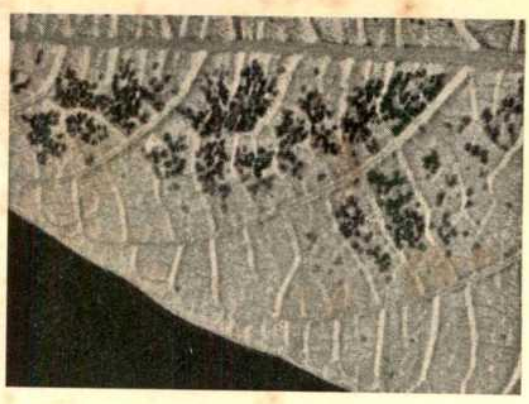

Fig. 2. The reaction of the bean leaf to *Xanthomonas phaseoli* var. *fuscans* showing well-defined, typical lesions. (×2, lower surface)

In these experiments both *X. malvacearum* and *X. phaseoli* var. *fuscans* multiplied in the tissue of either cotton or bean leaves. When both species were sprayed on to bean leaves at a concentration of 5×10^7 bacteria per ml. similar symptoms were apparent after 48 hr. Both species induced the tissues to become slightly water-soaked in appearance, *X. malvacearum* to a lesser degree than *X. phaseoli* var. *fuscans*. After this time the symptoms became markedly different. The areas of leaves sprayed with *X. malvacearum* dried rapidly, forming light-brown necrotic areas (Fig. 1), while those sprayed with *X. phaseoli* var. *fuscans* became progressively more water-soaked, resulting in typical angular leaf spots (Fig. 2). When the concentration in inoculum was reduced to 5×10^3 bacteria per ml., *X. malvacearum*, 'trained' and 'untrained', caused no symptoms to develop on bean leaves whereas *X. phaseoli* var. *fuscans* caused typical infection.

Thus, in these experiments there was no change in the host specificity of two cultures of *X. malvacearum* or in the one of *X. phaseoli* var. *fuscans*, a marked contrast to the evidence presented by Dye, in whose paper three important points are omitted. (1) He did not mention whether the change in virulence was sudden or whether there was a gradual increase in severity of infection symptoms. He only stated that on the fourth inoculation, lesions were allowed to develop for seven days and that a progressive disease was produced by all twenty species of *Xanthomonas*. (2) He did not compare his 'adapted' bacterium with the original culture. (3) He did not reverse the experiment, that is, attempt to adapt *X. phaseoli* to any one of the twenty species of host plant. It is thus difficult to see how he can claim that a change did in fact occur in any of the twenty *Xanthomonas* species.

Because a close physiological and biochemical relationship exists between many of the 'phytopathogenic species' of *Xanthomonas*[2], it is generally considered that many of these, which have been named after the original hosts, should be regarded as having the status of formae speciales[3], the differentiation of which is host specificity. If a further classification of the genus *Xanthomonas* is to be based on host reaction, the environmental conditions under which the host plants are grown, together with such considerations as the maturity of the host plant at time of inoculation, the inoculation technique or techniques, and the concentration of inoculum, must all be standardized.

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LETTERS TO THE EDITORS

PHYSICS

Resonant Scattering of the 14-keV. Iron-57 γ-Ray, and its Interference with Rayleigh Scattering

When radiation is scattered by a resonator, the question of its identity of frequency and coherence of phase with the incident radiation is not simply answered except for an infinitely narrow incident line, when the scattering is fully coherent (see, for example, the discussion by Heitler[1], written in the context of atomic resonances but equally relevant to nuclear ones).

Coherence may be experimentally proved by observing interference between the resonance radiation and some other form of scattering that is known to be coherent; for γ-rays, one would naturally look for interference with the Rayleigh (elastic electronic) scattering. In the long-studied 411 keV. resonance of mercury-198, such interference is unobservable[2], because of the thermal broadening of the line as well as for other reasons. It might just be observable in samarium-152, where the natural width of the 961-keV. line is not completely negligible[3,4] in comparison with the thermal; but the best conditions appear to be provided by the very narrow low-energy lines discovered by Mossbauer[5] in which a substantial part of the radiation is unaffected by recoil or thermal broadening.

After preliminary experiments in collaboration with Dr. B. S. Sood, in which the resonant scattering in metallic iron of the 14-keV. line of iron-57 was found to have the expected intensity, we decided that a foil of 65 per cent iron-57, electroplated on thin copper by the Isotope Division, Atomic Energy Research Establishment, Harwell, would give comparable amplitudes of resonant and Rayleigh scattering at convenient angles. We in fact chose an angle of 43 ± 2°, which would include the (211) Bragg reflexion. The geometry of the apparatus is indicated in Fig. 1: the source[6], about 20 mc. of cobalt-57 in a matrix of iron-56, was mounted on a 30 c.p.s. vibrator so that the exact energy of the emitted radiation could be oscillated through the resonant energy.

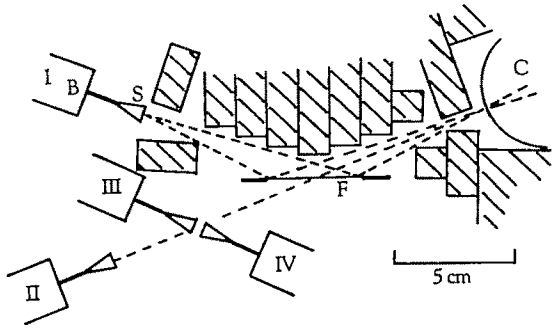

Fig. 1. Diagram of experimental arrangement. *B*, vibrator; *S*, source; *C*, proportional counter; *F*, iron foil. The shaded blocks are heavy alloy shielding. The different positions of the source and vibrator are: I, for scattering; II, for transmission; III and IV, for checking absence of shift in transmission

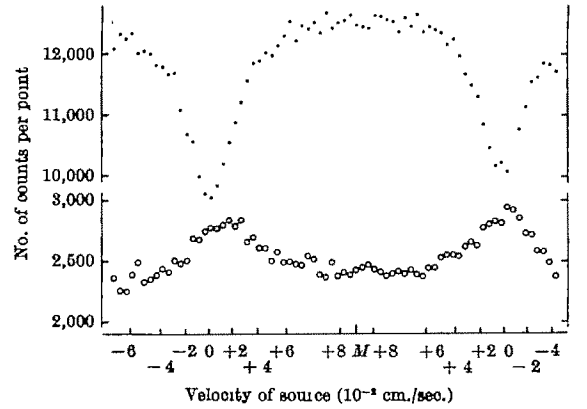

Fig. 2. Plots of intensity versus velocity for transmission (dots) and scattering (circles). The zero of the velocity scale is fixed only by the position of the transmission minima. Positive velocities are for the source approaching the foil. The position *M* on the velocity scale is the point at which the acceleration reverses

Auxiliary apparatus enabled the intensity of transmission through, or scattering from, the foil to be plotted automatically as a function of speed, the abscissæ of the resultant graphs extending over rather more than half a cycle of vibration, so that passages through zero velocity in both senses of acceleration were displayed.

Fig. 2 shows the transmission minima and scattering maxima obtained; it will be seen that the scattering peaks are somewhat broader and slightly nearer to one another than are the absorption minima.

The reduced separation of the peaks was, however, due entirely to the shift of one of them; presumably the whole pattern had suffered an instrumental drift during the long periods of operation that were necessary. We repeated the measurements with the apparatus set to display negative, instead of positive, speeds at the centre, alternating transmission and scattering measurements and adding the results of all sets of each kind. Fig. 3 shows that the peaks now appeared, as expected, more widely spaced than the dips, with no evidence of general drift. Thus, assuming the transmission dips to occur at exactly zero velocity, we can say that the maximum scattering occurs when the source is approaching the scatterer with a velocity corresponding to a fraction of the line-width.

It remains to verify that the dips correspond precisely to zero velocity; this need not be so if source and scatterer materials are not identical. This point was checked at the suggestion of Mr. D. A. O'Connor, by successive transmission experiments with the source assembly set in the positions marked III and IV in Fig. 1; this amounts to reversing the velocity-scale about the true zero. No change in the dip position was found.

If there is some coherence of phase between resonant and Rayleigh scattering, we should expect them to be in quadrature at exact resonance, moving towards coincidence of phase on the high-frequency side. Thus, on top of the constant intensity of the Rayleigh and the sharply peaked contour of the

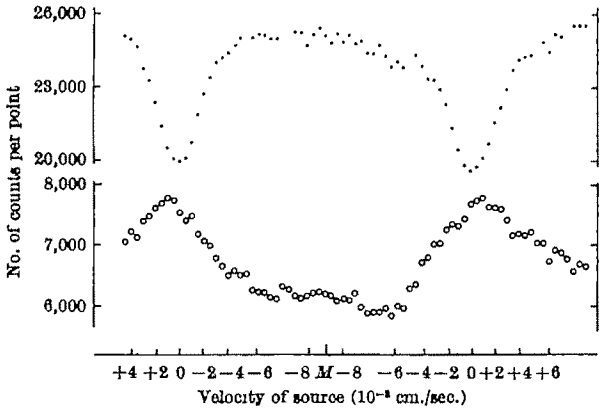

Fig. 3. Plots of intensity versus velocity for a separate experiment in which, as indicated on the velocity scale, negative velocities are displayed in the centre

resonant scattering, there should be added a dispersion-type curve representing the interference between them, with its maximum a fraction of a line-width to the positive side of zero velocity. The observed shift and broadening are probably to be explained in terms of such coherence, but the measurements are not yet detailed enough to show clearly the asymmetry of line-shape that is also to be expected or to determine what percentage of coherence exists; full coherence is not to be expected when the incident line is of similar breadth to that of the resonance.

We have also observed the resonant scattering from ordinary iron (2·2 per cent iron-57) at a mean angle of 90°, in the presence of a relatively large intensity of Rayleigh scattering. We found neither shift nor broadening of the scattering resonance, which is consistent with the expectation that, at this angle of scattering in a magnetic dipole transition, the resonant component will be polarized at right angles to the Rayleigh.

It is to be expected that the narrow-line resonance radiation will show, in its scattering from crystals containing iron-57, interference phenomena similar to those of X-rays. Interesting differences may arise from the resonant absorption which accompanies the scattering, from the narrowness of the line as compared with X-ray lines, and from the simple way in which the exact energy, and with it the phase of the resonant scattering, may be varied.

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Specific Fall-out Activity in Precipitation as a Function of Sampling Height

IN 1956–57 Herbst *et al.*[1] found a definite increase with height in the fall-out activity in vegetation from an altitude of 800–1,000 m. and upwards. This was ascribed partly to the slow growth of the vegetation with increasing height and consequently greater accumulation of activity on it, and partly to greater fall-out at increased heights. Small[2] suggested in 1958 from examination of the variations in the natural activity of the air (radium B and C), compared with the meteorological conditions at ground-level, that during inversion conditions the vertical transport of bomb debris from above would decrease. By comparing the fall-out in a precipitation collector situated in the top of a 123-m. mast with that in corresponding collectors at ground-level, I found[3] for the period September 1958–March 1959 more fall-out in the former than in the latter.

It was therefore decided to examine the fall-out activity in precipitation collected in different heights. At Risø, a 123-m. meteorological mast has been built for micrometeorological measurements[4]. At heights of 0, 7, 23, 39, 56, 72, 96 and 123 m. I fixed, at a distance of 1 m. out from the mast, eight 1-litre polyethylene bottles each provided with a 154 cm.² polyethylene funnel. The bottles were changed on the first of every month.

After the bottles had been collected, the amount of rain-water in each was measured and strontium-, cæsium- and cerium-carrier was added. The content of each bottle was then analysed for strontium-90 and -89, cæsium-137 and cerium-144 by the method of Osmond *et al.*[5]. The activities are given in pc./m.², and in pc./l., and are traced to the middle of the month. All the isotopes were determined for each of the ten months March–December 1959, except strontium-89 which was too weak in activity in the last months of the year for a reliable determination. A table with all the results of the measurements is given in Risø Report No. 14 (ref. 6). Table 1 gives the annual average values for the specific activity at the different heights.

A regression analysis on the figures in Table 1 shows for all the isotopes an increase in specific activity with the height. Strontium-90 displays an increase in activity of 15 per cent per 100 m., cæsium-137 of 19 per cent, cerium-144 of 27 per cent and strontium-89 of 31 per cent.

A regression analysis of the results for the ratio strontium-89/strontium-90 (see Table 2) shows an increase in that ratio with height of 13 per cent per 100 m.

The present work shows that it is possible to detect a change in the specific activity in precipitation even within a difference in height of 100 m. (The increase in total fall-out with the height is still more significant, due to increasing amount of precipitation, when ascending[4].)

The reason for this difference in specific activity must be due to the varying contribution of dry fall-out in the different rain-collectors, as it would be

Table 1. AVERAGE SPECIFIC ACTIVITY IN PRECIPITATION FOR THE PERIOD MARCH–DECEMBER 1959

Height (m) \ Isotope	Strontium-90 (pc./l.)	Strontium-89 (pc./l.)	Cæsium-137 (pc./l.)	Cerium-144 (pc./l.)
0	14·9	217	14·8	195
7	14·6	174	18·9	189
23	16·5	164	20·3	175
39	16·6	204	20·9	233
56	16·2	214	22·6	233
72	15·9	205	19·2	212
96	17·0	242	22·0	240
123	18·0	257	21·2	251
Mean	16·2	210	20·0	216

Table 2. AVERAGE OF RATIO OF STRONTIUM-89 TO STRONTIUM-90 FOR THE PERIOD MARCH–AUGUST 1959

Height (m.)	Ratio of strontium-89 to strontium-90
0	7·5
7	7·1
23	7·5
39	6·1
56	7·0
72	7·4
96	8·2
123	8·3

difficult to imagine how the rain could be less radioactive when falling down through the air.

(Regression analysis has shown that all the results are significant at the 1–2 per cent level except cæsium-137 and the ratio strontium-89/strontium-90, which are significant only at the 10 per cent level.)

At an altitude of 60 m. above the Risø area, there are on the average inversion conditions during 25 per cent of the time[4]. In the lower regions inversion is more frequent, in the upper less. In accordance with Small's results[2], it would be reasonable to suppose that these inversion conditions are one of the reasons why more dry fall-out is found in the bottles placed at the upper part of the mast than in those at the lower. Another factor contributing to the difference in activity will be the increasing wind velocity with increasing height[4]; this will give rise to a greater deposit of airborne particles in the higher bottles than in the lower ones[7]. Hence we get a higher specific activity in rain when the sample is taken at an altitude of, say, 100 m. than at ground-level.

Furthermore, it seems probable that short-lived fission products from fall-out would show a more pronounced variation with height than long-lived products. This is to be expected if one assumes that the dry deposit is of greater particle-size than the deposit from rain. Larger and heavier particles would be deposited more readily than fine particles[7], and consequently the fine particles will consist preferentially of older fission products than coarse ones. As a consequence of this, the age of the fall-out will decrease with increasing sampling height of the precipitation. As an example, the age determined in March 1959 from the strontium-89/strontium-90 ratio was 170 days at 0 m. and 148 days at 123 m. above ground-level.

I thank Mr. Heinz Hansen and Mr. Ulf Christiansen for many stimulating and inspiring discussions, especially concerning the statistical evaluation of the results.

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Radiative Transfer of Energy in the Core of a Heated Tube

WHILE investigating the temperature distribution along a thin-walled tube heated by passing an electric current through it *in vacuo* we had naturally to calculate the radiative transfer of energy occurring in the hollow core of the tube[1]. Taking the tube to be a circular cylinder of diameter D, and considering an annular ring of width dx, the net gain in energy by the ring due to radiative transfer can be readily calculated. If the ring is not too near the ends, this is found to be equal to:

$$4\pi\sigma D^3T^2\ (dT/dx)^2\ dx + \frac{4}{3}\pi\sigma D^3T^3\ (d^2T/dx^2)dx$$

which may be expressed in the form:

$$\frac{d}{dx}\left(\frac{4}{3}\pi\sigma D^3T^3\ dT/dx\right)dx$$

where σ is Stefan's constant of radiation, and the emissivity of the walls is taken to be unity. It is as though the hollow core had a thermal conductivity of magnitude:

$$\varkappa_r = \frac{16}{3}\sigma DT^3 \qquad (1)$$

One may compare this with the expression obtained by Bosworth[2] for the radiational conductivity of a very hot gas, in which the photons emitted by the molecules, as distinguished from the molecules themselves, are regarded as diffusing into the gas, his expression being:

$$\varkappa_{rg} = \frac{16}{3}\sigma l_0T^3 \qquad (2)$$

where l_0 is the mean free path of the photons, which may be taken to be the reciprocal of the absorption coefficient of the gas for the photons. Indeed, the radiational conductivity of the hollow core may be regarded as the limiting case of the conductivity of a hot gas filling the core, when the pressure of the gas is reduced to zero and the free path of the photons is thus limited by the dimensions of the tube. In this limiting case the source of the photons will recede to the walls. Taking (2) to remain valid in this limiting case also, and comparing (1) with it, one can see that the mean free path of the photons in the hollow core is just D.

There is a close analogy between expression (2) for the radiational conductivity of a gas at high temperatures, and that for the lattice conductivity of a dielectric crystal at low temperatures, in which the transport of energy is by the low-frequency thermal elastic waves or phonons in the medium[3]. The closeness of the analogy arises ultimately from two factors: the upper limit to the wave number set by the Brillouin zone ceases to be of significance for these low-frequency waves, and, secondly, the frequencies are proportional to the wave numbers, as for the photons in a gas. These are also just the factors that lead to the T^3 law for the lattice specific heat.

The expression obtained by Casimir[3] for the lattice conductivity of a dielectric cylinder at temperatures low enough for the free path of the phonons to be limited by its diameter is analogous to that obtained here for the radiational conductivity of the hollow core—again as though the mean free path so limited is just D.

When the emissivity of the walls falls short of unity, one has to know how the fraction $(1 - \varepsilon)$ of the incident radiation that is not absorbed is returned to the enclosure. When it is in the form of specular reflexion, it is found that the thermal conductivity of the core is on this account increased by a factor $(2 - \varepsilon)/\varepsilon$, which is similar to the factor obtained by Berman, Simon and Ziman[4] in their expression for the lattice thermal conductivity of a cylindrical specimen at low temperatures, and also similar to the 'coefficient of slip' of a rarefied gas in its passage through a narrow tube[5].

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New Delhi. Aug. 23.

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Infra-Red Spectrum of Praseodymium Nitrite

IN researches undertaken in this Laboratory, it has been necessary to characterize certain species in the thermal decomposition of a number of metal nitrates. In order to do this, it has been found useful to obtain the spectra of a number of metal nitrites. Nitrites are known to occur in the course of decomposition of a number of metal nitrates[1]; it has been found that praseodymium nitrite is a transient product in the thermal decomposition of praseodymium nitrate[2]. Praseodymium nitrite also appears as an intermediate in the interaction of nitrogen dioxide on praseodymia (Honig, J. M., and Vratny, F., unpublished work).

The majority of the nitrites used for comparison were obtained from commercial sources. Praseodymium nitrite was prepared by the method of Dutta[3] and Ferrari, Cavalea and Nordelli[4]. Stoichiometric quantities of praseodymium chloride and silver nitrite in aqueous solution were combined. The product was obtained by vacuum evaporation of the water. The viscosity of the ensuing solution, difficulty in crystallization, etc., strongly resemble the nitrate in character[5].

The spectra of the powdered metal nitrites were obtained on a double-beam Perkin Elmer model 21 spectrometer using sodium chloride optics. The spectra were obtained by dispersing the solid in 'Nujol' and by forming a potassium chloride pellet. The spectra were essentially the same except in the case of barium nitrite, in which case there appeared to be a shift in the 1,282-cm.$^{-1}$ band to 1,240 cm.$^{-1}$ in 'Nujol'. The use of the dual technique is recommended to assure absence of exchange, etc.[6].

The spectra of the simple nitrites: sodium, potassium, silver and barium, are rather straightforward and follow the characterization formulated by Williams[7]. The band at about 830 cm.$^{-1}$ represents the ν_2 bending mode, the band at about 1,250 cm.$^{-1}$ is the ν_1 symmetric stretching, and the band at about 1,360 cm.$^{-1}$ is the ν_3 asymmetric stretching. The

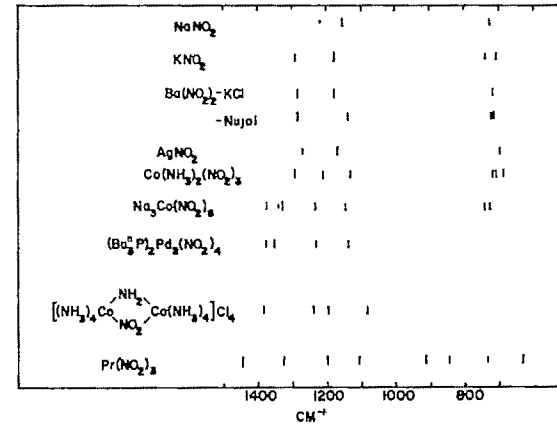
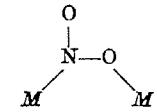
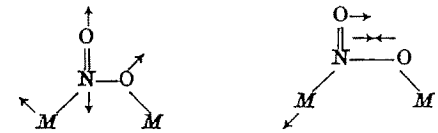


Fig. 1. Correlation diagram for various metal nitrites

splitting observed in the case of $Co(NH_3)_3(NO_2)_3$ occurs most probably in the ν_2 vibration and is configurational in origin. The spectrum of praseodymium nitrite is still more complex in that even greater splitting has occurred. The magnitude of the splitting is correspondingly greater than the field splitting observed in metal nitrates[8]. The distinction between nitro- and nitrite-linkage, as occurs with silver and sodium nitrite[9], is not a determining factor in this case. Recent work reported by Gatehouse[10] has shown that changes can be expected in the spectra of metal nitrites when the nitrite groups are arranged in either a *cis* or *trans* arrangement as in the case of $Co(NH_3)_2(NO)_3$, or when the nitrite group gives rise to a bridging structure, namely:



The spectra for two such compounds, reported by Gatehouse, are given in Fig. 1 along with other observed spectra. The two important modes of vibration for the bridging structure are:



at about 6·8 and 8·3μ, respectively. It can be seen that four characteristic bands occur in the high-energy region of the spectrum.

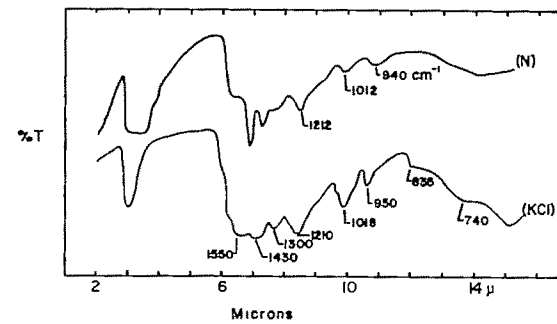


Fig 2. Infra-red spectrum of praseodymium nitrite in 'Nujol' and potassium chloride pellet

The splitting produced in praseodymium nitrite strongly suggests a similar bridging structure. For purposes of comparing band intensities, the spectrum of praseodymium nitrite is reproduced in Fig. 2.

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CHEMISTRY

Invariance of Molecular 'Inverse' Force-constants

IN the quadratic form:

$$V = \tfrac{1}{2}\Sigma_1^n\Sigma k_{rs}q_rq_s \qquad (k_{rs} = k_{sr}) \qquad (1)$$

representing the harmonic approximation to the potential energy of a vibrating molecule, the 'force constants' k_{rs} depend on the definition of the internal co-ordinates q_i used to represent small changes in the molecular configuration. For example, a full analysis[1] of the vibrations of $^{14}NO_2$ and $^{15}NO_2$, with co-ordinates q_1 and q_2 the NO bond stretches, gives for the stretch and stretch-interaction constants $k_{11} \equiv k_{22}$ and k_{12} the following values (in units 10^5 dynes/cm.): (i) 10·884 and 1·9914 and (ii) 15·507 and 6·614 in the two cases where the third co-ordinate is (i) the ONO angle distortion and (ii) the change in OO distance. Thus the interpretation and comparison of force-constants obtained by different co-ordinate analyses present difficulties, which naturally increase with molecular complexity.

'Inverse' force-constants, h_{rs}, may be defined as the elements of the matrix $\{h_{rs}\}$ inverse to $\{k_{rs}\}$. A changed definition or choice of the internal co-ordinates q_r corresponds to a linear transformation, and the necessary invariance of V in (1) under this transformation implies that the h_{rs} can be transformed like the dyad or set of products q_rq_s. Thus if new co-ordinates $q_3, \ldots, q_n$ (linear combinations of the old $q_1, \ldots, q_n$) are chosen, leaving the old q_1 and q_2 as members of the new set, then the elements h_{11}, h_{12} and h_{22} are unchanged; and in general, the inverse force-constants corresponding to any unchanged co-ordinates are invariant. This can be verified with precision by using full sets of force-constants k_{rs} for NO_2 in cases (i) and (ii) above.

This invariance of inverse force-constants holds similarly for the potential energy in the vibrations of a single symmetry class, where the k_{rs} are symmetry-co-ordinate force-constants, and a partial change is made in the choice of symmetry co-ordinates.

It has often been found useful tentatively to transfer one or more force-constants k_{rs} from one fully analysed molecule to another containing a similar atomic group. The present considerations suggest that it might be more suitable to transfer the corresponding *inverse* force-constants h_{rs}.

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Re-assessment of the Electron-spin Resonance Splitting Constants of Several Well-known Free Radicals

THE hyperfine splitting constants of the electron-spin resonance spectra of several well-known free radicals in solution have been re-measured recently. In some cases discrepancies with the values quoted in the literature have been found.

The particular case examined was the detection and identification by electron-spin resonance of a free radical produced during the thermal cracking of hydrocarbons, as the perinaphthenyl radical (it is hoped to publish details of this work in due course). It was found that the values of the splitting constants for the perinaphthenyl radical differed from those already reported[1]. In order to check the calibration of the magnetic field, the splitting constants of several well-known free radicals were measured, and the values obtained in the present work are compared with those reported in the literature in Table 1. The accuracy of the magnetic field calibration is confirmed by the agreement obtained for the last two free radicals listed. (Similar agreement has been obtained for several other free radicals.)

Table 1. HYPERFINE SPLITTING CONSTANTS FOR FREE RADICALS IN SOLUTION

Free radical	Hyperfine splitting (oersted) This work	Literature	Ref.
Perinaphthenyl	6·30 ± 0·1 1·82 ± 0·05	7·3 2·2	1
DPPH *	8·9 ± 0·2	10	2
B and K †	11·9 ± 0·2	13·5 ; 11·0	2 ; 3
Coppinger's ‡	5·9 ± 0·1	4·9 ; 5·7	4 , 5
p-Benzosemiquinone	1·45 ± 0·05 2·34 ± 0·05	1·0 ; 1·3 { 2·368 ± 0·001 2·37 ± 0·01	6 7
Hydrogen atom	512 ± 10	505·4 ; 508·7	8 ; 9

* α,α′-Diphenyl-β-picrylhydrazyl.
† 1,3-Dimethyl-1-(phenylimineoxide)-butylidene-3-N′-phenyl-N′-oxynitrogen.
‡ 2,6-Di-*t*-butyl-4-(3,5-di-*t*-butyl-4-oxo*cyclo*hexa-2,5-dienylidene methyl)phenoxy.

In view of the potential use of electron-spin resonance for identifying unknown free radicals, the need for an accurate measurement of the hyperfine splitting constants cannot be emphasized too strongly. The apparatus used for measuring the magnetic field was relatively simple, consisting of a proton resonance probe and a *BC* 221 crystal-controlled frequency meter. In most cases the derivative electron-spin

resonance spectra were obtained and field markers superimposed on the recorder trace. In a few instances the spectra and the proton resonance signal were displayed on an oscilloscope and the hyperfine splittings measured directly.

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Hydrogen-bonding in Calcium-deficient Hydroxyapatites

MANY calcium phosphates precipitated from solution give the X-ray diffraction pattern of hydroxyapatite but depart from the ideal stoichiometry, $Ca_{10}(PO_4)_6(OH)_2$, of this compound. Pure hydroxyapatite can be prepared only under hydrothermal bomb conditions[1,2], whereas the appearance of hydroxyapatites with low Ca/P ratio from aqueous preparations seems to be the rule rather than the exception.

Index of refraction, density, and X-ray diffraction data have shown that it is possible to have calcium ions missing randomly from certain positions in the hydroxyapatite structure[3]. To effect electrical neutrality, it was suggested that hydrogen bonds, in the proper proportion, were present between the oxygens of adjacent orthophosphate groups[3]. Evidence is presented here to confirm the presence of hydrogen bonds in a series of hydroxyapatites, with low calcium, in proportion to the missing number of calcium ions.

A series of hydroxyapatites deficient in calcium were prepared by methods outlined in an earlier publication[4], and examined by X-ray diffraction to make certain that each preparation was a single phase. The samples were analysed for calcium gravimetrically[5], and for phosphorus by a differential spectrophotometric method[6]. Average indices of refraction of the samples, obtained by the double-diaphragm method of oblique illumination[7], confirmed the X-ray and chemical evidence that these samples were calcium-deficient hydroxyapatites. Details of all physical and chemical analyses will be given in a later publication.

The samples all show an infra-red absorption band near 3,400 cm.$^{-1}$, which corresponds to a hydrogen-bonded O–H stretching frequency. Weighed mixtures of the various calcium-deficient hydroxyapatites and potassium ferricyanide were prepared and examined in a commercial infra-red spectrophotometer. Spectra were obtained from a pressed film of the sample held between two sapphire windows of a sapphire pressure-cell[8]. The base-line technique was used to calculate the molar absorbance from the absorption band. The hydrogen-bond content was determined quantitatively by comparing the absorbance at 3,400 cm.$^{-1}$ with that of potassium ferricyanide at 2,105 cm.$^{-1}$. The latter was used as an internal standard to correct for the unavoidable differences in thickness of film of the samples.

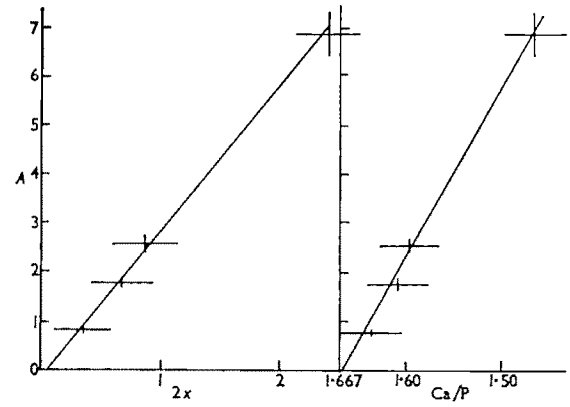

Fig. 1. Right. Plot of relative molar absorbance, A, at 3,400 cm.$^{-1}$ against the Ca/P molar ratio of a series of calcium-deficient hydroxyapatites
Left. Plot of absorbance values (A) against the number of gram atoms of H per mole (x) of calcium-deficient hydroxyapatite as calculated by theory (ref. 3). Standard deviations in ordinate and abscissa are indicated at each point. A was calculated by dividing the absorbance per mole at 3,400 cm.$^{-1}$ by the absorbance per mole of internal standard (potassium ferricyanide) at 2,105 cm.$^{-1}$

Fig. 1 shows that in a series of low-calcium hydroxyapatites examined, the infra-red absorption due to the hydrogen-bonded O—H group is inversely proportional to the Ca/P ratio. If the general formula for hydroxyapatite is assumed[3] to be $Ca_{10-x}H_{2x}(PO_4)_6(OH)_2$, it is then possible to plot the relative molar absorbance, A, against $2x$ (the gram atoms of hydrogen). Fig. 1 shows that such a plot is a straight-line function, indicative of the validity of the formula assumed.

The value of A approaches zero as the Ca/P molar ratio approaches 1·67, that is, the ratio for pure hydroxyapatite. Thus when the hydrogen-bond content is zero (that is, when $x = 0$), the compound is the end member, hydroxyapatite, which contains no hydrogen-bonding but only exhibits the O—H stretching frequency of free hydroxyl ion near 3,700 cm.$^{-1}$.

The hydrogen-bonded O—H stretching frequencies observed in the samples of calcium-deficient hydroxyapatites were all found to be near 3,400 cm.$^{-1}$. This indicates that the oxygen-to-oxygen distance of the O—H—O bonds did not change with varying hydrogen content. By means of the criteria of Lippincott and Schroeder[9], the probable O—O distance calculated from the O—H stretching frequency can be estimated at 2·85 Å. This is a reasonable distance between oxygen atoms of adjacent orthophosphate groups clustered around the three-fold axes of hydroxyapatite as calculated from the refined atomic parameters of this crystalline species[10]. It is not possible to say specifically from the present results which oxygen atoms are involved in the hydrogen-bonding. However, it is reasonable to assume that the hydrogen bonds will be as near as possible to the missing columnar calcium positions on the three-fold axes, since electrical neutrality will be maintained locally in a crystal.

This experiment has implications beyond the synthetic calcium phosphates discussed here. It has been suggested that the mineral portions of bone and tooth tissue are calcium-deficient hydroxyapatites[3,11]. The possible presence of hydrogen bonds in these materials may provide a much needed parameter for an estimation of the stoichiometry of these biological hydroxyapatites under varying conditions. In addition, there are many non-stoichiometric, inorganic systems in which hydrogen-bonding between electronegative ions may provide a balance between chemical perfection and imperfection due to missing cations.

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The 1,2-Propylenediaminetetra-acetato-cobaltate(III) Anion

IT is implicit in a recent theory[1] of stereospecific effects in metal complexes containing optically active diamines that the optical isomers of complexes containing only one such diamine molecule should have exactly similar conformations.

To test this matter, the infra-red spectrum in the sodium chloride region of L-potassium (*d*-propylenediaminetetra-acetato)-cobaltate(III) trihydrate was compared with that of DL-barium (*dl*-propylenediaminetetra-acetato)-cobaltate(III) octahydrate. The spectra, in 'Nujol' mulls, were identical, as predicted by theory[1]. It is of interest that the infra-red spectra of *d*- and *dl*-propylenediamine tetra-acetic acids are not quite identical[2]. This was attributed to differences in hydrogen bonding.

A further point of interest is that the spectra of the cobalt complexes show a single strong carboxylate peak at 1,647 cm.$^{-1}$. This is good evidence for hexa-co-ordination by propylenediaminetetra-acetate, and is directly analogous to the single strong peak in the infra-red spectrum of the (ethylenediaminetetra-acetato)-cobaltate(III) anion (ref. 3). The spectra of complexes with copper(II), zinc and nickel show a splitting of this peak, presumably due to penta-co-ordination.

The cobalt complexes used were prepared by the methods given by Dwyer and Garvan[2]. Attempts to make complexes of formula $(Co(HPDTA)X)^-$, where PDTA is the propylenediaminetetra-acetate ion and X is the bromide or nitrite ion, by methods like those used by Schwarzenbach[4] in making the corresponding complexes of ethylenediaminetetra-acetate were unsuccessful. However, the reaction mixture from the attempted introduction of nitrite ion had a visible absorption spectrum which differed from that of the (propylenediaminetetra-acetato)-cobaltate(III) anion.

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BIOCHEMISTRY

Effect of Electrolytes on the Activity of Glutamic-Oxalacetic Transaminase

IN their method for the determination of glutamic-oxalacetic transaminase without precipitation of protein, Mohun and Cook[1] conducted transamination between aspartic and α-ketoglutaric acid to glutamic and oxalacetic acid in a phosphate buffer solution of $pH = 7.5$. Similarly, Yatzidis[2] used a 2 per cent solution of dipotassium hydrogen phosphate for incubation of the system previous to determining the enzyme activity in the serum.

Transaminase activity is known to be enhanced by iron Fe^{2+} and magnesium ions[3,4] and impeded by mercury and cyanide compounds[5]. Introduction of nickel, cobalt, aluminium and manganese ions was found to produce no variation in the activity of the enzyme[6].

As defined by Cabaud[7], the unit of transaminase activity is that of 1 ml. of serum giving rise to 1 μgm. of pyruvic acid in the system incubated. The activity of the serum investigated is determined by the use of a standard graph obtained from extinction measurements in hydrazone solutions of various pyruvic acid concentrations.

In the present investigation, which was carried out according to the method proposed by Mohun, the composition of the fundamental solution containing the substrate, that is, aspartic and α-ketoglutaric acid, was made to vary. In addition to the buffer solution, some electrolyte solutions as well as pure distilled water were used as solvents, simultaneously with, or instead of, the buffer. The experimental

Table 1

No.	Medium	Electrolyte introduced, in mgm. per sample	*p*H of system	SGO-T in Cabaud units
1	Phosphate buffer according to Mohun	9.4	7.5	22
2	Buffer–water (1 : 3)	2.4	7.5	33
3	Distilled water	—	5.0	34
4	Sodium chloride	8.2	4.8	25
5	Sodium chloride + (buffer–water (1 : 3))	10.6	7.4	24
6	Potassium chloride	9.5	4.8	29
7	Calcium chloride	1.4	4.9	43
8	Magnesium chloride	2.0	4.9	49

results are shown in Table 1, and prove that the activity of the enzyme increases as mineralization of the system decreases and acidity rises, attaining 34 Cabaud units in a medium of distilled water. The presence of sodium chloride and potassium chloride does not induce such activity. On the contrary, addition of calcium chloride or magnesium chloride to the solution incubated raises serum transaminase activity above the level obtained in an aqueous solution without electrolyte admixture, in spite of the relatively small amounts of calcium chloride and magnesium chloride introduced (greater amounts of calcium chloride provoke precipitation of sediment with substrate).

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Isocitratase as an Enzymic Indicator of Metabolic Pathways

MANY micro-organisms form major quantities of *iso*citratase only when grown on substrates the catabolism of which ultimately produces acetate, and the provision of even small quantities of intermediates of the tricarboxylic acid cycle represses this formation of the enzyme[1-3]. This property can be utilized to decide between alternative modes of microbial degradation of growth substrates if one such alternative leads ultimately to the formation of acetate (or acetyl coenzyme *A*) and the other does not.

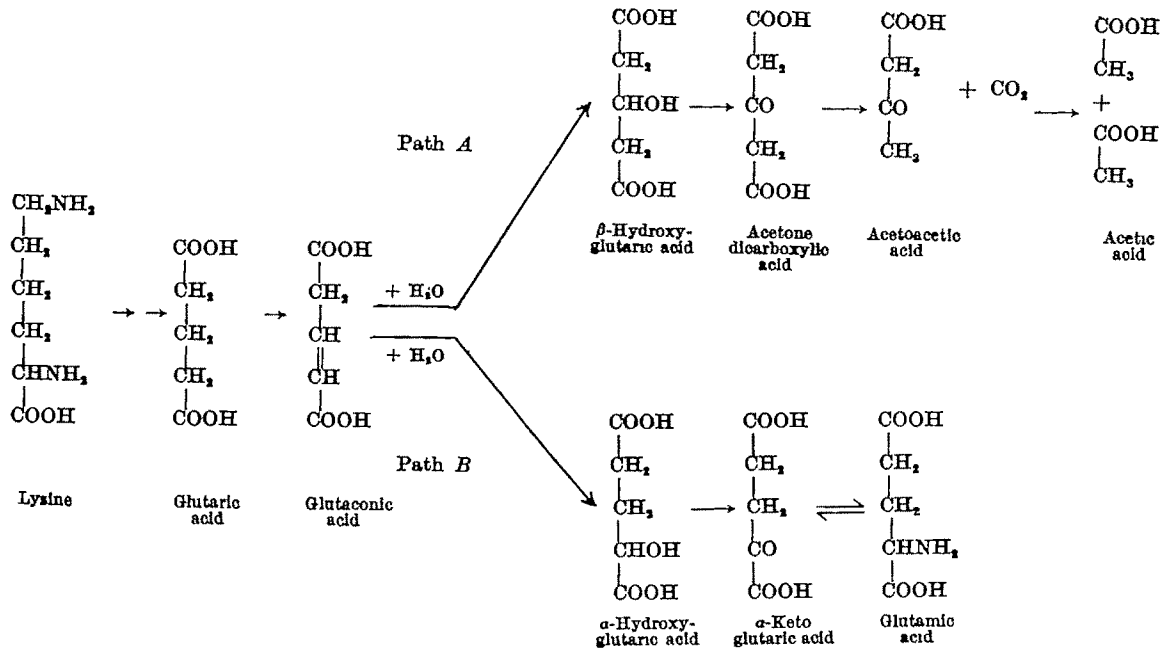
Table 1. *iso*CITRATASE ACTIVITY IN CELL-FREE EXTRACTS OF *Pseudomonas ovalis* CHESTER GROWN ON VARIOUS CARBON SOURCES

Carbon source for growth	Specific activity of *iso*citratase
Lysine	4·8
Glutaric acid	5·1
Acetone dicarboxylic acid	4·8
Acetoacetic acid	5·0
Acetic acid	5·2
α-Hydroxyglutaric acid	0·04
α-Ketoglutaric acid	0·05
Glutamic acid	0·05

Pseudomonas ovalis Chester was grown at *p*H 7·2 in 50 ml. of medium (ref. 1) containing 50 m*M* ammonium chloride, 50 m*M* phosphate, essential salts and the carbon source at 50 m*M* concentration. Extracts were prepared from the washed cells as previously described (ref. 1) and assayed for *iso*citratase (ref. 12). The levels of the enzyme in the extracts are expressed as the specific activity (μmoles of glyoxylate formed from *iso*citrate/hr./mgm. protein)

An example of this is the catabolism of lysine. Studies with mammals and mammalian tissue preparations have established[4-7] that lysine is catabolized via pipecolic and α-amino-adipic acids, to glutaric acid. The subsequent fate of glutaric acid is, however, in some doubt. Evidence has been obtained both for its β-oxidation to acetate[5,7-9], via acetone dicarboxylic acid and acetoacetate (path *A*), and its alternative α-oxidation[5,10,11] to α-ketoglutarate or glutamate via α-hydroxyglutarate (path *B*); the relative quantitative contribution made by these routes is not clear.

In an attempt to assess the relative importance of these two pathways in *Pseudomonas ovalis* Chester, the organisms were grown on media containing respectively lysine, or the sodium salts of glutaric, acetone dicarboxylic, acetoacetic, acetic, α-hydroxyglutaric, β-ketoglutaric and glutamic acids as sole sources of carbon. The *iso*citratase activity of extracts of cells thus grown was measured[12] (Table 1). Growth on the first five carbon sources listed in Table 1 (lysine and the substrates of path *A*) was accompanied by high and uniform levels of *iso*citratase, which indicates that their catabolism led chiefly to acetate. Growth on the last three substrates (the substrates of path *B*) led to formation of only traces of the enzyme.



Although these results do not provide evidence that the first five carbon sources listed are necessarily interrelated and are intermediates in the microbial degradation of lysine, they nevertheless show that the pathways of their catabolism are similar in leading to acetate, and different from the modes of degradation of the last three carbon sources. Since the specific activity of *iso*citratase after growth on lysine is closely similar to that produced after growth on postulated intermediates of its oxidation via path *A* and on the ultimate product, acetate, these results are consistent with its catabolism via this or some similar route also leading to acetate, and rule out path *B* as of quantitative importance in this organism. These findings are also in agreement with those of Andreoli and Wolfe[13], that oxidation of glutaric acid by an organism isolated from soil involves β-oxidation rather than α-oxidation.

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Estimation of Magnesium and Purification of Chlorophyll from *Chlorobium thiosulphatophilum*

Chlorobium thiosulphatophilum was grown under conditions similar to those described by Larsen[1]. '*Chlorobium* chlorophyll' (bacterioviridin) was extracted from the cells with 80 per cent methanol, transferred to ether, washed with water and dried over anhydrous sodium sulphate. The volume of the solution was reduced by evaporation under nitrogen, and the bulk of the chlorophyll precipitated by the addition of petroleum ether (b.p. 60–90). The chlorophyll was collected on talcum and washed with petroleum ether (b.p. 30–60) until the washings were colourless. The chlorophyll was removed from the talcum with acetone, transferred to ether, and washed with water. After drying, the solution was concentrated under vacuum, an equal volume of petroleum ether (b.p. 60–90) containing 4 per cent tetrahydrofuran added, and the solution adsorbed on to a sucrose column. The tetrahydrofuran was employed as a means of preventing precipitation of the chlorophyll in the column[2]. The column was developed by stepwise elution with *iso*propyl alcohol (0·75–2·0 per cent) in petroleum ether (b.p. 60–90°) containing 2 per cent tetrahydrofuran. The chlorophyll zone was cut out, dissolved in ether, and chromatographed as before. The absorption spectrum of the chlorophyll in ether was obtained on a Cary recording spectrophotometer. Peaks at 650, 575, 530, 425, and 406 mμ indicated that this chlorophyll was the '650' type described by Stanier and Smith[3], and that the organism studied was similar to or identical with *Chlorobium thiosulphatophilum*, strain *L*.

The magnesium content of the purified chlorophyll was determined spectrophotometrically by formation of a magnesium complex with sodium 1-azo-2-hydroxy-3-(2,4-dimethylcarboxanilido) - naphthalene-1′-(2-hydroxy-benzene-5-sulphonate)[4]. The purified chlorophyll, containing 0·5–10 μgm. of magnesium, was evaporated in a platinum dish, ashed with sulphuric acid, and collected as described by Koski and Smith[5]. The procedure was modified by keeping the total volume of water to less than 5 ml., and using 95 per cent ethanol for rinsing. The *p*H of the ethanolic solution of magnesium was adjusted to be slightly acid to phenolphthalein and transferred to a 25 ml. volumetric flask. Five ml. of the naphthalene-sulphonate reagent (0·15 mgm./ml. in 95 per cent ethanol) and 0·5 ml. of 0·08 *M* borax solution were added, the solution brought to volume with 95 per cent ethanol, and mixed. After 1 hr. the absorbance of the solution at 510 mμ was measured in a Beckman *DU* spectrophotometer using a distilled water blank and the concentration of magnesium in the solution calculated from a standard curve. The spectrophotometric sensitivity of this method is 0·0008 μgm. of magnesium/cm.^{2} as compared with a sensitivity of 0·006 μgm. for the titan yellow method.

Assuming that there is a 1:1 molar ratio of magnesium and chlorophyll, the calculated molar extinction coefficient at 650 mμ in ethyl ether is $99{\cdot}7 \times 10^3$. Using the value for the specific extinction coefficient at 650 mμ obtained by Stanier and Smith[3] for '*Chlorobium*-chlorophyll-650' (113·5 l./gm. cm.) the calculated molecular weight of the chlorophyll was 879.

This work was carried out under the auspices of the U.S. Atomic Energy Commission.

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Tryptic and Phosphatase Action on Certain Synthetic Phosphorylated Peptides

WITH the development of a new procedure for the synthesis of O-phosphorylated peptides, in which di-*p*-nitrobenzyl phosphorochloridate is used as the phosphorylating agent[1], we have had occasion to study the action of alkaline and acid phosphatase on certain synthetic substrates.

A preliminary report of our results seems to be justified from the fact that a correlation between chemical structure and phosphatase action is strongly suggested. Moreover, additional information on the inhibitory spectrum of phosphoserine[2] was gained by the synthesis of α-carbethoxy-L-lysyl-L-leucyl-L-(O-phospho)serine and the action of trypsin on it.

So far as the latter case is concerned, the key intermediate, α-carbethoxy-(ε-carbobenzoxy)-L-lysyl-L-leucyl-L-serine benzyl ester (I), was prepared in a similar series of reactions used in the preparation of α-carbethoxy-(ε-carbobenzoxy)-L-lysyl-L-serylglycine benzyl ester[3]; the product had $[\alpha]_D^{29}$ − 19·6° (c. 1 in glacial acetic acid). Analysis: calc., $C_{33}H_{46}N_4O_9$; C 61·6; H 7·1; N 8·7; found: C 61·6; H 7·1; N 8·6. Hydrogenolysis of it produced α-carbethoxy-L-lysyl-L-leucyl-L-serine (II) with $[\alpha]_D^{25}$ − 28·5° as 1 per cent solution in glacial acetic acid.

Phosphorylation[1] of I and subsequent removal of protecting groups with palladized charcoal afforded α-carbethoxy-L-lysyl-L-leucyl-L-(O-phospho)serine (III), m.p. 245–250° (Kofler block), $[\alpha]_D^{25}$ − 24·5° (c. 1 in glacial acetic acid.) Analysis: calc., $C_{18}H_{35}N_4O_{10}P$; N 11·2; P 6·2; found: N 10·9; P 6·1.

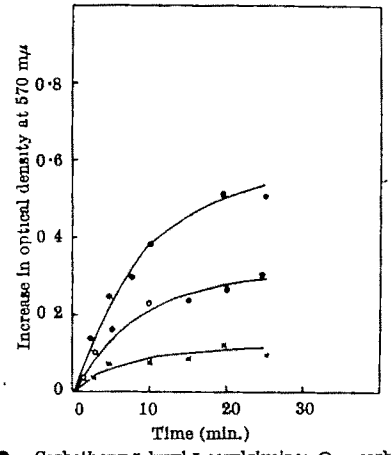

Fig. 1. ●, α-Carbethoxy-L-lysyl-L-serylglycine; ○, α-carbethoxy-L-lysyl-L-leucyl-L-serine; x, α-carbethoxy-L-lysylglycyl-L-serine. Hydrolysis of substrates (0·01 M) with 1 per cent trypsin (three times crystallized, Fluka preparation), pH 8·2 (tris buffer) at 25° C

The result of the tryptic action on substrate II is indicated in Fig. 1. Evidently, compound II is hydrolysed faster than α-carbethoxy-L-lysylglycyl-L-serine (obtained from hydrogenolysis of α-carbethoxy-(ε-carbobenzoxy)-L-lysylglycyl-L-serine benzyl ester[1]) and slower than α-carbethoxy-L-lysyl-L-seryl-glycine It must be emphasized, though, that the colour yield given by the splitting products has not been taken into account; but, so far, only *iso*leucyl peptides are reported to give very low colour yield with the ninhydrin reagent[4].

Compounds II and III were incubated with trypsin at pH 8·2 at 25° and the incubation mixtures were then checked by paper chromatography at different intervals up to 2 hr. In contrast to II, compound III was extremely slowly attacked by trypsin. Only traces of the splitting product, L-leucyl-L-(O-phospho)-serine, could be detected. Even after 18 hr. when II was completely hydrolysed, compound III gave a faint spot at the position of L-leucyl-L-(O-phospho)-serine.

It might be of interest to note that the splitting of II by trypsin is not inhibited in the presence of III. Similarly, α-carbethoxy-L-lysyl-L-(O-phospho)-seryl-

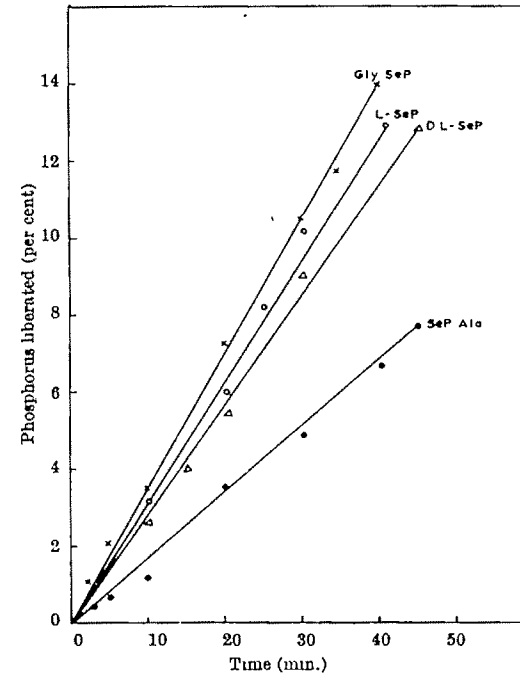

Fig. 2 Dephosphorylation of substrates (0·01 M) with alkaline phosphatase (0·1 mgm./ml., crude preparation, Fluka) in barbiturate buffer (0·2 M) pH 9·4 at 38° C L-SeP = L-phosphoserine; D,L-SeP = D,L-phosphoserine

glycine (m.p. 260–262°, Kofler block) does not retard the hydrolysis of α-carbethoxy-L-lysyl-L-serylglycine, when both substrates, in the ratio 1:1, 2:1 and 3:1, are incubated with trypsin. Since no competitive inhibition was observed under these experimental conditions, it seems reasonable to assume that the resistance of the above-mentioned phosphopeptides towards trypsin is due to the intense electrostatic field which results from the vicinity of a strongly acidic (phosphoric acid) and a basic group (ε-amino group of lysine).

It should be recalled that L-(O-phospho)seryl-L-glutamic acid, isolated by Posternak and Pollaczek, was resistant to the dipeptidase action, but sensitive

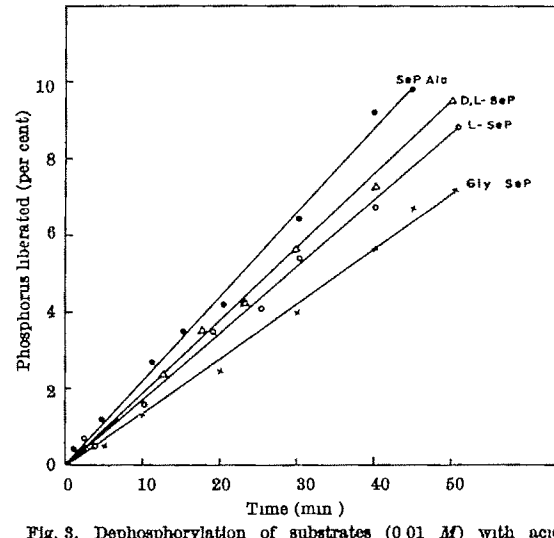

Fig. 3. Dephosphorylation of substrates (0·01 M) with acid phosphatase (0·1 mgm./ml., Lot 8055 Nutritional) in citrate buffer (0·1 M) pH 4·9 at 38° C.

to this enzyme after dephosphorylation[5]. Another tetrapeptide Ileu.SeP.Val.Arg. was only slowly attacked by leucine aminopeptidase, while the hexapeptide, Lys.Glu-NH_2.Ileu.SeP.Val.Arg., readily yielded a mixture of lysine, glutamine, glutamic acid and a large amount of the tetrapeptide possessing an amino-terminal *iso*leucyl residue[6].

Provided that essential phosphopeptides are produced during the breakdown of caseins, one could assume that, in this connexion, the phosphoserine residues might play an important part in controlling the selective splitting of peptide bonds. Additional support to this assumption is offered by the phosphatase specificity observed with certain synthetic substrates tested so far.

It is apparent from Fig. 2 that alkaline phosphatase dephosphorylates glycyl-D,L-(O-phospho)-serine (Gly.SeP) considerably faster than L-(O-phospho)-seryl-L-alanine (SeP.Ala), calculated as the monohydrate.

Acid phosphatase, on the other hand, was found to dephosphorylate L-(O-phospho)seryl-L-alanine faster than glycyl-D,L-(O-phospho)serine. The amount of phosphorus liberated was determined by the method of Fiske and SubbaRow[7].

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Ubiquinone (Coenzyme Q) in Insects

Lester and Crane[1] found that while tissues of vertebrates contain mostly the Q_{10}-homologue of ubiquinone (coenzyme Q), certain insects, notably the house-fly, *Musca domestica*, and the cabbage white butterfly, *Pieris rapae*, are characterized by the presence of the Q_9 homologue, that is, a ubiquinone with a side-chain of 9, instead of 10, isoprenoid units.

In continuation of our previous work on quinone-dependent respiratory systems in insects[2,3], we made an analysis of ubiquinone in the hawk-moth, *Celerio euphorbiae*. The fresh tissue was saponified, extracted with ether, the extract washed with water, concentrated to dryness, and the residue dissolved in absolute ethanol. The absorption of ultra-violet light due to the ubiquinone present in the ethanolic solution showed a peak at 272 mμ; but we found it impossible to shift it to 291 mμ by reduction with potassium borohydride. In order to purify the material, the ethanolic solution was kept at $-15°$ for 2 days, the precipitate which had appeared was removed, and the supernatant solution instilled on Whatman chromatographic paper No. 1, impregnated with 'Vaseline'. The chromatogram was developed in 95 per cent ethanol, and the paper area corresponding to the ubiquinone eluted with absolute ethanol. In this solution it was possible to demonstrate the characteristic shift of the absorption maximum from 272 to 291 mμ, which occurs after reduction.

In order to identify the ubiquinone homologue obtained from the hawk-moth, the chromatographic method of Page *et al.*[4] was used. However, instead of dimethylformamide, 95 per cent ethanol was employed for developing the chromatograms. In this way, it has been possible to achieve a much better separation of authentic samples of the Q_9 and Q_{10} homologues, which had been prepared from the yeast *Torula utilis*, and ox heart, respectively, using a modified method of Crane *et al.*[5].

In addition to the hawk-moth, *Celerio euphorbiae*, desiccated material from two other species of insects has been examined, namely, the pupae of *Sphinx pinastri* (Lepidoptera) and the adult insects of *Anatis ocellata* (Coleoptera). Just like the hawk-moth, the other two species have been found to contain the Q_{10} homologue of ubiquinone.

A detailed account of the experiments will be published in *Acta Biochimica Polonica*.

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The Epoxide Nature of the Carotenoid, Neoxanthin

IN his extensive investigation of the xanthophylls of leaves, Strain[1] described a common, widely distributed carotenoid which he named neoxanthin. Neoxanthin has since been reported by other workers, and the evidence suggests that, together with lutein and violaxanthin, it is one of the three major xanthophylls of leaves[1,2]. Despite its common occurrence, however, all that is known of this pigment is due to Strain.

Neoxanthin is characterized by: (1) its tight adsorption on chromatographic columns of magnesium oxide or aluminum oxide, where it is found above lutein, violaxanthin, and flavoxanthin; (2) its characteristic absorption spectrum, similar in shape and position to violaxanthin, and with more pronounced fine structure than lutein; (3) its solubility—neoxanthin is readily soluble in alcohol but only sparingly soluble in petroleum ether. On partition between 60 per cent aqueous methanol and petroleum ether, the pigment is found almost entirely in the hypophase[1].

Goodwin and Jamikorn[3] reported the presence of neoxanthin in the green flagellate, *Euglena gracilis*. Recently we too have found a pigment in this species which has similar spectral and adsorptive properties to the neoxanthin described by Strain. Strain worked much with barley. We have therefore compared this carotenoid to neoxanthin isolated from barley (*Hordeum*).

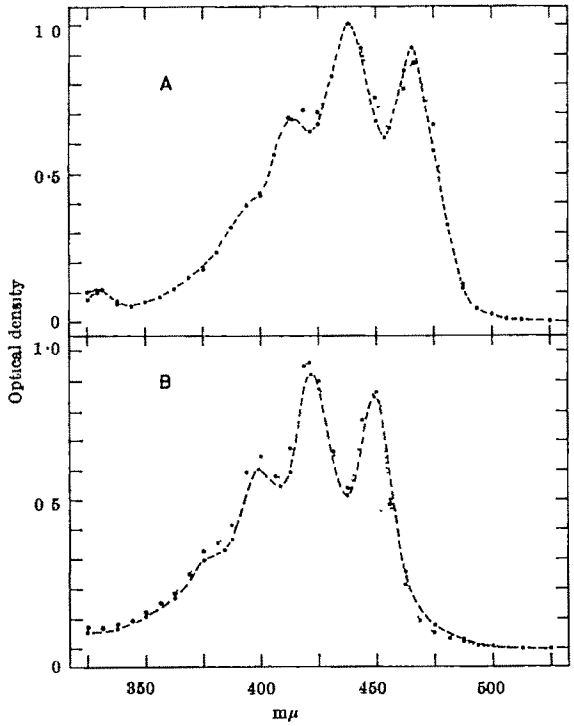
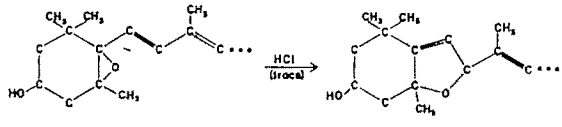


Fig. 1. (*A*) Absorption spectrum in ethanol of neoxanthin isolated from *Euglena* (dashed curve) and barley (dotted curve)
(*B*) Absorption spectrum in ethanol of the furanoid oxide produced from neoxanthin in the presence of traces of dilute hydrochloric acid

The tissues were dried by grinding with anhydrous sodium sulphate and the pigments extracted with acetone and ethanol. After saponification, the carotenoids were shaken into benzene, leaving the chlorophyll in the aqueous hypophase. The carotenoids were chromatographed from 10 per cent acetone in petroleum ether on a column of aluminium oxide. The neoxanthin fraction from *Euglena* was purified further by crystallizing the pigment from diethyl ether–petroleum ether. Further details of extraction and chromatography will be given elsewhere[4].

Fig. 1*A* is the absorption spectrum of neoxanthin in ethanol. The major peaks of absorption are at 466 and 437 mμ, as compared with 467 and 437 mμ reported by Strain[1].

As shown by Fig. 1*B*, the addition of a trace of hydrochloric acid results in a hypsochromic displacement of about 18 mμ. This shift is characteristic of the isomerization of a single 5 : 6 epoxide (I) to the 5 : 8 furanoid oxide (II), with the removal of one double bond from conjugation[5].



(I) (II)

No separation of the pigments from the two sources could be achieved in a mixed chromatogram on a column of aluminium oxide (Merck) 'weakened' by the addition of 5 per cent water. The column was developed slowly with 40 per cent acetone in petroleum ether; 100 per cent acetone; 2 per cent and finally 4 per cent ethanol in acetone. With the addition of ethanol to the eluant, the carotenoid migrated slowly as a single band.

Table 1. PARTITION COEFFICIENTS OF NEOXANTHIN

Source	Ratio of pigment in epiphase (petroleum ether) to pigment in hypophase (aqueous methanol): 60% methanol	50% methanol
Euglena	8:92	37:63
Barley	10:90	34.66

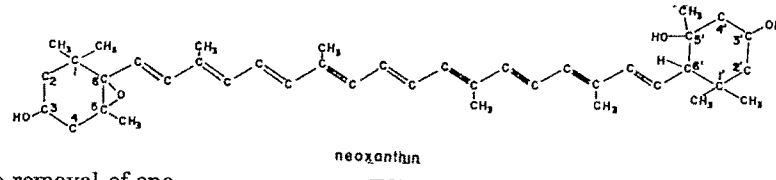
Quantitative partition coefficients, measured by the method of Petracek and Zechmeister[6], are given in Table 1. There can be little doubt that the pigment isolated from *Euglena gracilis* and neoxanthin isolated from barley are identical, and that this pigment is a mono-epoxide carotenoid. The degree of purification we feel accounts for the minor differences in absorption spectra.

From its spectral similarity to violaxanthin (ref. 1 and unpublished work by us) and neurosporene[7], this pigment appears to have only nine conjugated double bonds. Inasmuch as the epoxide group is in the 5:6 position, 5′:6′ must be saturated. Neoxanthin is much more hypophasic in partition tests than antheraxanthin (3,3′-di-hydroxy-5:6-epoxy-β-carotene)[4]. This and the firm adsorption during chromatography indicate the presence of a fourth polar group, such as a third hydroxyl.

Table 2. ELEMENTARY ANALYSIS OF NEOXANTHIN (DATA FROM STRAIN (1))

	Predicted for. $C_{40}H_{56}O_4$	$C_{40}H_{58}O_4$	Observed (average and range of four analyses)
C	79 93	79·70	79 87 (79·02–79 70)
H	9 41	9·69	9 67 (9·50–9 78)

Strain, from his elementary analysis, suggested that the results fit the general formula $C_{40}H_{56}O_4$. We believe his results could be somewhat better represented by the formula $C_{40}H_{58}O_4$ (Table 2). On the basis of these results, the spectral characteristics, behaviour on partition, and adsorption we propose the following tentative structure (III) for neoxanthin:



neoxanthin

(III)

Neoxanthin 3,3′,5′(or 6′)-tri-hydroxy-6′(or 5′)-hydro-5 6-epoxy-β-carotene).

It should be pointed out that this structure is a possible intermediate in the formation of the diepoxide, violaxanthin.

It also appears likely that foliaxanthin, a monoepoxide of unknown structure reported by Cholnoky *et al.*[8] as present in the leaves and fruit of the yellow paprika, is identical with neoxanthin.

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A Method for concentrating Solutes of High Molecular Weight

CONCENTRATION of diluted aqueous solutions of labile solutes of high molecular weight, such as proteins, is often difficult in the laboratory as well as on a technical scale. We wish to present a mild concentration method, which seems to be useful in such cases.

This method is founded on the special property of a cross-linked dextran 'Sephadex' (Pharmacia, Uppsala (Sweden), which, even after swelling to a gel in aqueous media, will not admit large molecules, while there is little or no restriction of the diffusion of smaller molecules. If, therefore, dry 'Sephadex' is added to a solution, a concentration of solutes of high molecular weight is obtained corresponding to the amount of water taken up by the swollen grains. At the same time, salts and other solutes of low molecular weight are removed to an extent that ionic strength and *p*H remain approximately constant during the procedure.

As an example of the applicability, we wish to report an experiment where the liquid medium from a culture of *Polyporus versicolor* was concentrated prior to the isolation of cellulase. The purification of this enzyme will be described in greater detail elsewhere (Petterson, G., Cowling, E., and Porath, J.).

7·5 litres of clarified culture medium were divided into three equal portions and 750 gm. 'Sephadex *G*-25' were added to each of these. The sieve fraction of this material was 50–100 mesh and its water regain was 2·6 gm. per gm. of dry 'Sephadex'. The thick suspension was stirred for 10 min. to obtain complete swelling of the gel, after which the gel grains were separated from the concentrated enzyme solution in a basket centrifuge (*M.S.E.* 3000). The centrifugation was started with a moderate centrifugal field, which was progressively augmented as the flow decreased. The filter cake was then washed by spraying a small amount of water centrally. The centrifugates and washes were pooled and subjected to an additional concentration step. At this stage the volume of the solution was small enough to be handled in one operation. After a third treatment the volume was reduced to an extent which made further purification by traditional methods more convenient. The concentration in three steps was accomplished in less than 4 hr. in spite of the large number of operations. (It should be possible to reduce the time required to about 1 hr. by omitting the washings and by using a larger centrifuge in the first step.) The process was followed by determination of the cellulase activity as measured by the increase in the number of reducing end-groups[1]. The results obtained are given in Table 1.

Table 1. CONCENTRATION OF CELLULASE WITH 'SEPHADEX *G*-25'

	Enzyme solution (ml.) In	Out	Test quantity (ml.)	Activity (units per ml.)	Total activity
Original sample	7,500		1·0	0·532	4,000
First step					
Main fraction	7,500	3,045	1·0	1·245	3,790
First wash	300	300	1·0	0·400	120
Second wash	300	274	1·0	0·105	29
Second step					
Main fraction	2,930	1,130	0·5	3·816	4,310
First wash	117	122	0·5	2·196	268
Second wash	117	92	0·5	0·418	39
Third step					
Main fraction	1,020	410	0·1	8·48	3,480
First wash	41	34	0·1	2·58	88
Second wash	41	31	0·1	0·46	14
Third wash	41	26	0·1	0·19	5

The determination of activity is somewhat uncertain, as can be seen in the value for the main fraction of the second step. It is evident that this value is too high when compared to the original activity. According to the results in Table 1, the cellulase is almost quantitatively recovered in the 15-fold concentrated solution. The low activities in the washes show that it is possible to separate the concentrate almost completely from the swollen gel-grains quite easily.

For the application of the method described here, the following requirements must be fulfilled by the water-absorbing substance: (1) it should swell rapidly in water; (2) it should be easily and quantitatively separable from the concentrate; (3) it should be insoluble and not contaminate the concentrate; (4) it should not adsorb solutes which are to be concentrated.

Generally all these demands seem to be satisfied by 'Sephadex', if an appropriate particle size is used. Its upper limit is determined by requirement (1), and requirement (2) determines the lower limit. According to our own experience, only a small amount should pass a 100-mesh sieve.

Several procedures have been tried to separate the swollen gel-grains from the concentrate. The method described here, using a basket centrifuge, is particularly suitable for concentrating large volumes, while filter adapters in centrifuge tubes have been used when the concentration is carried down to a 1-ml. volume. The separation can, of course, also be made by filtration with suction or pressure; but losses are in general higher. Experiments have also been made to separate the concentrate in a column. For this purpose the suspension of gel in the concentrate is poured into a column and the concentrate is displaced by water. The method gave satisfactory results when the packing was carried out in such a way as to give a sharp boundary between the concentrate and the displacer.

Concentration with 'Sephadex' has been used for other substances sensitive to evaporation or freeze-drying, such as choline esterase, pancreatic lipase, phosphatases, and phosphodiesterases. Concentration of pepsin has been described by one of us[2]. In connexion with paper electrophoresis, this method has been used routinely.

Generally, very high recoveries have been obtained, amounting to more than 90 per cent at 10–20-fold concentration. In connexion with experiments involving some proteins of low molecular weight (cytochrome *c* and a phosphatase from *E. coli*), some complications have appeared. A considerable part of the activity remained in the gel and could be recovered only after extensive washing of the filter cake. Difficulties will probably arise also in the concentration of very viscous solutions.

It is of practical importance that the 'Sephadex' could be regenerated. This was done by first washing with water, followed by two suspensions of the material in ethanol, and drying at 80° C. The dried substance could then be used for new concentration experiments without any detectable difference in its properties.

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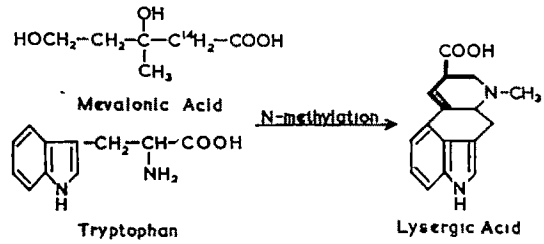
Biogenesis of Lysergic Acid in Ergot

SEVERAL schemes have been proposed for the biogenesis of the medicinally valuable lysergic acid moiety of the ergot alkaloids[1–5]. Recently, it was shown by Taber and Vining[6], and later verified by Baxter *et al.*[7], that tryptophan (β-^{14}C) serves as a precursor for lysergic acid. Gröger and co-workers[8] demonstrated that tryptophan (β-^{14}C) is also a precursor for the chemically related clavine alkaloids, which are produced by certain strains of ergot; but the carboxyl group of tryptophan does not enter the molecule. The nature of the precursor of the remaining portions of lysergic acid and of the clavine alkaloids has remained a puzzle. Groger[9] demonstrated that, when acetate (1-^{14}C) was fed to saprophytic cultures of ergot, the radioactivity was incorporated into the clavine alkaloids. Since the alkaloids were not degraded, the biogenetic significance of this work is not clear.

Mevalonic acid has been recognized as a key compound in the biogenesis of isoprenoids, terpenoids, and steroids. In 1959, Groger[9] added mevalonic acid to the saprophytic culture medium, but found no significan increases in total production of clavine alkaloids. We have found that mevalonic acid serves as the precursor for the *iso*pentenyl portion of lysergic acid:



So far as we are aware, this is the first demonstration of mevalonic acid serving as a biogenetic precursor for an alkaloid. (Since this communication was written, clavine alkaloids have been derived from mevalonic acid by Birch, A. J., *et al.*, *Z. Naturforsch.*, 15, b, 141; 1960.)

A series of cultures of *Claviceps purpurea* (*PRL* 1578) were grown in batches of 40 ml. of liquid nutrient medium in 125-ml. flasks. After 15–30 days, 1 μc. of radiologically pure mevalonic acid-2-^{14}C (21·9 mgm. = 1 mc.) was added to each flask. Two weeks later the medium and the mycelium were separated by filtration, the medium made alkaline with ammonia, and the alkaloids extracted with chloroform. The mycelium was dried, finely powdered, and defatted with petroleum ether. The alkaloids were extracted with ammoniacal ether. The two alkaloidal extracts were evaporated to dryness, and the residues were dissolved in a mixture of chloroform and *iso*propanol (3 : 1); a portion was spotted on formamide-impregnated paper[9] and chromatographed (descending) with carbon tetrachloride/chloroform/benzene (7 : 2 : 1). In this solvent system the ergot alkaloids are separated well and in order of increasing R_F values: ergotamine, ergosine, ergotaminine, ergosinine, ergocornine plus ergocristine, ergocryptine, ergocorninine plus ergocristinine, and ergocryptinine; the water-soluble ergometrine and ergometrinine remain at the origin.

Ergotamine and ergosine were eluted separately from the carbon tetrachloride–chloroform–benzene–chromatogram with 50 per cent ethanol and hydrolysed according to the method of Jacobs and Craig[10]. The hydrolysate was chromatographed with butanol/acetic acid/water (4 : 1 : 1) on Whatman No. 1 paper. Autoradiograms showed the radioactivity to coincide exactly with the location of lysergic acid (R_F 0·40) as established from its fluorescence under ultra-violet light and the blue colour given by this indolic compound with Ehrlich's reagent. The behaviour of the compound was identical to that of authentic lysergic acid and to the behaviour of lysergic acid in the hydrolysate of pure ergotamine.

For the separation, identification, and isolation of ergometrine a second portion of the alkaloid mixture was chromatographed (descending) in butanol–acetic acid–water on Whatman No. 1 paper. In this solvent system ergometrine has an R_F of 0·60 while the peptide-type alkaloids have an R_F of 0·85. Both these fluorescent radioactive areas were eluted separately with 50 per cent ethanol, the eluate hydrolysed and chromatographed (descending) with butanol–acetic acid–water on Whatman No. 1 paper. In both cases the lysergic acid was found to be radioactive as revealed by autoradiograms. All the radioactivity of the alkaloids resided in the lysergic acid.

Mevalonic acid did not enter appreciably the general metabolism of the mould. More than 90 per cent of the radioactivity of converted mevalonic acid-2-^{14}C was found incorporated into the lysergic acid portion of the ergot alkaloids. The petroleum ether fraction of the mycelium contained less than 10 per cent of the total added radioactivity. The amino-acids which were extracted from the mycelium showed no radioactivity.

A more detailed and extended account of this work will be published elsewhere.

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PHYSIOLOGY

Rectifying Properties of Heart Muscle

A FACTOR of likely importance in the genesis of the long-lasting action potentials of vertebrate heart muscle is the influence of membrane potential on the potassium permeability of the fibres. That a difference here exists between cardiac muscle and nerve is evident from Weidmann's[1] demonstration of a low slope conductance during the plateau of the action potential. But little information is so far available on the voltage dependence of the membrane conductance under conditions designed to avoid the generation of action potentials.

To study this point, so far as the technical limitations imposed by the structure of cardiac muscle at present allow, excised Purkinje fibres from sheep ventricles were used. While sharing the essential electrical properties of myocardial tissue, these fibres do not produce a mechanical response on depolarization; they are also insensitive to parasympathomimetic substances so that choline chloride or sucrose may be used as a substitute for extracellular sodium chloride to abolish excitability.

Fig. 1, *A* and *B*, shows how the membrane conductance of a Purkinje fibre in sodium-deficient solution depends on the direction and magnitude of the polarizing current. An outward current of 0·31 μamp., for example, produced the same voltage deflexion as is caused by nearly twice as great an inward current. Allowing for the cable properties of the fibre, this means that the conductance to a depolarizing current may be about four times less than to a hyperpolarizing current. Since the contribution of chloride ions to the membrane conductance of cardiac muscle is small[2], a decrease in the potassium conductance presumably occurs on depolarization. The direction of the potassium conductance change in Purkinje fibres is thus opposite to the predominant change in nerve[3], but has a parallel in skeletal muscle[4].

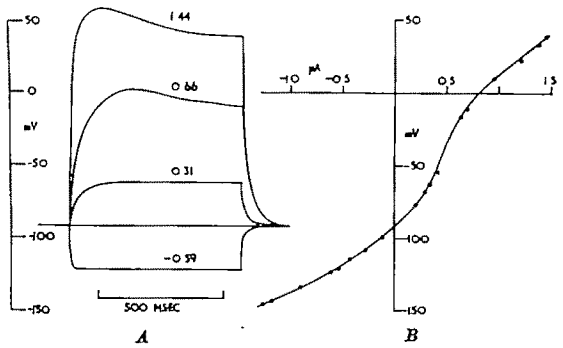

Fig. 1 *A*. Superimposed tracings of electrotonic potentials from a sheep's heart Purkinje fibre. Sodium ions in Ringer's solution replaced by choline. Depolarization is shown in an upward deflexion from a resting potential of −92 mV. Two closely spaced KCl-filled intracellular electrodes were used to record the membrane potential and to pass practically rectangular current pulses of a strength indicated by the figures on each record. *B*, Current-voltage relation for the same preparation Ordinate, membrane potential at end of current pulse lasting 700 m.sec. Abscissa, total membrane current

With strong depolarizing currents a decline in the electrotonic potentials during the pulse may be observed, suggesting a gradual increase in conductance. This second effect probably accounts for the S-shaped relation between the amplitude of the electrotonic potential at the end of a long pulse and the polarizing current (Fig. 1 *B*), but over the physiological range the conductance remains below its value at the resting potential.

The slope conductance decreases appreciably over the range occupied by the slow diastolic depolarization in spontaneously beating preparations[1]. This alinearity may require consideration in interpreting the resistance changes observed during the pacemaker potential[5].

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Cardiac Action and Pacemaker Potentials based on the Hodgkin–Huxley Equations

SINCE the equations describing the nerve action potential were formulated by Hodgkin and Huxley[1], the range of phenomena to which they have been shown to apply has been greatly extended. Huxley[2] has applied them to the influence of temperature on the propagated response and to the repetitive firing observed in low calcium concentrations. More recently, Fitzhugh[3] has shown that the long action potentials induced by tetraethylammonium ions in squid nerve may also be reproduced.

The computations described in this communication were carried out with the aim of reconstructing the long-lasting action potential and pacemaker potential of cardiac muscle. Although this work was done independently, the results agree with those of Fitzhugh in showing that action potentials of long duration may be accounted for by Hodgkin and Huxley's formulation of the membrane properties. The description of the potassium current, however, differs from that used by Fitzhugh and provides a better description of the conductance changes.

The equations I have used to describe the sodium current are very similar to Hodgkin and Huxley's,

those for h (the variable describing the availability of sodium carriers) being based on Weidmann's[4] experiments on the availability of sodium carriers in Purkinje fibres.

The behaviour of the potassium battery in cardiac muscle differs from that in nerve in that the potassium conductance (G_K) falls when the membrane is depolarized[5]. A small delayed increase in conductance appears to be present when large currents are used, but this is not great enough for the conductance of the depolarized membrane to exceed the resting conductance. For the purpose of setting up equations to describe this behaviour, it is convenient to suppose that potassium ions move through two types of channel in the membrane. In one, G_K is an instantaneous function of the membrane potential and falls when the membrane is depolarized. A simple empirical equation has been used to describe the current in this channel. In the other type of channel the rectification is in the opposite direction and occurs with a delay. The conductance of this channel may be described by Hodgkin and Huxley's equations for delayed rectification with two modifications. First, the magnitude of this conductance must be small; accordingly the maximum conductance ($\overline{G_K}$) has been made less than 1/50 of that in nerve. Secondly, the time constants have been made very much longer to take account of the slow onset of the effect.

The membrane capacity was taken as 12 μF./cm.^{2} (ref. 4), and the absolute values of the various conductances were adjusted to give a resting membrane resistance of about 2,000 ohms/cm.^{2} (ref. 4).

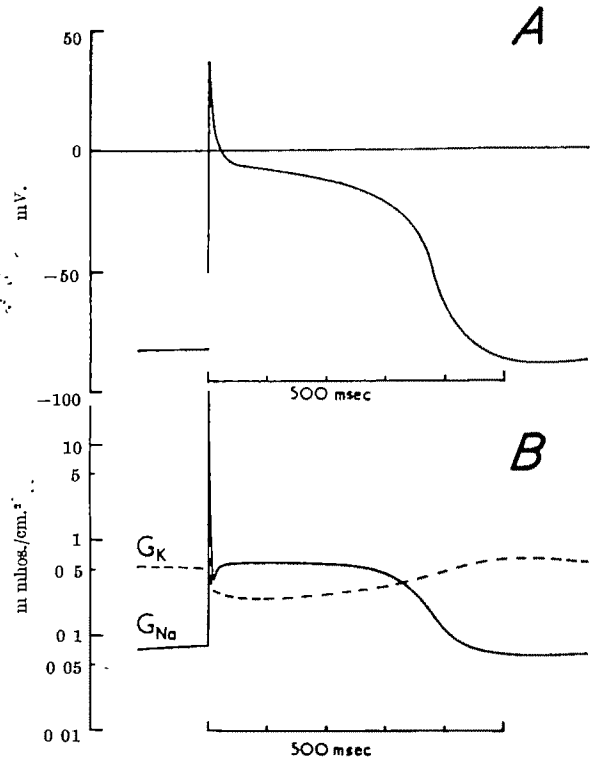

Fig. 1. A, Computed action potential. The integration was started by displacing the membrane potential to −60 mV., which is equivalent to a very short cathodal pulse of 3 6 × 10^{-7} coulombs/cm.^{2}. B, Time course of computed conductance changes on a logarithmic scale. G_K, potassium conductance, G_{Na}, sodium conductance. The potassium and sodium equilibrium potentials were set at −100 mV. and + 40 mV. respectively

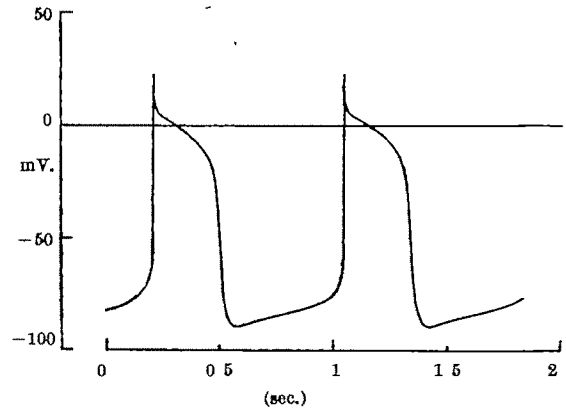

Fig. 2. Solution to equations in which the membrane potential is unstable in diastole so that pacemaker activity occurs. In this case, the potential at which the steady state sodium and potassium currents are equal and opposite is −38 mV. and an unstable state at this potential corresponds to a second solution to the equations

The equations were set up on a digital computer and were integrated by a numerical approximation using a step length of 0·05 m.sec. during the initial spike of the action potential and 0·3 m.sec. during the slower phases. In this connexion I should like to thank Dr. R. A. Buckingham, director of the University of London Computer Unit, for permission to use *Mercury* for this purpose, and Dr. M. J. M. Bernal and other members of the Computer Unit staff for advice on programming.

It was found that computed responses resembling action potentials of different durations could be obtained by inserting appropriate values for the constants in the equations for m (the variable describing the activation of sodium carriers). One of the solutions is shown in Fig. 1. It can be seen that the general shape of the action potential (A) corresponds very closely to that observed experimentally in Purkinje fibres[4]. The time-course of the computed conductance changes is shown in Fig. 1B. After an initial 'spike', the sodium conductance (G_{Na}) settles down to a value during the plateau which is about 8 times its resting value. G_K by contrast is below its resting value throughout the duration of the plateau.

The total membrane conductance ($G_K + G_{Na}$) rises during the plateau, but the slope conductance (determined by adding current to the equations at different times during the integration) was found to decrease. This is the result of a decrease in the sodium slope conductance which becomes negative towards the end of the plateau. Although the slope conductance during the plateau falls to a value which is equal to the resting conductance, the decrease was not so great as that observed experimentally[4]. This may be the result of a defect in my equations which over-estimate the potassium current produced by large depolarizations of the membrane.

If a large enough repolarizing current is added to the equations during the plateau, an all-or-nothing repolarization is initiated. The threshold for this phenomenon is about −30 mV. at the middle of the plateau, which is in fair agreement with that found experimentally by Weidmann[4].

In these equations there is always at least one potential at which the steady state sodium and potassium currents are equal and opposite. In the computations just described, this forms the resting potential and the system is stable unless excited. A

small change in the constants in the equations for m is sufficient to make the system unstable in diastole, and pacemaker activity then occurs. Such a solution is shown in Fig. 2. However, in order to bring about repolarization in this case a larger delayed potassium conductance had to be assumed. It is not yet known whether this is a necessary feature of the equations and further computations are being made to test this point. Nevertheless, the sensitivity of the computed pacemaker potential to changes in ionic conductance has been shown to correspond quite well with the experimental information available[6].

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Relative Vascularity of Certain Anatomical Areas of the Brain and Other Organs of the Rat

IT need scarcely be pointed out that for the meaningful interpretation of the results of work where an exogenous material is administered to an animal and the assay performed on dissected areas of tissues with their content of blood, as is usually the case, it is frequently necessary to know the contribution of blood to the respective areas. This is particularly true if the concentration of a given substance is much greater in the blood than in the tissues.

Several approaches were made by different investigators[1-5] to determine the vascularity of the central nervous system of the cat, but so far as we know, nothing similar has been reported for the rat since the earlier work of Craigie[8]. He used the method of direct capillary counts of specimens from animals injected with carmin gelatin to determine the relative vascularity, but the limitations of this method are obvious. Furthermore, it has not included all the anatomical areas of interest to us. In 1955 Oeff and König[7] reported the blood content of several organs of the rat including whole brain in the non-bled out, bled out, and perfused animals using erythrocytes labelled with phosphorus-32. They did not, however, determine the blood content of the various anatomical areas of brain. In their work on the cat, Barlow *et al.*[1] have approached this problem using human serum albumin labelled with iodine-131 and demonstrated the relative vascularity by means of densitometric measurements of the autoradiograms.

Their technique consisted of killing the animal by intracardiac injection of a saturated solution of potassium chloride, dissecting out the brain, hardening it on a bed of dry ice followed by sectioning. The whole operation was performed at room temperature (29°). They observed that "tissue radioassay data of an anatomical structure within a single animal and of the same structure from animal to animal showed wide variation and were, therefore, useless for quantitative purposes. It is clear that dissection-sampling technique inadvertently included varying amounts of large blood vessels containing highly concentrated radioactivity giving rise to gross inconsistencies". However, by selecting areas on the autoradiogram corresponding to tissue areas containing blood within only small blood vessels and capillaries and avoiding large blood vessels, they were able to obtain values in good agreement with those found by others using capillary counting techniques. The problem referred to by Barlow *et al.* is a general one and arises also in distribution and metabolism work where such techniques are utilized.

It seems that the major factors which contribute to the inconsistencies in similar experiments are: (1) Varying amounts of residual blood that is retained in the brain tissue as a result of the varying loss which is inevitable in the process of dissection. (2) Contamination from blood which is also unavoidable. It is not difficult to see that in this case, where there is a tremendous concentration gradient from blood to the adjoining tissue, how adversely this situation can affect the results. (3) Since the operation is performed at room temperature, there is some condensation of moisture on the cold surface of brain slices which may lead to spreading, leaching, and further contamination of areas. The influence of these factors is greater when one is dealing with the very small areas of brain. In the present work, we have avoided these difficulties by using the following technique.

White male rats, weighing 250–300 gm., were injected by the tail vein with 10 μc./100 gm. of human serum albumin labelled with iodine-131 (*RISA*, Abbott). Pentobarbital sodium (4 mgm./100 gm.) was also administered along with the albumin to facilitate withdrawal of blood by intracardiac puncture, minimizing at the same time influences of stress on the animal. At the end of 15 min., 1 ml. of blood was withdrawn from the heart, and the animal was killed by rapid immersion in acetone–carbon dioxide mixture (−78°). It was then transferred to a refrigerated room (−10°), allowed to remain for 1 hr., and all subsequent operations were carried out there. The brain was chiselled out of the frozen animal with a 6 mm. wide chisel and after removal of the meninges and the larger blood vessels on the surface, 2–3 mm. thick serial coronal sections were obtained by free-hand sectioning with a razor blade. The areas dissected from the central nervous system were: cerebral cortex, cerebral white matter, caudate nucleus, thalamus, hypothalamus, hippocampus, inferior colliculi, cerebellar cortex, medulla and spinal cord. Similarly, sciatic nerve, kidney cortex, kidney medulla, periphery of the left lateral lobe of liver, skeletal muscle, and adrenals were also dissected. Of these, the cerebral white matter and the cerebellar cortex were the most difficult to dissect with any degree of assurance. It is to be noted that during the whole operation, in view of the fact that it is performed in the refrigerated room on the frozen animal, there was neither loss of blood nor contamination by blood; nor was there any spreading of activity from the blood as a result of condensing moisture. The areas dissected were homogenized in 1·5 ml. of water, 1 ml. of the homogenate transferred to weighed glass tubes and the radioactivity determined in a well-type scintillation counter. The tubes containing homogenate were then dried to constant weight in a desiccator. Table 1 shows the results from 15 animals. The results are expressed as a ratio of the specific activity of the area over the activity of a microlitre of hæmolysed blood of the same animal taken at the time of killing, times 10^2. An absolute determination of the vascularity was not attempted in this investigation, but it merely sought to establish a set

Table 1. RELATIVE BLOOD CONTENT OF DIFFERENT AREAS OF THE BRAIN AND CERTAIN OTHER ORGANS OF THE RAT

Area	$\frac{\text{counts/min./mgm dry wt}^*}{\text{counts/min./}\mu\text{l. blood}} \times 10^3$
Cerebral cortex	8 49 ± 0 59
Cerebral white	3·33 ± 0 33
Caudate nucleus	5 53 ± 0 11
Thalamus	5 67 ± 0·13
Hypothalamus	3 61 ± 0 29
Hippocampus	5 38 ± 0 36
Inferior colliculi	8 32 ± 0 63
Cerebellar cortex	10 95 ± 0·68
Medulla	5 25 ± 0·35
Spinal cord	3 33 ± 0 33
Sciatic nerve†	3·37 ± 0·44
Kidney cortex	67 60 ± 3·40
Kidney medulla	140·70 ± 15·50
Liver	81 80 ± 4 03
Skeletal muscle	3·84 ± 0 34
Adrenals‡	117 20 ± 11·58

* Means of 15 experiments ± standard error
† Means of 11 experiments ± standard error
‡ Means of 4 experiments ± standard error

of ratios which is adequate for the intended use of this information.

The experimental conditions for this work were carefully chosen so that identical conditions could be adapted for studies concerning drug distribution and permeability changes within the central nervous system. We are at present investigating two classes of compounds: one that enters the brain tissue rapidly and one that does not cross the blood–brain barrier, and it is hoped that the results will show the usefulness of the technique and the validity of the results obtained with iodinated albumin. It may be concluded from the present experiments that: (1) the vascularity of the central nervous system of the rat is certainly not uniform and the interpretations arrived at in the past on the basis of the average value of 0·024 ml. of blood per gm. of brain tissue[8] may need reconsideration. (2) There is a variation (for the range see Table 1) from animal to animal in the blood content of various areas. This would suggest the need for study of a large number of animals, particularly in the case of a substance the blood concentration of which is not much different to the concentration in tissue. (3) The results presented in Table 1 provide a reference scale which is of use in the study of distribution of drugs within the central nervous system of rat when the contribution of vascularity is also to be taken into account.

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Isolation of Glomerula from Rat Kidney

IN contrast to the renal tubular system the glomerulum has not received as much attention biochemically as it deserves. This is mostly due to the difficulties in isolating a pure glomerular fraction. Only during the past ten years have a few methods been worked out which are, however, too complicated and time-consuming for the study of enzyme patterns in single normal or diseased animals. McCann's method[1], using manually isolated glomerula from frozen-dried sections, is limited by the small amount of tissue available for analysis. To obtain larger samples, attempts have been made to isolate the glomerula from crude kidney homogenate. Liberation of the glomerula from surrounding tissue was achieved by using a Potter–Elvehjem tissue homogenizer[2] with a mismatched plunger[3] or pushing the kidney through a fine-meshed wire gauze[4–8]. The purification of the glomerular fraction was performed either by repeated centrifugation[4], by filtration through a layer of glass balls[7], or by magnetic attraction following intra-arterial injection of iron trapped in the glomerula[8]. No detailed information on purity or yield of the glomerula was given. For enzyme work on normal and diseased glomerula a method had to be developed allowing rapid, and technically simple, isolation.

Table 1. DISTRIBUTION OF ALKALINE PHOSPHATASE IN FRACTIONS *H*, *M*, *T* AND *G*

Fraction	*N*	μM *p*-Nitrophenol/min./mgm. protein $\bar{X}$	s
H ('homogenate')	8	0 651	0 220
M (medulla)	7	0 030	0·015
T ('tubular material')	7	0·662	0·293
G (glomerula)	5	0·180	0 030

This was achieved by pushing out the glomerula of the surrounding tubules in a homogenizer with an ill-fitting pestle[3], centrifuging the resulting crude homogenate against an osmotic gradient and eliminating impurities by sieving several times through graded nylon mesh sieves. The capsule of kidneys of rats weighing 180–200 gm. is stripped off, the hilar structures and the medulla (Table 1: fraction *M*, 20 per cent w/v, homogenate in isotonic sucrose) dissected away. The remaining cortex is cut into small pieces with scissors, suspended in isotonic sucrose (final concentration 20 per cent, w/v) and coarsely ground in a Potter–Elvehjem apparatus[2] using an unmatched plunger until the tissue pieces have disappeared (fraction *H*). The suspension is then put through a nylon *HD* 250-μ mesh sieve (obtained from Zuricher Beuteltuchfabrik A.G., Am Schanzengraben 15, Postfach 1123, Zurich 22). In the meantime, a plastic cylinder (Fig. 1,*b*) with a 100-μ mesh sieve as the bottom (*e*) was inserted into a centrifuge tube (*a*) filled with 25 per cent sucrose solution up to 2 cm. above the level of the sieve (*d*). 5–10 ml. of fraction *H* are layered on the hypertonic sucrose in the plastic tube (*c*), and centrifuged for 10 min. at 3,000 r.p.m. in a refrigerated centrifuge. There then appears at the top a yellowish viscous fluid containing microscopical particles which are believed to be of tubular origin because of their high content in alkaline phosphatase (fraction *T*). On the net are found small pieces of tubules and the majority of the glomerula. This material is resus-

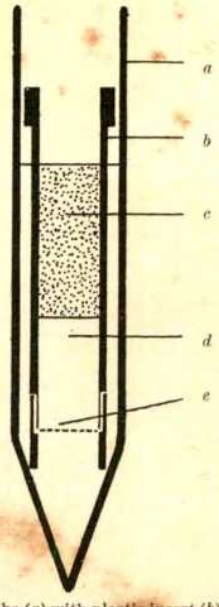

Fig. 1. Centrifuge tube (*a*) with plastic insert (*b*) for centrifugation through a mesh sieve (*e*) against an osmotic gradient (*c*/*d*)

pended in 8 per cent sucrose and filtered through a 150-μ sieve which eliminates most of the tubular fragments. The remaining impurities are removed by two or three more filtrations through 100–200-μ mesh sieves. A photomicrograph of the final glomerular fraction *G* is presented in Fig. 2 (courtesy of Prof. E. Hintzsche, director of the Anatomical Institute, University of Berne). Most of the glomerula are devoid of their capsule and only occasional specimens still show an intact Bowman capsule (right lower corner). It is important to carry out all the manipulations in the cold and to control the procedure by microscopic examination. Even so, the whole process can be completed within 1 hr. of killing the animals.

To determine the yield of glomerula, counts were made from fractions *H* and *G*. Assuming 27,000 glomerula per gm. rat kidney[9], 29 ± 8 per cent ($\bar{X} \pm s$; $N = 7$) of glomerula are recovered in fraction *H* and 7 ± 3 per cent in fraction *G*. This suffices for the assay of a number of enzymes and for manometric studies of the glomerula isolated

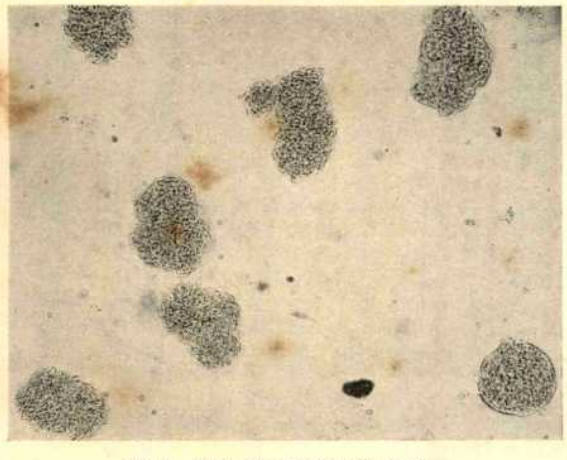

Fig. 2. Photomicrograph of fraction *G*

from one animal. To obtain a quantitative measure of the purity of the glomerular fraction, alkaline phosphatase activity was determined[10] in homogenates and based on protein content[11]. The results (Table 1) reveal a three-fold concentration of this enzyme in fractions *H* and *T* as compared to fraction *G*. Work on a number of other enzymes, oxygen uptake and glycolysis of isolated glomerula will be presented elsewhere.

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Active Transport of Sodium by Isolated Frog Skin in Relation to Metabolism of Acetate labelled with Carbon-14

Although it is well established that isolated frog skin uses energy for the active transport of sodium, little is known about the metabolic processes providing this energy. Huf[1] showed that monobromacetate caused a decrease in potential across the frog skin which could be reversed by pyruvic and lactic acids, but not by glucose. Similar results were obtained by Francis and Gatty[2].

These experiments suggest, but do not clearly establish, that exogenous metabolites can be used by the skin. The use of appropriate metabolites labelled with carbon-14 appeared to offer an approach to this problem. Preliminary work by one of us (K. Z.) done in the Department of Biophysics, Purdue University, indicated that the isolated frog skin could take up and metabolize a number of carbon-14-labelled compounds.

The short-circuiting technique of Ussing and Zerahn[3] was employed for determining sodium transport. The apparatus used was only slightly modified from that of Zerahn[4]. The skin was placed as a barrier between two glass compartments so that each could be individually filled with solution, stirred, drained and refilled with ease. The compartment facing the inner side of the skin was filled with Ringer solution to which was added the labelled metabolite to be studied, and vasopressin to obtain a higher rate of sodium transport. Streptomycin was also added to this solution in about half the experiments to reduce bacterial growth.

In other experiments, it was found that isotopic equilibrium is not attained in several hours of equilibration. A preliminary 2-hr. period of contact of the skin with labelled metabolite was therefore allowed, and the bathing solutions of this period were discarded. The medium from subsequent experimental periods was acidified and the released carbon

dioxide collected in a small volume of sodium hydroxide using a spiral absorption apparatus developed by Holm-Jensen (Holm-Jensen, J., unpublished work).

The radioactivity of carbon dioxide samples was compared to the radioactivity of the inside solution and thus permitted calculation of the amount of tracer metabolite utilized.

The labelled metabolites were obtained from Amersham and were generally used at a level of 0·5 μc. per period. Acetate was chosen as a representative metabolite and was used at a level of 1 m*M*.

During the transport period the compartment on the outside of the skin was filled with Ringer solution. In this way the sodium transport can be determined from the reading of the short-circuit current. Total production of labelled carbon dioxide and thus total labelled acetate utilization were determined.

To determine the amount of the radioacetate used which did not contribute to sodium transport, a blank period of non-transport was done during which the outside Ringer solution was replaced with distilled water. Other means of obtaining non-transport periods, such as the use of an applied potential of 150 mV. (inside positive), gave similar results.

Alternate 90-min. periods of non-transport and transport were carried out, and the average value of acetate carbon-14 used for two non-transport periods was subtracted from the value of the intervening transport period. The labelled metabolites contained some labelled carbon dioxide. No correction was made for this activity because it represented a minor fraction of the labelled carbon dioxide collected, and furthermore, calculation of the difference as above allows for the presence of a blank.

The following assumptions are made in the calculations: (1) Both the carbons of radioacetate contribute to production of carbon dioxide to about the same extent. This was confirmed in work with acetate-1-^{14}C and acetate-2-^{14}C. (2) For each mole of acetate metabolized, two molecules of oxygen are utilized. Since Zerahn[4] and Leaf and Renshaw[5] have shown that one molecule of oxygen is used for each 18 atoms of sodium transported, each mole of acetate used for transport will provide for the transport of 36 atoms of sodium. Each atom of sodium will thus require the use of 1/36 mole or 0·0278 mole of acetate. (3) From the net acetate used and the amount of sodium transported, the fraction of the sodium transport due to the use of the acetate of the medium is calculated.

The experimental findings are summarized in Table 1. It is clear that the added acetate can be utilized by the isolated frog skin as is indicated by the first two columns and that it is utilized for sodium transport is shown by the third column. The fraction of the sodium transport supported by the metabolism of the exogenous acetate is given in the last column. (This is, furthermore, the relative specific activity in per cent of the radioacetate added.)

Table 1. METABOLISM OF ACETATE-1-^{14}C BY THE ISOLATED FROG SKIN

μmole/hr. of labelled acetate used during			△ Sodium μmoles	μmole acetate per μmole sodium transported	Fraction of sodium transport by radioacetate (per cent)
Transport	No transport	Net			
0·216	0·139	0·077	5·8	0·0133	48
0·284	0·226	0·058	11·2	0·0052	19
0·442	0·226	0·216	15·0	0·0144	52
0·392	0·321	0·071	5·7	0·0125	45
0·466	0·329	0·137	10·5	0·0130	47
0·299	0·150	0·149	13·2	0·0113	41
0·344	0·180	0·164	13·2	0·0126	45
0·467	0·220	0·256	8·4	0·0304	109
0·312	0·165	0·147	11·8	0·0125	45
0·468	0·250	0·218	13·2	0·0165	59
0·386	0·203	0·183	12·3	0·0149	54

In similar work we have shown that lactate is used at a rate similar to acetate, but that glucose was metabolized to a smaller extent.

It can be concluded that: (1) The serosal surface of the isolated frog skin is permeable to exogenous acetate and lactate; (2) the skin can use these compounds for metabolism; (3) added metabolites can support sodium transport; (4) when the exogenous acetate is present at a level of 1 m*M*, an appreciable fraction of the total sodium transport can be directly related to the use of the added acetate.

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An Adaptive Change in an Inbred Mouse Strain maintained in a Cold Environment

A STRAIN of *A2G* mice (*Mus musculus* L.), maintained for a number of generations in a room kept at −3° C., has progressively improved in ability to cope with the cold. The mice were obtained from Glaxo Laboratories, and had a long history of sib mating. When the breeding was begun in the cold environment, a parallel colony was started at 21° C. (controls). Members of a single litter were used to start the two colonies: one pair was kept at 21° C. and the other transferred to −3° C. These initial pairs were the parents of the first generation of mice studied. All subsequent breeding pairs too were litter mates, and were selected at random at the age of 5 weeks. Reproductive performance was recorded to the age of 28 weeks. There were few barren pairs in the cold, and only one after the fourth generation. One control pair, in the fourth generation, failed to produce young. The methods used, and some of the physiological changes in the mice kept in the cold, have already been described[1-3,5].

The evidence of a secular change in the response to cold comes from the loss of young between birth and 21 days (weaning). Fig. 1 shows that the controls had a consistent infant mortality of about 22 per cent. The mice in the cold lost nearly 80 per cent of the young in the second generation, but by the ninth generation they were losing 10 per cent or fewer.

The loss of young born to first-generation pairs in the cold was significantly lower ($P < 0·05$) than to those of the second generation. Since the parents of the mice of the first generation had been reared at 21° C., it seems likely that these mice provided a better uterine environment and milk supply than the second-generation parents. Other data, not yet published, tend to confirm this.

The secular improvement could be due to changes either in maternal performance or in the young; both could be involved. There was no evidence of a pro-

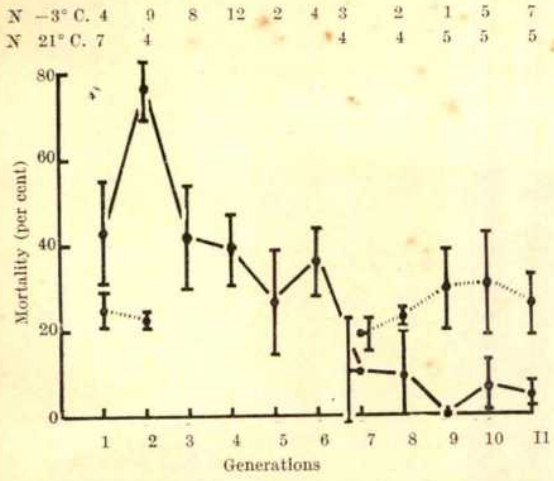

Fig. 1. Mortality between birth and 21 days, by generation. Continuous line: mice at −3° C.; broken line: controls. Each point is a group mean for pairs of one generation. Vertical lines represent standard errors. The numbers of pairs are shown at the top. No control data are available for generations 3–6

gressive increase in fecundity in the cold: in fact, the number of young born per pair did not change significantly in either temperature. The most probable sources of the improvement are (*a*) increased milk yield[6,8], (*b*) superior ability of the young to respond to the low temperature by increased heat production[3,4].

Whatever the physiological basis, the results require explanation in terms of either (1) a steady genetical change in the colony maintained at −3° C.; or (2) a cumulative maternal effect.

(1) The first hypothesis implies that the original strain was genetically heterogeneous despite its long history of sib mating (since mutation cannot account for a rapid progressive trend of the kind observed). If this were so, it would be necessary to assume that there were present genetical mechanisms which tended to maintain heterozygosis in the face of rigorous inbreeding. There are empirical grounds for rejecting this hypothesis, in the work of Deol *et al.*[7]: these authors give evidence that inbred mouse strains are genetically homogeneous, and that the formation of sub-lines is due to the occasional appearance of mutant genes which "tend to be fixed promptly in homozygous condition". The fact that the improvement continued even when the infant mortality was low is also against this hypothesis, since natural selection can occur only if the breeding of some members of each generation is diminished either by death or by reduced fertility.

There are also theoretical grounds for doubting whether heterozygosis at several loci could be maintained in an animal such as the mouse, since an excessively high loss of progeny would be required in each generation[9].

(2) The second hypothesis implies that the change is wholly one of 'nurture'. Survival in the cold demands extensive physiological adaptation. The young not only must themselves respond to the cold environment, but also may be influenced by the adaptive adjustments made by the mother: this effect could be through the environment either in the uterus or in the nest (the nest environment includes the milk supply). The hypothesis requires that the ill-effects of rearing the females in the cold were progressively reduced through a cumulative improvement in physiological adaptation to cold. There is no obvious argument against this, but there is little evidence to show how the change could have been brought about.

Neither hypothesis accounts for the fact that, from the seventh generation on, the infant mortality in the cold was consistently lower than in the warm. This implies that, in the long run, so far as survival during the first 3 weeks was concerned (though not in other ways), the cold environment was the superior one. Yet the infant mortality in the warm was similar to that reported by other workers; there is consequently no reason for thinking that there was anything wrong with the conditions in the warm room.

Whether the change in infant mortality was due to heredity or environment, it has implications for any experiments in which mice (and perhaps other mammals) are maintained for several generations in an environment very different from that of a control group. Just what these implications are depends on the exact nature of the change; this is being studied. The results will in any case be more fully reported and discussed later.

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Presynaptic Nature of Neuromuscular Depression in the Frog

WHEN a number of successive nerve impulses arrive at a curarized neuromuscular junction, the induced end-plate potentials show a gradual decrease in size (Wedensky-inhibition, or junctional fatigue). Two different mechanisms, though not exclusive of each other, are conceivable.

(1) The amount of acetylcholine liberated at the nerve endings might be decreased, presumably in consequence of the depletion of the store of transmitter substance[1–4].

(2) The sensitivity of the end-plate to acetylcholine might be decreased as a result of the desensitizing action of the transmitter.

Recently, Thesleff[5] reported that the latter mechanism was a main cause of the diminution of the size of the end-plate potential in the rat. In the following experiment it will be shown that, in contrast with the case in the rat, the first mechanism is the main cause of neuromuscular depression in the frog and that the latter mechanism plays only a negligible part, if any.

A recording micro-electrode was inserted at the end-plate region of a curarized sciatic-sartorius preparation of the frog. Constant quantities of acetylcholine were applied electrophoretically from a second micro-pipette containing a 1·1 *M* solution of the substance, which was located on one of the sensitive spots of the same end-plate. End-plate potentials were induced

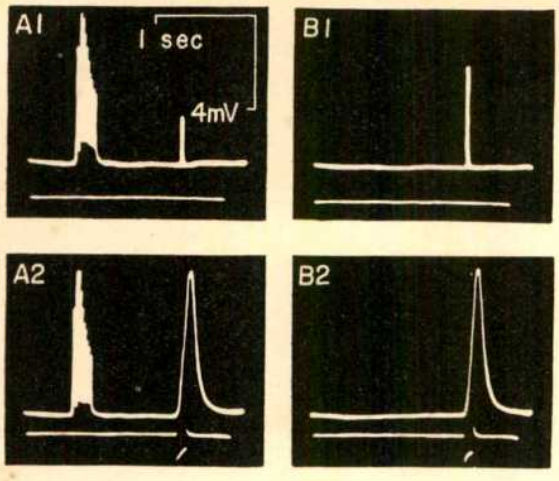

Fig. 1. End-plate and acetylcholine potentials following the conditioning repetitive stimulation. In each record, the upper trace shows the membrane potential recorded from the end-plate region. In the lower trace the strength of the current through the acetylcholine pipette was monitored.
A, End-plate potential (*A*1) and acetylcholine potential (*A*2) about 0·9 sec. after repetitive stimulation.
B, End-plate potential (*B*1) and acetylcholine potential (*B*2) 11 sec. after repetitive stimulation.
Conditioning stimuli were given every 20 sec. Neuromuscular transmission was blocked by *d*-tubocurarine 3×10^{-6}. The muscle was stretched by about 20 per cent of its resting length. Resting potential was 89 mV.
Monitor calibration: '4 mV.' scale = $1{\cdot}2 \times 10^{-7}$ A.

by supramaximal nerve volleys. End-plate and acetylcholine potentials were recorded at various intervals after the conditioning stimuli consisting of 10 successive nerve volleys at a frequency of 50 per sec.

Fig. 1 shows that about 0·9 sec. after the conditioning stimuli the size of end-plate potential is decreased by 55 per cent compared with that of the end-plate potential which is not preceded by repetitive stimulation. The amplitude of acetylcholine potentials, on the other hand, remains completely unchanged whether preceded by conditioning stimuli or not.

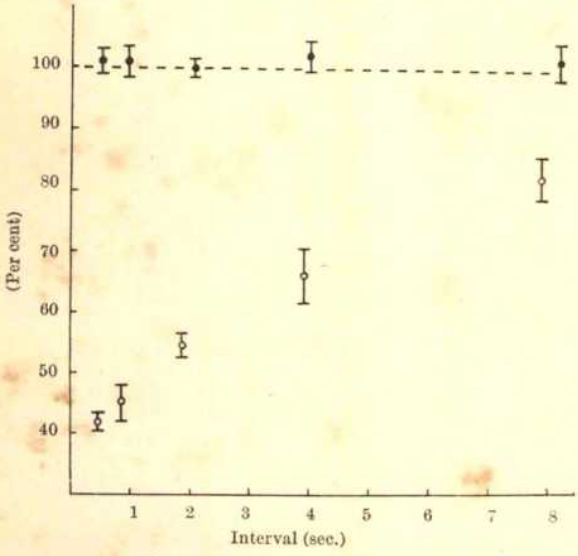

Fig. 2. Plot of amplitudes of end-plate and acetylcholine potentials after 10 successive nerve volleys. The same experiment as in Fig. 1.
Ordinate: Amplitudes of end-plate potentials (o) and of acetylcholine potentials (●) as percentage of those of unconditioned end-plate potentials and of unconditioned acetylcholine potentials respectively. Each point and vertical line represent mean value and ± *S.D.* respectively calculated from five determinations. Abscissa: Intervals between the end-plate or the acetylcholine potentials and the conditioning stimuli

The amplitude of end-plate potentials and that of acetylcholine potentials at increasing intervals after conditioning stimuli are given in Fig. 2 as a percentage of amplitudes of end-plate and acetylcholine potentials which are not preceded by repetitive stimulation.

Essentially the same result was obtained from the preparation in which the activity of cholinesterase was completely inhibited by prostigmin 2×10^{-6}.

It is concluded from this experiment that the sensitivity of the end-plate to acetylcholine remains entirely unchanged even when the amplitude of the end-plate potential is markedly decreased after repetitive stimulation. This conclusion is in good agreement with the earlier suggestion[1,2] of the presynaptic nature of neuromuscular depression, but makes a sharp contrast with the result obtained by Thesleff in the rat. The difference between Thesleff's result and ours might be due to use of a different species; or, the diminution of the response to acetylcholine after conditioning stimuli observed in the rat might have been caused by the mechanical movements, since even a very minute movement suffices to abolish completely the response to acetylcholine.

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Actions of the Decarboxylase Inhibitor, α-Methyl-3,4-dihydroxyphenylalanine, in the Dog

Alpha-methyl-3,4-dihydroxy-DL-phenylalanine was shown by Sourkes[1] to be a potent inhibitor of the decarboxylation of 3,4-dihydroxyphenylalanine *in vitro*. This action was confirmed by animal studies in which the pharmacological actions of 3,4-dihydroxyphenylalanine and 5-hydroxytryptophan were decreased by administration of this compound[2,3]. Further evidence of the activity of α-methyl-3,4-dihydroxy-DL-phenylalanine *in vivo* was obtained by Smith[4], who reported that levels of serotonin in the brains of mice were decreased after parenteral administration of this compound. More recently, Oates *et al.*[5], in this Laboratory, observed a decrease in the formation of serotonin, tryptamine and tyramine from the precursor amino-acids when 1·0–6·0 gm./day of α-methyl-3,4-dihydroxy-DL-phenylalanine were administered to hypertensive patients. Associated with this decrease in amine production was the development of transient sedation and a lowering of the blood pressure.

In the present investigation, intravenous administration of α-methyl-3,4-dihydroxy-DL-phenylalanine was found to decrease the blood pressure and to produce sedation of the unanæsthetized dog, thus making it possible to study these actions of the inhibitor by pharmacological and biochemical techniques not

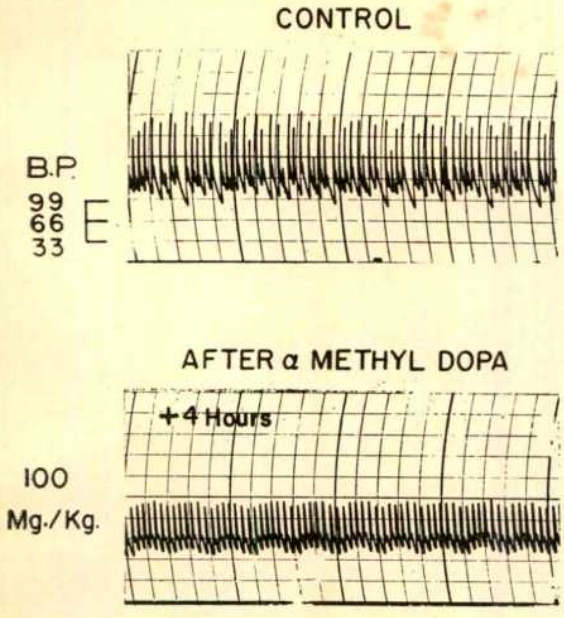

Fig. 1. Femoral arterial pressure of an unanæsthetized dog before (above) and 4 hr. after intravenous administration of 100 mgm./kgm. of α-methyl-3,4-dihydroxy-DL-phenylalanine. The scale to the left of the upper tracing is in mm. mercury. The heavy vertical lines signify 10-sec. intervals

applicable in man. Blood pressure was recorded from the femoral artery in five unanæsthetized, semi-trained, mongrel dogs by direct puncture or by cannulation of the artery under local anæsthesia. The pressures were measured electronically by means of a Statham transducer and Grass polygraph. In each animal, intravenous administration of 100–200 mgm./kgm. of α-methyl-3,4-dihydroxy-DL-phenylalanine produced reductions in arterial pressure ranging from 30/10 to 60/30 mm. mercury (Fig. 1). The hypotension did not begin until 2–3 hr. after drug administration and the maximum effect was usually not observed for 4–6 hr. The blood pressure returned to normal values within 24 hr., and in three of the animals repeated administrations of α-methyl-3,4-dihydroxy-DL-phenylalanine on 2–7 subsequent days produced equivalent hypotensive effects. At the time the blood pressure was reduced, there was no consistent change in heart-rate, no alteration in the response to tilting the animal through 90°, and no relaxation of the nictitating membrane. In most experiments, the animals appeared to be quietened by the inhibitor, but they were easily startled by noise. Injections of saline in the same animals had no effect on blood pressure recorded under identical conditions.

Heart contractile force was measured by a Walton strain gauge arch in seven vagotomized, anæsthetized, open-chest dogs as previously described[6]. The pronounced and prolonged increments in heart contractile force produced by 10–20 mgm./kgm. of L-3,4-dihydroxy-DL-phenylalanine or DL-metatyrosine, injected intravenously, were found to be completely inhibited by intravenous administration of 100–200 mgm./kgm. of α-methyl-3,4-dihydroxy-DL-phenylalanine. This total inhibition remained for 30 min. after drug administration and then gradually decreased so that the responses of 3,4-dihydroxy-DL-phenylalanine and metatyrosine were essentially back to control-levels in 4–6 hr. In these and similar experiments, the cardiovascular effects of l-norepinephrine, dopamine and tyramine were not significantly altered. The increments in heart-rate and contractile force produced by stimulation of the presynaptic fibres to the stellate ganglion were also not blocked by administration of α-methyl-3,4-dihydroxy-DL-phenylalanine, indicating that the function of the sympathetic ganglion and nerves was intact.

In order to correlate the pharmacological actions of the inhibitor with biochemical changes, preliminary determinations of decarboxylase inhibition and serotonin-levels in the brain (caudate nucleus) and norepinephrine in the heart (atria) were obtained in thirteen additional dogs. Eight dogs were killed by bleeding under barbiturate anæsthesia at 3, 5, and 24 hr. after intravenous administration of α-methyl-3,4-dihydroxy-DL-phenylalanine as shown in Table 1. Five dogs were killed in a similar manner to serve as controls. Serotonin-levels and decarboxylase inhibition were determined by previously described techniques[7]. Trichloracetic acid extracts of tissues were purified by absorption on alumina and the eluates were assayed fluorimetrically for norepinephrine by a modification of the trihydroxyindole method[8]. The high fluorescence of α-methyl-3,4-dihydroxy-DL-phenylalanine or of its metabolites remaining in the tissues prevented determination of norepinephrine levels in the 3- and 5-hr. samples. Accordingly, two additional experiments were carried out with a related decarboxylase inhibitor, α-methyl-3-hydroxy-DL-phenylalanine (α-methyl metatyrosine), which does not interfere with norepinephrine determinations.

Table 1. EFFECTS OF DECARBOXYLASE INHIBITORS ON LEVELS OF SEROTONIN IN THE BRAIN AND NOREPINEPHRINE IN THE HEART

No. of dogs	Inhibitor	Dose (mgm./kgm.)	Time (hr.)‡	Serotonin (caudate nuclei) (μgm./gm.)	Norepinephrine (atria) (μgm./gm.)
5	Control	—	—	1·03	2·41
2	α-methyl dopa*	200	3	0·43	—
2	α-methyl dopa	200	5	0·78	—
2	α-methyl dopa	200	24	1·13	1·88
1	α-methyl dopa	500	24	1·00	1·77
1	α-M.M.T.†	200	5	0·41	1·74
1	α-M.M.T.	400	5	0·50	1·53

* α-methyl-3,4-dihydroxy-DL-phenylalanine.
† α-methyl-3-hydroxy-DL-phenylalanine.
‡ Time in hours after administration of inhibitors.

The results of the serotonin and norepinephrine determinations are shown in Table 1. As may be noted, there was a decrease in the serotonin-levels in the brain to values 60 per cent lower than those of the control animals in 3 hr., but in the 5-hr. specimens the serotonin-levels had returned to 80 per cent of control values. These changes in serotonin content appeared to be related to decarboxylase inhibition for in 3 hr. there was 40 per cent inhibition, but there was no inhibition demonstrable in the 5-hr. specimens. These *in vitro* determinations of decarboxylase inhibition, therefore, correlated well with the inhibition of the cardiac actions of 3,4-dihydroxy-DL-phenylalanine and metatyrosine *in vivo*. Norepinephrine-levels were decreased slightly 5 hr. after α-methyl-3-hydroxy-DL-phenylalanine and 24 hr. after α-methyl-3,4-dihydroxy-DL-phenylalanine. Serotonin-levels and decarboxylase inhibition were approximately the same in the specimens obtained 5 hr. after administration of α-methyl-3-hydroxy-DL-phenylalanine as in the specimens obtained 3 hr. after α-methyl-3,4-dihydroxy-DL-phenylalanine.

The results of this work indicate that the pharmacological effects of α-methyl-3,4-dihydroxy-DL-

phenylalanine in the dog do not appear to be related to decreased function of the peripheral sympathetic nerves or to an adrenergic blocking action. The preliminary biochemical work demonstrates that α-methyl-3,4-dihydroxy-DL-phenylalanine is a potent decarboxylase inhibitor and decreases serotonin-levels in the dog. These changes, however, did not appear to be temporally related to the pharmacological effects in the unanæsthetized dog. The decrements in norepinephrine-levels in the heart were not pronounced and were probably of little pharmacological significance since the response of the heart to stimulation of cardiac sympathetic nerves was unaltered. Additional work is being carried out to determine whether the pharmacological actions of α-methyl-3,4-dihydroxy-DL-phenylalanine and similar compounds are related to decarboxylase inhibition.

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HÆMATOLOGY

Glucose-6-phosphate Dehydrogenase Deficiency, Haptoglobin Groups, Blood Groups and Sickle Cell Trait in the Bantus of West Belgian Congo

SINCE the demonstration that red blood cells of almost 10 per cent of American Negroes are deficient in glucose-6-phosphate dehydrogenase[1,2], one can suppose that the same defect exists in West Africa. The semi-quantitative test described by Motulsky[3] is particularly suitable for a rapid and efficient screening of the male subjects in a given population.

We made such a survey among the adult male Bantus of Leopoldville, capital of the Belgian Congo. More than 75 per cent of the inhabitants of this town originated from the west parts of the country. Among 522 adult males, we found 112 deficient subjects (21·5 per cent). This percentage is one of the highest hitherto discovered in adult males (Table 1). We have found by our own experience that, among deficient males, the glutathione stability test according to Beutler[4] gives the same results as the screening test proposed by Motulsky.

Table 1. RACIAL INCIDENCE OF GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY IN MALE SUBJECTS

Origin	Deficient percentage	Screening method
Sardinians (ref. 5)	8	Glutathione stability test
American Negroes (ref. 1)	8·8	Glutathione stability test
Iranians (ref. 6)	9·8	Glutathione stability test
Non-Ashkenazic Jewish (ref. 7)	11·2	Glutathione stability test
Nigerians (ref. 8) (two tribes)	6·14–16·9	According to Motulsky
Congolese Bantus	21·5	According to Motulsky

To obtain a more complete view of the genetic pattern of these Bantus, we performed a survey, determining in each of a group of 150 adult male subjects the following genetically inherited characteristics of the blood: A, B, O and D blood groups, sickle cell trait (paper and starch-gel electrophoresis at *p*H 8·6 coupled with falciformation test), haptoglobin groups (according to Laurell[9] on starch-gel electrophoresis) and glucose-6-phosphate dehydrogenase activity in erythrocytes (according to Motulsky).

Table 2

Origin	Phenotype percentage A	B	AB	O	Origin	Phenotype percentage D	d	D^u
Congolese male Bantus	26·2	21·2	5·8	46·8	Idem	94	3·3	2·6
Belgians (Hubinont, ref. 10)	43·3	7·9	3·4	45·4	Belgians (Moureau, ref. 11)	82·4	17·6	

As already known, the phenotypes B and D are more frequent among Bantus than among Caucasians (Table 2). Nevertheless, the genes of A, B, O, and rhesus blood groups are not closely linked with the genes responsible for the glucose-6-phosphate dehydrogenase deficiency, as indicated by a χ^2 test.

Phenotype number	AB	A	B	O
Non-deficient	7	30	28	58
Deficient	2	11	5	15

$\chi^2 = 1·5$, P between 0·7 and 0·5.

The Congolese Bantus have one of the highest sickle cell trait incidence in the world. Figures of 25–30 per cent in the west and central parts of Belgian Congo are quoted by Vandepitte[12]. In our group of 151 male adult Bantus, we found 33 subjects with the genotype AS (21·8 per cent). Although almost equal in incidence, the enzyme deficiency and sickle cell trait do not appear to be linked.

Tested number	AS	AA
Non-deficient	25	93
Deficient	8	25

$\chi^2 = 0·376$, P between 0·7 and 0·5.

We did not find any person belonging to the haptoglobin genotype 0–0, as described by Allison[13]. It appears from the literature that the percentage of haptoglobin groups varies according to different races. Congolese Bantus present the highest percentage for haptoglobin group 1–1 and the lowest for haptoglobin 2–2 hitherto described (Table 3). There is no apparent linkage between the genes of glucose-6-phosphate dehydrogenase deficiency and those of haptoglobin groups.

Phenotype number	1–1	1–2	2–2
Non-deficient	62	42	5
Deficient	20	11	0

$\chi^2 = 1·72$, P between 0·3 and 0·5.

Table 3. RACIAL INCIDENCE OF HAPTOGLOBIN GROUPS

Origin	Phenotype percentage			Gene percentage	
	1—1	1—2	2—2	1	2
Indians (ref. 14)	1·8	14·6	81·7	0·09	0·91
Bushmen (ref. 15)	10·8	36	53	0·29	0·71
Swedish (ref. 16)	15	47	38	0·38	0·61
Ivory Coast (ref. 17)	49	42	9	0·70	0·30
Congolese Bantus	59	37·5	3·5	0·77	0·22

Summarizing, we can assert that Congolese Bantus are characterized by a high incidence of S hæmoglobin, glucose-6-phosphate dehydrogenase deficiency, haptoglobin 1, B and D blood group genes. These facts support the hypothesis of poor admixture of foreign blood in this population.

This particular genetic pattern induces some pathological consequences and raises a few questions.

(1) In the Bantu, the incidence of hæmolytic disease of the newborn by anti-D iso-antibodies is quite uncommon.

(2) Clinicians must bear in mind the possibility of hæmolytic crisis in patients lacking glucose-6-phosphate dehydrogenase, induced by drugs like 8-aminoquinolines, naphthol derivates, sulphones and nitrofurazone. This last-named drug is certainly dangerous as demonstrated by one of us in a Bantu patient[18]. As the enzyme activity in erythrocytes of deficient Bantus is 1/5–1/8 of a normal control (Sonnet, J., and Haumont, A., unpublished work), it is likely that deficient Bantus are not so sensitive as Caucasian males, whose enzyme deficiency is almost complete.

(3) The parallelism between the high incidence of sickle cell trait and enzymatic deficiency in the Bantus, as compared with American Negroes, suggests that, in a tropical environment, an identical underlying cause could exert a positive selection on both kind of carriers. As suggested by Motulsky, the mechanism of this advantage could be a protection against *Plasmodium falciparum* infection.

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Hæmagglutination of Cells treated with Antibiotics

PREVIOUSLY, we directed attention to the occurrence in certain sera of an antibody-like factor capable of causing hæmagglutination of group O, Rh-negative red cells modified by exposure to penicillin[1,2]. The reaction appears to be specific and is inhibited by preliminary mixing of the sera with penicillin.

We have extended this work to try to determine the presence of hæmagglutinating factors for erythrocytes modified by other antibiotics. Negative results were obtained with streptomycin, dihydrostreptomycin and tetracycline. However, from a series of 1,700 routine hospital blood bank sera tested, six were found capable of agglutinating chloramphenicol-modified cells. Titres ranged from 1/2 to 1/128, when the sera were diluted in 0·85 per cent saline and incubated at 37·0° C. for 1½ hr. followed by spinning at 1,000 rev./min. for 1 min. before reading.

Sensitized cells were prepared by adding 250 mgm. of chloramphenicol to 4·0 ml. of fresh blood in 4·0 ml. of Alsevers solution. Incubation at 37·0° C. for 1 hr. was followed by storage at 4·0° C. overnight. For use, 2·0 ml. of suspension were washed four times in 20·0 ml. of saline and resuspended to make an approximate 10 per cent suspension. Red cells exposed to a mixture of penicillin and chloramphenicol were agglutinated in the presence of each homologous positive serum.

The hæmagglutinin against chloramphenicol-modified cells appears to be similar to that against penicillin-modified cells. Both are stable on heating, and the reaction is inhibited in the presence of the appropriate antibiotic. In each instance dilution in 30 per cent bovine albumin solution leads to an approximate four-fold reduction in titre. None of the sera against chloramphenicol-modified cells gave a positive antiglobulin test. Solutions of urea (20 per cent), sodium salicylate (5·0 per cent), and glycerol in saline (20 per cent) inhibited both reactions, suggesting that the nature of the physical associative interaction between the molecules may be one of hydrogen bonding.

We considered previously the possibility of an immune origin for the penicillin-modified cell hæmagglutinin, penicillin acting as a haptene in conjunction with some tissue protein[1]. Of 30 such sera 28 were derived from patients with a history of previous penicillin therapy. However, of the six sera agglutinating chloramphenicol-modified cells, five were obtained from patients with no previous history of chloramphenicol treatment. The highest titre serum (1/128) came from a patient aged six years who had apparently never received any antibiotic therapy. It may be that there has been previous antigenic stimulation by some substance or compound with a common determinant group to chloramphenicol or, alternatively, the reaction might be due to the presence of some naturally occurring factor in certain sera. If so, the specificity of the reaction seems remarkable. One serum will not agglutinate erythrocytes modified by the heterologous antibiotic, nor will penicillin inhibit the agglutination of chloramphenicol-treated cells with the homologous serum and vice versa. If not of immune origin, the apparent narrow specificity of the reaction requires further elucidation.

By starch-gel electrophoresis we have demonstrated hæmagglutinating activity in the pre-albumin moiety of positive sera against penicillin-modified cells. In

only one of 24 sera have we found activity in the γ-globulin fraction, and this serum gave a positive antiglobulin test in addition to having the characteristic agglutinating fraction in the pre-albumin zone. The suggestion is made that some antibiotics may function as haptenes and produce true immune hæmagglutinin of γ-globulin type, but that certain sera may contain an additional fraction in the pre-albumin moiety which may or may not be of immune origin. The nature and further characteristics of this factor are under investigation.

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Separation of Human Serum Albumins

THE presence of several protein components in human serum albumin was recently demonstrated[1–3] by two-dimensional zone electrophoresis (filter paper followed by starch gel)[4]. Their identity with albumin was determined by two-dimensional zone electrophoresis[3]. The proteins are not related to those described by Knedel[4] or by Gitlin *et al.*[5]. During our work on normal human sera, several new proteins were observed which had the same mobility as albumin by filter paper electrophoresis (at *p*H 8·6), but which when subjected to electrophoresis in starch gel in a discontinuous system of buffers[7] migrated more slowly than albumin. These proteins can be divided into two main groups: the members of the first group are immunologically related to albumin and one of them is present in sera in about 50 per cent of all normal adults and children. These proteins will be referred to as 'albumin-like proteins'.

A second group of proteins was also found which possessed a mobility on filter paper similar to, but not identical with, that of albumin. They migrate at the same rate as the 'slow' portion of the albumin and in starch gel can be separated from albumin only in a discontinuous system of buffers. These proteins are not immunologically related to albumin and will be referred to as 'quasi-albumins'. Their presence in sera was found in 61 of the 64 individuals screened.

Proteins of either or both these groups may be present or absent in a serum for a given individual. Fig. 1, *a*, *b*, *c*, shows diagrammatically the three possible combinations of the occurrence of these proteins. A detailed description of the distribution and some of the properties of the proteins will be given elsewhere.

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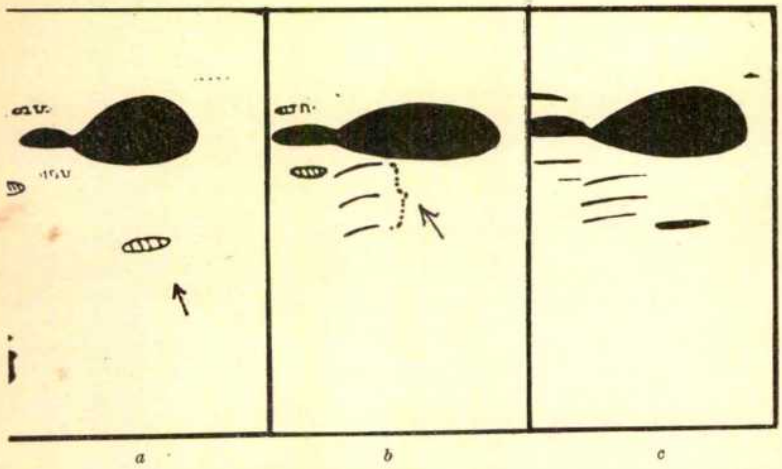

Fig. 1. Diagrams (traced from photographs) of two-dimensional zone electrophoretic patterns of human sera showing the separation of albumins (only albumin(s) and α-1-globulin regions shown). *a*, position of the 'albumin-like' protein; *b*, positions of 'quasi-albumins'; *c*, pattern of an individual with both groups of proteins

PATHOLOGY

Spontaneous Cytomegalic Inclusion Body Disease involving Lacrimal Glands of Cæsarian-derived (so-called) Pathogen-free Rats

HISTOLOGICAL study of lacrimal glands in laboratory rodents revealed cytological changes, for example, nuclear polymorphism and inclusions characteristic of cytomegalic inclusion body disease in rats of the Sprague–Dawley strain; no other organs were involved. Lesions occurred in both intra- and ex-orbital glands of males only at an age of six months or older and with an incidence of 100 per cent. Similar observations have recently been published for eight rat colonies of different geographical locations[1]. The disease is apparently widespread among laboratory rats. Guinea pigs, a variety of mouse strains, both golden and Chinese hamsters, Wistar and Fisher rats, either commercially obtained or bred and raised in the Roscoe B. Jackson Laboratory, were free of the disease.

Our Sprague–Dawley colony was derived from stock animals purchased several years ago from a local breeding farm. For a number of years now, this breeder has since specialized in the production of Cæsarian-derived pathogen-free animals. Routinely Cæsarian-derived Sprague–Dawley pups are foster-suckled on germ-free Lobund strain mothers (alpha-colony) and on attaining breeder size

transferred to pathogen-free surroundings. Cæsarian sections are performed in sterile plastic isolaters ('Trexler' type) and pathogen-free conditions for Cæsarian-derived Sprague–Dawley breeders maintained by an elaborate barrier system (sterilizer and lock system). Eight generations of pathogen-free Cæsarian-derived Sprague–Dawley rats have so far been obtained, interrupted only by introduction of new germ-free Lobund rats.

Pathogenic bacteria and parasites have never been demonstrated from any of the Cæsarian-derived Sprague–Dawley rats. Lacrimal glands, however, from *both* males and females (100 per cent) disclosed cytomegalic inclusion body disease at about six months or older. Transmission experiments were conducted with cell-free filtrates prepared by grinding glands with pestle and mortar, 'Carborundum' and tissue culture fluid (dilution 1:10) fortified with aqueous penicillin-streptomycin, centrifuged at 3,000 r.p.m. for 30 min. and filtered through bacteria-tight *EK*-Seitz filter pads. Sprague–Dawley new-borns were inoculated intraperitoneally, 0·1 ml., and intracerebrally, 0·03 ml. Death of 20 per cent occurred within one month from systemic cytomegalic inclusion body disease. Surviving animals, both males and females, killed at intervals of 55, 63 and 71 days, showed extensive lacrimal gland involvement only. Similarly inoculated new-born mice remained healthy and no microscopic lesions were detected.

The problem of viruses in both pathogen- and germ-free animals should be investigated systematically and adequate tests devised for virus detection. Although it is possible to raise animals in the absence of bacteria, protozoa and helminths, elimination of all viruses may be more difficult. It seems significant that at the Lobund Institute filtrable agents had been isolated from cæca of rats that were raised germ-free for several generations[2]. Tentative identification of these agents classified them serologically in the group of *ECHO* viruses. Also, at the National Institutes of Health, from the salivary glands of germ-free rats an agent was isolated that could be propagated on rabbit kidney cells[3].

From evidence cited it would seem that the pathogen- and germ-free state does not necessarily apply to viruses. As shown here, so-called pathogen-free animals may in fact contain infective viruses. Although viruses may be occult both clinically and microscopically, viral antibodies may or may not be detectable in infected host's serum. The presence or absence of humoral antibodies to cytomegalic inclusion body disease virus in so-called pathogen-free Sprague–Dawley rats is under investigation; also, attempts are being made to find out the virus state prevailing in this disease as compared with latent murine lymphocytic choriomeningitis and swine influenza in which neither virus nor viral antibodies are detectable by direct means. Transmission of the virus in pathogen-free rats has to be studied from an epidemiological viewpoint; it may enter postnatally (for example, viruria, occular discharge) or prenatally by way of placental transfer (following viræmia, for example, herpes). In pathogen-free rats virus multiplication does indeed occur in lacrimal glands of females, but the presence of virus in conventional females appears to be masked. Morphological studies with the light- and electron-microscope will be presented in a separate description of the fine structure, as well as pathogenesis of inclusions.

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Schistosomiasis and Urinary β-Glucuronidase Activity

Boyland, Wallace and Williams[1] have shown that the activity of urinary β-glucuronidase is increased in patients suffering from bladder cancer and suggested that 'spontaneous' urinary bladder cancer could be caused by unmasking carcinogens which were inactive as β-glucuronides, but active when liberated by β-glucuronidase in the urine.

Bladder cancer is not uncommon in East Africa. The Cancer Registry of the Kampala Cancer Research Committee has noted 68 cases out of a total of 1,800 cancer cases over the past 4 years.

The role of schistosomiasis in the ætiology of bladder cancer is controversial[2], and as part of a programme of investigations into the background of cancer in East Africa, the effects of schistosomiasis on urinary β-glucuronidase activity are being studied. 24-hr. samples of urine are collected and the β-glucuronidase activity is estimated by a slight modification of the method of Boyland, Gasson and Williams[3].

Preliminary results on a limited number of male East African natives showed that the normal range of activity was fairly narrow and was lower than that quoted by Lewis and Plaice[4] for Europeans on a units per ml. basis, but slightly higher when expressed as activity per 24 hr.

The urine of patients suffering from intestinal schistosomiasis (*Schistosoma mansoni*) showed an increase in activity above the normal range and those with urinary schistosomiasis (*S. hæmatobium*) showed a well-marked increase.

Table 1. URINARY β-GLUCURONIDASE ACTIVITY

Group	N	Units/ml.	*S.D.*	Units/24 hr.	*S.D.*
African normals	18	0·95	0·29	1,475	120
S. mansoni	8	1·59	0·91	1,970	573
S. hæmatobium	7	3·08	2·18	4,560	1,710
European normals[4]	32	1·05	0·55	1,405	893

After treatment with 'Nilodin' (lucanthone hydrochloride, Burroughs Wellcome) or sodium antimonyl tartrate, the activity of the enzyme dropped rapidly and, in cases where the series were long enough, reached the normal range, and in one case was still normal after 58 days. This drop was well marked in the *S. hæmatobium* series, but longer series are required for *S. mansoni*. Details of the longest series are given in Table 2.

Since urinary schistosomiasis is accompanied by hæmaturia, two cases of sterile hæmaturia unassociated with schistosomiasis were studied. Both gave results which were within the normal range. Exten-

Table 2. THE EFFECT OF TREATMENT ON β-GLUCURONIDASE ACTIVITY

Schistostoma hæmatobium						*Schistostoma mansoni*					
Case	Pre-treatment		Post-treatment			Case	Pre-treatment		Post-treatment		
	units/ml.	units/24 hr.	Day	units/ml.	units/24 hr.		units/ml.	units/24 hr.	Day	units/ml.	units/24 hr.
OB	6·00	7,020	1	4·96	6,150	*OL*	1·25	2,920	1	0·96	1,330
			2	3·52	4,720				2	0·90	1,190
			3	2·30	3,400	*NA*	3·66	2,120	1	2·93	1,640
OP	6·57	7,750	1	4·95	5,000				2	2·80	1,490
BA	1·20	3,480	1	0·97	2,570	*OK*	1·74	3,000	1	1·74	2,460
			8	0·64	1,760	*OC*	—	—	1	1·06	2,440
MW	2·50	5,580	1	2·10	5,100				2	1·54	3,230
			8	1·23	1,970				3	1·36	2,900
KA	2·63	4,400	1	1·85	3,090	*AL*	1·75	1,980	6	0·93	1,020
			2	2·63	2,820						
			3	2·58	1,680						
			58	1·32	1,630						

sions of this work are being undertaken and will be published elsewhere.

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Induction of Tumours by Polyoma in Adult Hamsters

THE relative non-susceptibility of adult versus new-born or very young animals to tumour induction by certain viruses has been interpreted as the expression of either of two possibilities: (1) presence in the young animal of cells intrinsically more susceptible to the virus infection and to the proliferative response; (2) lack in the young animal of an adequate immunological response.

In the case of tumour induction by polyoma, much emphasis has been placed on the fact that it is the undifferentiated mesenchymal cells in the new-born hamster which are susceptible to the proliferative response[1]. Thus the proliferative response to infection and the appearance of the tumour would depend on the availability of such cells. Results presented here show that the tumour can be induced by polyoma in adult hamsters, and special attention has been paid to the influence of the immunological process on the outcome of polyoma infection in terms of tumour production. Twenty male Lakeview hamsters 6 weeks old were divided into two groups: 10 animals were inoculated subcutaneously and 10 intra-peritoneally with a single dose of 0·2 mm. of a tissue culture preparation of polyoma virus (*M*–11–9*A*). Of the group inoculated intraperitoneally, 5 died between the 8th and 15th week after inoculation; only one could be autopsied, and the cause of death was found to be a massive intraperitoneal hæmorrhage, originating in a broken hæmorrhagic cyst in the liver; a similar picture was found in another animal dying 24 weeks after inoculation. In this same group, one animal, 13 months after receiving the inoculum, developed a subcutaneous nodule in the left flank which rapidly enlarged, reaching a diameter of 5 × 3·5 × 5 cm. In no other areas were proliferation or necrotizing lesions observed. In the group inoculated subcutaneously, 3 animals were lost; 4 developed subcutaneous tumours 24, 35, 36, and 44 weeks after the inoculation, respectively. The tumours were very similar to those observed after inoculation in new-born hamsters, being characterized by large, hæmorrhagic necrosis with very pronounced vascular formations in the viable part. The remaining 4 animals in the two groups were killed 14 months after inoculation and failed to show proliferative lesions.

In summary, 7 out of 11 hamsters which were inoculated at 6 weeks of age and in which necropsy could be done showed tumours of the liver or of the subcutaneous tissue 3–14 months after inoculation. No other tumours were found in any other organ, suggesting that the tumour had developed at the site of inoculation. The tumours were in all respects identical to those observed in new-born animals, and, in the case of the subcutaneous lesions, grew very rapidly. Hæmagglutinin-inhibiting antibodies were found in all 7 of the animals tested, 3 with tumours and 4 without tumours at 11 and 14 months after the virus inoculation. Thus the only difference between new-born and adults after an equal amount of virus inoculation appears to be that in adults the latent period preceding the appearance of the tumour is greatly prolonged and that the tumour appears only at the site of inoculation. Cells capable of proliferative and neoplastic response to polyoma must, then, be present and available to the virus in the adult animal as well—probably throughout its life—although it cannot be excluded that the number and the areas of these cells may be decreased in the adult animal. It would seem that the difference between the new-born and adult animals can be better explained on the basis of immunological activity. Several observations point in this direction: high titres of polyoma hæmagglutination-inhibiting antibodies are reached in the adult hamsters by the 4th–5th day, while in the new-born similar titres are found only at the 6th–7th day (Defendi, V., unpublished work); inoculation of adult lymphoid tissue in the new-born

before the virus is given increases the latency period before tumour appearance and decreases the actual number of tumours per animal[2]; when the lymphoid tissue inoculated originated from animals with antibodies to polyoma, the actual incidence of tumours decreases by 60 per cent, with tumours present only at the site of inoculation (Defendi, V., unpublished work). Briefly, when inoculated with adult lymphoid tissue, the new-born hamster responds to the polyoma in much the same way as the adult. One attractive hypothesis that could be formulated is that in the adult animal the considerable replication of the virus found in the new-born[3] does not occur, or that the virus is rapidly neutralized, decreasing the probability of tumour initiation in organs remote from the site of inoculation. It should also be kept in mind that the virus concentration at equal inocula is much lower in the large adult animal than in the new-born.

In relation to the problem of new-born versus adult susceptibility to polyoma, it has been found in another animal (mouse) that adult salivary gland *in vitro* is just as susceptible to tumour induction by polyoma as is the fœtal gland, and that X-ray treatment makes the adult mouse susceptible to the oncogenic action of polyoma[4].

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HISTOLOGY

Mineralization of Rat Enamel

THE initial stages of the mineralization of tooth enamel have been studied using electron microscopical techniques applied to ultra-thin sections of developing molars and incisors of 1–10-day-old white rats (*Rattus norvegicus*). The specimens were fixed in either Palade's[1] or Dalton's[2] fixative, embedded in 'Araldite' and cut without demineralization using a diamond knife.

Tooth enamel is a highly mineralized tissue consisting of tightly packed orientated apatite crystals in intimate association with an organic substance 75 per cent of which contains citric acid, peptides and a glycoprotein, the remainder being a protein of the keratin type. There is considerably more mineral than organic matter, the mineral contributing approximately 96 per cent by weight, organic material approximately 1·5 per cent and the rest water.

It is generally accepted that the keratinous organic matrix of the enamel is fibrous and that its formation precedes the mineralization process. The exact role of the ameloblast cell in enamel formation is a matter still under consideration. I believe[3] that fibrillogenesis occurs extra-cellularly, the fibres forming from a granular precursor substance which is elaborated and secreted by the ameloblasts, the

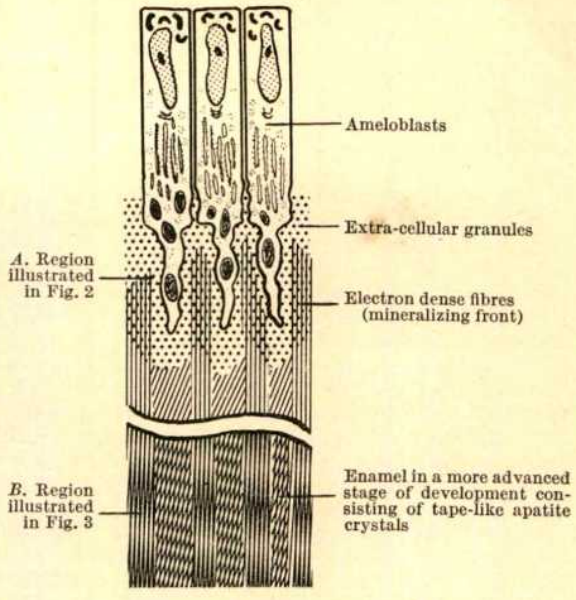

Fig. 1. Diagram of amelogenesis

granules being discharged from the formative end of the cell into the extra-cellular environment. This concept is illustrated diagrammatically in Fig. 1. The newly secreted organic material in the extra-cellular region between the cells appears first to consist of granules with an electron density equal to that of the intra-cellular 'Palade' granules. Some granules then become arranged in poorly defined columns giving rise to what appear to be orientated fibres. An abrupt change to very electron dense fibres marks the next stage in enamel formation (Fig. 2). In an earlier publication[4] I designated the region undergoing this change as the 'formative front' of the enamel matrix. This 'front' is marked by a striking contrast between the granules (diam. 50–70 Å.) which have a low electron scattering capacity and fibres (50–100 Å. × 0·1μ–1·0μ) (Fig. 2) which have a much greater electron-scattering property. The fibres, which have a periodicity of 50–70 Å., become arranged in parallel rows, the strands of which appear to be cross-linked in places by electron-dense granules; this results in an appearance rather like the rungs of a ladder. In the depths of the enamel where mineralization is more advanced, both granules and fibres are replaced by 'tape-like' crystals which give a diffraction pattern characteristic of apatite. The transition from fibres to 'tape-like' crystals, which might be expected to be a gradual process, is difficult to detect with certainty in 'bright-field' electron micrographs.

Diffraction patterns characteristic of apatite were obtained from selected areas of the formative front of the enamel matrix and from various places in the deeper layers of the newly formed enamel up to 30μ from the formative zone (positions *A* and *B*, Fig. 1). A progressive change from extremely small crystallites of approximately 100 × 500 Å., to larger crystallites of approximately 500 × 1000 Å., was calculated from the angular breadth of the diffracted beam from the 002 and 300 crystal planes. The smallest crystallites are situated in the electron dense region of the formative front of the enamel matrix (Fig. 2) whereas the larger crystallites are situated away from the

formative zone in the deeper layers of the enamel matrix.

Crystallite size calculated from the orientated electron diffraction patterns is greater than the observed size of the electron-dense particles (50–70 Å.) associated with the electron-dense fibres in transmission electron micrographs (Fig. 2). Calculation of crystallite size from the breadth of diffraction lines is most accurate when applied to diffraction patterns from cubic crystals where the crystallite size falls within the range 100–1000 Å.[5]. Cubic and non-cubic crystals below this size-range may therefore give diffraction patterns having poor intensity, and a diffuseness which contributes to large errors in calculations of crystallite size.

By interposing a small aperture below the object plane in such a way as to permit the passage of only part of the diffracted electron beam, it is possible to produce a 'dark-field' diffraction image which shows the position and size of those crystallites suitably orientated in respect to the electron beam. Such an image appears as a bright point on a dark background. Measurements of the crystallites visible in dark-field micrographs of the formative front reveal a size-range of 50–100 Å. in the zone nearest to the forming front. Moreover, the bright regions in dark-field correspond in position to the electron-dense regions in bright-field electron micrographs.

From the evidence provided by the diffraction patterns, and both dark-field and bright-field electron micrographs, it is concluded that the abrupt change to a high electron density of the fibres at the formative front is due to the multiple deposition of very small apatite crystallites which form centres from which further crystal growth takes place. This growth leads to the formation of the 'tape-like' crystals which can be obtained from the deeper layers of the enamel (Fig. 3). As a result of these observations I would now prefer to call this region of changing electron density the 'mineralizing front' rather than the formative front of the enamel matrix.

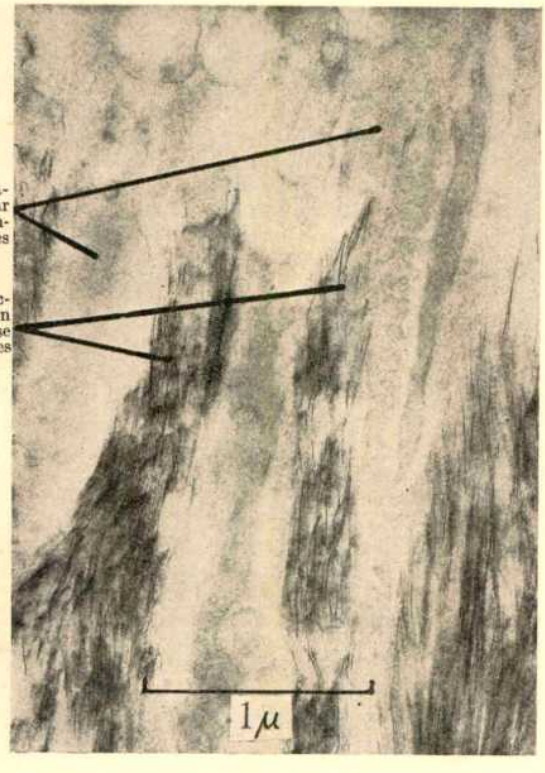

Fig. 2. 'Mineralizing front', the junction between extra-cellular granules and electron-dense fibres, region *A* in Fig. 1

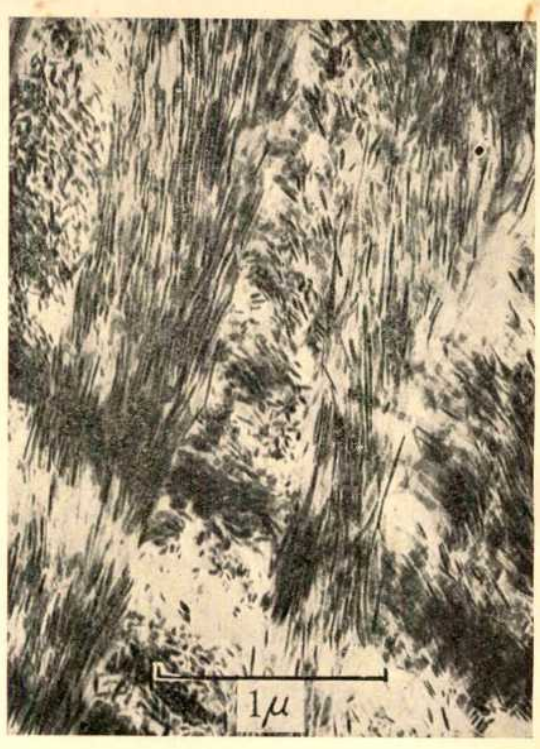

Fig. 3. Tape-like crystals of enamel in a more advanced stage of mineralization, region *B* in Fig. 1

It has been suggested by Frank and Sognnaes[6] that in enamel mineralization, crystal nucleation and growth are by epitaxy with the organic matrix. This may well be true since in dark-field electron micrographs small crystals can be detected spaced by regular intervals. These intervals may presumably represent the position of some structure which is not opaque to electrons and which could therefore represent the position of the organic material. Epitaxy could also explain the particularly high degree of orientation of the apatite crystals in different regions of tooth enamel. Crystallization by epitaxy commencing from multiple centres could also influence the mode of crystal growth and perhaps regulate size and packing of the crystals.

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RADIOBIOLOGY

Radioactivity in Wool

WITH the development of highly sensitive γ-ray detectors, it has become possible to carry out non-destructive measurements of the low levels of γ-ray activity emitted by various biological materials. Since γ-ray measurements may be made rapidly without any special preparation or modification of the material measured, the application of this technique to agricultural research problems has much to recommend it. The advantages of the non-destructive γ-ray measurement technique appear to justify exploratory research to determine if such measurements may be used to estimate other factors to which they may be related[1].

In the course of such a line of exploratory research γ-ray measurements were made on raw and scoured wool. A recently developed low-level γ-ray detector employing plastic scintillators was used in this work[2]. Simultaneous two-channel operation was used in making γ-ray radioactivity measurements. The upper channel was set to measure γ-radioactivity of from approximately 1·2 to 2·5 MeV. energy. The lower channel measurements represented γ-radioactivity of from approximately 0·6 to 1·0 MeV. energy plus a substantial spill-over of counts from the upper channel energy band. When a standard consisting of 1·00 lb. of potassium chloride mixed with 13·00 lb. of granulated sugar was counted using these channel settings, the net counting-rate for the potassium-40 γ-radioactivity in the lower channel was approximately 80 per cent of the net counting-rate observed in the upper channel. Since the resolution of our system is not adequate to identify unknown γ-ray emitters, no corrections for spill-over have been applied in Table 1.

Table 1. γ-RAY RADIOACTIVITY OF SAMPLES OF GREASE WOOL AND SCOURED WOOL

Samples	Lower channel (net counts/min./lb.)	Upper channel (net counts/min./lb.)
	Mean ± *S.D.*	Mean ± *S.D.*
Maryland grease wool	690 ± 111	731 ± 129
New Mexico grease wool	1,382 ± 57	669 ± 101
Idaho grease wool	1,565 ± 107	929 ± 76
Idaho scoured wool	46 ± 12	25 ± 4

γ-Ray measurements were made with samples of grease wool weighing between 8·6 and 10·0 lb. The grease wool samples were placed for counting in a fibre drum 11½ in. in diameter and 21 in. long. The wool had been sheared in the spring of 1959 from sheep from Maryland, New Mexico and Idaho. The 6 samples of Maryland grease wool were taken from pooled wool, while the 6 samples from the other locations were each taken from individual fleeces. Measurements were also made of 6 scoured wool samples from 1958 Idaho wool. Each of these samples, which weighed between 4·0 and 5·6 lb., was an entire fleece.

The mean values and standard deviations for each group of 6 samples are presented in Table 1. The scoured wool samples emitted a much lower amount of γ-ray radioactivity than did the grease wool samples. Domestic grease wool may contain 25–80 per cent impurities[3]. The major impurities in grease wool are grease, suint, and dirt. The suint or dried perspiration is quite high in potassium content. Since all potassium in Nature contains an essentially constant proportion of the γ-ray emitter, potassium-40 (ref. 4), with an energy of 1·46 MeV., it is probable that the upper channel measurements reflect the presence of suint in the grease wool samples. Grease wool may contain 5–40 per cent dirt content[3]. It will be noted that the lower channel net counts per min. per lb. values for grease wool from the three locations vary more widely than do the upper channel values. Natural radioactivity from soil[5] as well as fall-out debris may be factors contributing to the lower channel counts.

The γ-ray radioactivity of the clean wool is only a small fraction of that found in grease wool. Thus the bulk of the content of grease wool emitting γ-rays is associated with its impurities. Work is being carried out in our laboratories to determine if γ-ray measurements, which can be made non-destructively in a few minutes, may serve as an index for predicting the percentage of impurities present in grease wool and the relative proportions of the major impurities.

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An Effect of Tritiated Thymidine on the Incorporation of Thymidine into Chromosomal Deoxyribonucleic Acid

IN the course of a series of experiments designed to test for possible anomalies in the synthesis and behaviour of chromosomal deoxyribonucleic acid resulting from the use of tritiated thymidine, the possibility arose that the tritiated precursor could interfere with the normal course of synthesis and partition by destroying the integrity of the deoxyribonucleic acid molecule or otherwise modifying the normally operative control mechanisms. This possibility was examined by comparing the incorporation of thymidine labelled with carbon-14 into meristematic cells in the presence and absence of tritiated thymidine.

Vicia faba roots were incubated for a period of 10 hr. in three different media: ^{14}C-2-thymidine (New England Nuclear Corporation), 2·7 μc./μmole, 1 μc./ml.; tritiated thymidine (Schwarz Bio Research Inc.), 3,000 μc./μmole, 5 μc./ml.; ^{14}C-2-thymidine and

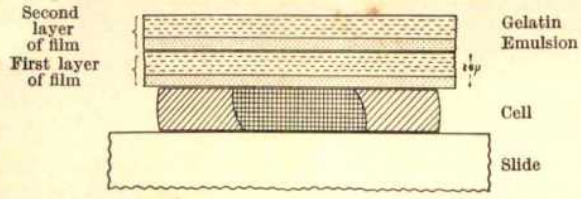

Fig. 1. Diagrammatic illustration of a two-layer stripping film preparation

tritiated thymidine with a final specific activity of 16 μc./μmole and a concentration of 6 μc./ml. The roots were fixed, briefly hydrolysed, squashed and covered with two layers of Kodak *AR*-10 stripping film (Fig. 1). After 19 days of exposure the autoradiographic preparations were developed and analysed by visual grain counts. The first film layer served as an effective screen against tritium β-particles: relative to the first layer, grain densities in the second layer for carbon-14 were about 50 per cent and for tritium about 0·5 per cent. The second layer over cells labelled with tritium alone showed a grain density over nuclei which was only 2 above background. This number was subtracted from the counts of doubly labelled nuclei in the main analysis which was carried out in the second layer of ^{14}C-thymidine and ^{14}C-thymidine-^{3}H-thymidine labelled cells. The results of this analysis are plotted in Fig. 2 and represent pure carbon-14 grain numbers.

These results demonstrate that tritiated thymidine enhances the incorporation of thymidine labelled with carbon-14 and lead to the conclusion that incorporation of tritiated thymidine into deoxyribonucleic acid cannot be assumed to measure normal amounts of synthesis of the acid but does in fact bring about modifications. (The possibility that carbon-14–thymidine itself produces similar difficulties is theoretically less likely, but cannot be easily evaluated in an experiment of this design.)

It is of interest to note in this connexion recent reports of chromosome breakage and reduction in mitotic index[1], increased mutation frequency[2] (both attributed to tritiated thymidine) and the demonstration of structural modifications in tritiated deoxyribonucleic acid[3]. These results, together with those presented here, form a broad spectrum of detectable modifications in the deoxyribonucleic acid molecule brought about by the introduction of tritium-labelled components. The finding of Pelc and LaCour[4] of

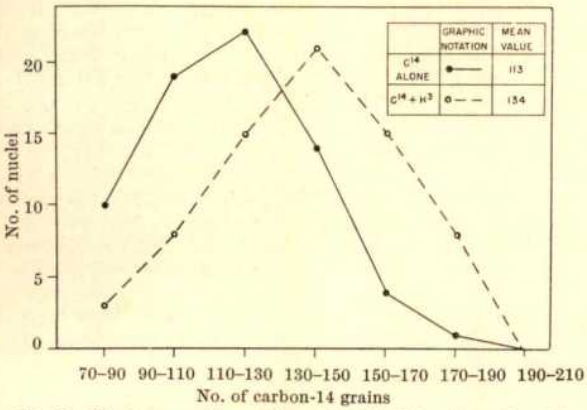

Fig. 2. The incorporation of thymidine labelled with carbon-14 in the presence and absence of tritiated thymidine

excessive incorporation of tritiated thymidine in cells where similarly extensive incorporation has not been noted with other labelled precursors, and the apparent lack of quantitative correspondence between tritiated thymidine incorporation and cytochemically demonstrable deoxyribonucleic acid increase in puffed regions of polytene chromosomes[5,6] may also prove to be examples of tritiated thymidine effects rather than evidence for metabolic activity of deoxyribonucleic acid.

The results reported here are not unexpected in view of the extremely high ionization density produced by tritium β-particles and the complex structure of the deoxyribonucleic acid molecule[7,8]. It is somewhat surprising that a measurable effect is elicited by tritiated thymidine in as low a specific activity as was used in the present experiment (less than 16 μc./μmole). The explanation of this circumstance may lie in the sensitivity of the detection system we have employed, that is, the use of a tracer to measure disturbances produced by another.

A discussion of the possible nature of the modifications introduced by tritiated thymidine into chromosomal deoxyribonucleic acid behaviour is in preparation and will be published together with further data on the effect of this precursor on total levels of deoxyribonucleic acid.

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Influence of Thyroid on Radiophosphorus Metabolism in Fish

INFORMATION concerning the endocrinological regulation of mineral metabolism in fishes is lacking. The problem is particularly interesting because the parathyroid gland which regulates the normal calcium and phosphorus content within the body in higher vertebrates is supposed to be absent in fishes. I have tried to find out if the thyroid had any control over the mineral metabolism in yearling salmon, *Salmo salar* L.[1,2]. Since surgical thyroidectomy is not possible in fishes, an attempt was made to destroy the thyroid follicles by anti-thyroid drugs. Successful destruction could not be achieved since the fishes were treated with thiourea for a very short time. The result of the experiments suggested that when fish were treated with thiourea for a short time, thyroid was indirectly stimulated by thyrotropin secreted by the pituitary and so the uptake of phosphorus-32 was more than in the controls; in thyroxine-injected fish the uptake was a maximum because the stimulation was direct.

Complete thyroidectomy has been achieved by repeated injections of radioiodine[3]. In the present

investigations, goldfish, *Carassius auratus* L., were injected intraperitoneally with 40, 30, 20 and 10 μc. of iodine-131 respectively for 4 months—one injection every month. Histological examination of the thyroid after this period showed that radioiodine had selectively destroyed all the thyroid follicles. Another group of goldfish were injected with 0·4 ml. of 0·1 per cent thiourea three times a week for 2 weeks. Then for the next 3 weeks the volume of injection was reduced to 0·2 ml. The thyroid in this case became hypertrophied and hyperplastic, with increased number of very small follicles. The height of the cell was greatly increased and the colloid was very scanty. A third group of goldfish was maintained to serve as control. For every injection proper precautions were taken not to disturb the osmotic balance in the fish.

The foregoing groups of fishes were then subjected to three different sets of treatments. Fishes were given three injections of physiological saline, extract of acetone-dried goldfish pituitary gland (to supply them with additional quantity of thyrotropin) and 0·1 per cent L-thyroxine (Nutritional Biochemical Corp.) respectively on alternate days. The volume injected at a time was 0·2 ml. Radiophosphorus was then added to all the aquaria. The antibiotic tetracycline was put in the aquaria to eliminate any bacterial activity. Table 1 shows the amount of radiophosphorus absorbed in various sets.

Table 1. PHOSPHORUS-32 ABSORBED BY THE VARIOUS GROUPS OF FISHES INJECTED WITH PHYSIOLOGICAL SALINE, PITUITARY, AND THYROXINE

	Injections given	Phosphorus-32 absorbed (per cent)
Iodine-131-injected fish	*A* Physiological saline	22·9
	B Pituitary	24·6
	C Thyroxine	34·6
Thiourea-injected fish	*A* Physiological saline	26·7
	B Pituitary	37·9
	C Thyroxine	45·9
Controls	*A* Physiological saline	45·0
	B Pituitary	58·3
	C Thyroxine	66·2

The conclusions drawn from the experiments are that radioiodine completely destroyed the thyroid follicles and so the radiophosphorus uptake was low (22·9 per cent), approximately half that of the controls (45·0 per cent). Injections of pituitary extract did not have much effect (uptake 24·6 per cent). This could be explained by the complete destruction of thyroid; thyrotropin of the pituitary which has the thyroid-stimulating function could not produce any effect. But the injections of the thyroid hormone, thyroxine, increased the uptake from 22·9 to 34·6 per cent (50 per cent increase).

The uptake of radiophosphorus in thiourea-injected fishes (26·7 per cent) resembles that of fishes injected with iodine-131, but the injections of pituitary extract increased the uptake in these fishes from 26·7 to 37·5 per cent (40 per cent increase). This is because the thyroid follicles had only become hypertrophied and hyperplastic and as a result of the loss of colloid they were inactivated. Thyrotropin of the pituitary, therefore, could cause stimulation leading to an increased uptake. When thiourea-treated fish were given thyroxine injections the uptake (45·9 per cent) came to the normal level of controls (45·0 per cent). In the latter, pituitary and thyroxine injections raised the uptake of radiophosphorus from 45·0 to 58·3 and 66·2 per cent respectively. The results show that thyroid has positive influence over the mineral metabolism in fish, but it cannot be said definitely at present whether this control is direct or is indirect through some intermediate agency. Further work is in progress and the detailed report of this work will be published elsewhere.

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BIOLOGY

Interspecific Differences in Strontium Uptake by Pasture Plants as a Function of Root Cation-Exchange Capacity

VOSE and Koontz[1] have reported differences in strontium contents of pasture plants. As there is evidence that the uptake of cations may be influenced by the root cation-exchange capacity of plants[2–4] it was of interest to compare the observed variation in strontium uptake among the plants with the corresponding root cation-exchange capacities.

Root cation-exchange capacity measurements of several of the plants used by Vose and Koontz[1] had previously been made by a method based on that of Drake *et al.*[4,5] and these results are shown in Table 1. It must be stressed that these results have only limited application as root cation-exchange capacity has been shown to vary with different levels of nutrition[6]. However, when the level of nutrition is similar for all plants (as was the case in the experiments of Vose and Koontz), then the plants should show much the same relative differences in root cation-exchange capacity. Varietal differences in exchange capacity between the plants tested in New Zealand and those used by Vose and Koontz may also cause some perturbation of the results.

By applying Donnan distribution laws to the root membrane–soil solution–soil colloid system, it may be predicted that the higher the cation-exchange capacity of the root surface, the greater will be the proportion of divalent cations within the root micellar solution[7]. As this initial adsorption on the root surface is the first stage of nutrient absorption by plants and, in dilute solutions, appears to have a considerable effect on the quantity and ratio of ions

Table 1

Plant	Root cation-exchange capacity (m.equiv./100 gm. oven-dry roots)
Bromus inermis	25
Lolium perenne	20
Phleum pratense	23
Phalaris tuberosa	18
Dactylis glomerata	23
Medicago sativa	48
Trifolium repens	42
T. pratense	46
Lotus corniculatus	36

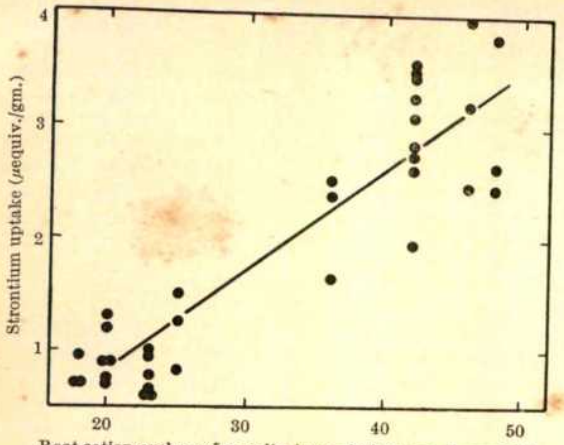

Fig. 1. Strontium uptake (from Vose and Koontz (ref. 1)) as a function of root cation-exchange capacity: $y = 0{\cdot}091x - 1{\cdot}01$; $r = 0{\cdot}91$

absorbed, it would be expected that the uptake of strontium would increase with increase in root cation-exchange capacity. The highly significant correlation between the uptake of strontium recorded by Vose and Koontz[1] and the root cation-exchange capacity (Fig. 1) indicates that the predicted effect of root cation-exchange capacity differences on ion uptake may be a strong factor in determining interspecific differences in uptake of strontium.

The exchange capacity figures used here differ from those obtained by Drake *et al.*[5]. However, the results of these workers significantly correlate with the strontium uptake in a similar manner to those shown here.

While the strontium content varied greatly among species, the calcium to strontium ratio remained constant[1]. This lack of discrimination between the two divalent ions by all species is to be expected if it is accepted that exchange reactions on the root surface determine the ratio of ions absorbed by the plants.

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A Possible Mechanism of Cell-Wall Formation

GOLDACRE[1] has shown that if a surface film of a lipo-protein on water is compressed, it tends to form folds and ultimately cigar-shaped fibres consisting of a double lipo-protein layer with water inside and outside. It was suggested that such fibres could have been a reaction-space for the original formation of living cells. Danielli[2] formed double lipo-protein layers by dropping dense protein solution through an oil layer into a less-dense protein solution. In this case, the film was spherical in shape and included a layer of oil. Sigwart and Nassenstein[3] have formed spherical shells of water in benzene by ejecting benzene drops from a nozzle preferentially wetted by water.

I have observed an alternative method of formation of a spherical shell of oil stabilized with protein and separating two aqueous phases. A dilute (0·1 per cent) aqueous solution of bovine plasma albumin is placed in a beaker beneath a layer of petroleum ether (80–100° C.); air is then bubbled into the liquid for a few seconds. Spherical shells of the type formed by Danielli[2] may be observed afterwards in the water. Their sizes range up to 2–3 mm. Most of the shells rise to the oil–water interface, but some disintegrate, leaving one small oil droplet.

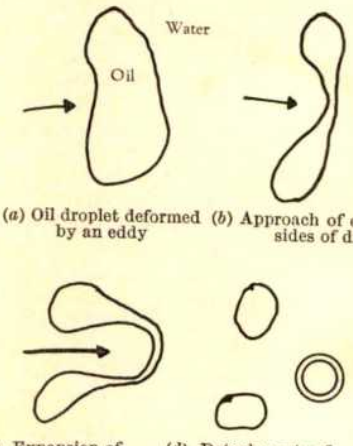

Fig. 1. Formation of a spherical shell

The mechanism of formation of the spherical shell is believed to be the deformation of an oil droplet by an eddy in the way illustrated on Fig. 1. Spherical shells containing air ('inverse bubbles') have been formed in a similar manner[4]. This mechanism of formation of protein-stabilized lipid shells seems to be at least as likely in Nature as those suggested by earlier workers[1,2]. Given a 'primeval soup' of the right composition, the only physical requirement for the mechanism is turbulence.

Thanks are due to the Department of Scientific and Industrial Research for financial assistance while this work was carried out.

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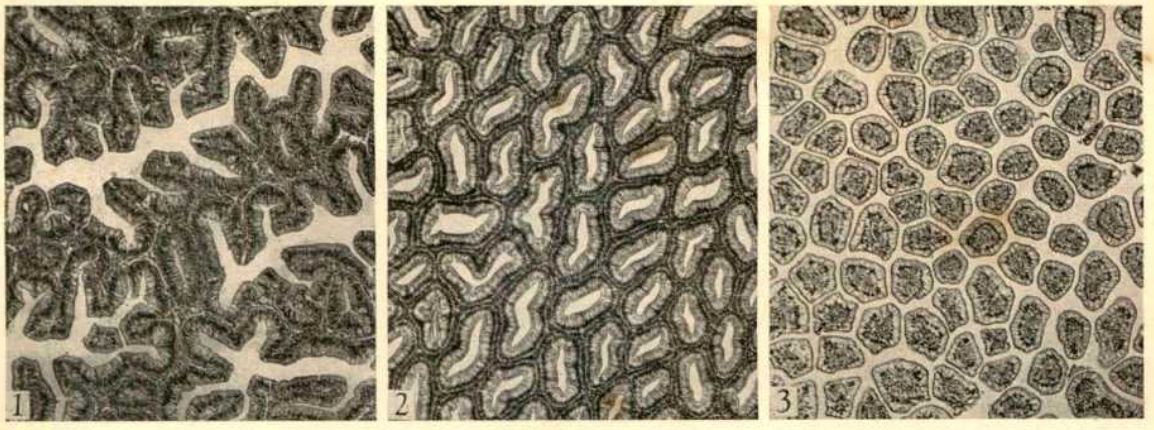
The Intestine in Members of the Genus *Raja* and Host-specificity in the Tetraphyllidea

IT was recently found that some species of the genus *Raja* could be distinguished solely on differences in the morphology of their spiral valves, in particular, from the form of their mucosæ. A brief account of the latter is given here because, so far as I know, these differences have not been described previously. In addition, it is thought that variations of this kind may



Figs. 1–3. Facial sections near the surface of the mucosa and from the middle region of the spiral valve of *Raja*. (1) *Raja montagui*. (2) *Raja clavata*. (3) *Raja naevus*

explain, in part, the high degree of host specificity found in the Tetraphyllidea, and may have a bearing on specificity in other orders of the Cestoda. A more detailed account of the work will be published elsewhere.

A facial section near the surface of the mucosa of *Raja montagui* shows (Fig. 1) that villi are absent. Instead the surface is composed of variously arranged and folded ridges which join to form a complicated network. The spaces between the ridges become progressively shallower and less in volume from the anterior to the posterior region of the intestine. Furthermore, these ridges are not always at the same level and therefore the surface of the mucosa has a corrugated and an irregular appearance. In *Raja clavata*, however, the surface is relatively smooth but composed of a fine regular network of ridges (Fig. 2), the intervening spaces leading into tubular crypts which are deeper in the anterior region. *Raja naevus* can be distinguished from these two species because well-developed villi are present (Fig. 3). *Raja brachyura* possesses a mucosa which at first glance is like that of *Raja montagui*, but the ridges are not identical in their detailed structure. The mucosa of *Raja micro-ocellata* resembles that of *Raja clavata*, but a noticeable difference occurs in the form of the muscular layers in the walls of their intestines.

The above differences may be of value, because it is not always easy to identify species of the genus *Raja* on other characters. Parker[1] described and figured variations in the mucosa of different species and in individuals of the same species of the genus. The specimens of *Raja* that I have examined so far, however, have not revealed a significant variation in different individuals. It is possible, therefore, that Parker was dealing with two species in his account of the mucosa of *Raja montagui*. One of his figures supports this view, as it resembles the mucosa of either the spiral valve of *Raja clavata* or that of *Raja micro-ocellata*. It may have been the former, in view of its abundance at Plymouth and because it can occasionally be confused with *Raja montagui*. On the other hand, the external features of *Raja micro-ocellata* are very distinctive.

The variations found in the intestine of *Raja* are not unlike those previously described in some teleost fishes; and although they suggest that a correlation may occur between feeding habits and the structure of the intestine, the possibility of a direct relationship will require a very careful analysis. Little is known of the feeding habits of rays, but preliminary observations suggest that some species of *Raja* may be more selective in their feeding habits than hitherto believed. If a correlation between food and the structure of the intestine does occur in this genus, it will obviously have a very important bearing on the specificity of their cestode parasites.

In recent work on the Tetraphyllidea of elasmobranchs caught off the British Isles, I have been able to confirm that host-specificity is very well marked in these cestodes. I stated earlier[2] that a correlation occurs between the morphology of the intestine in elasmobranchs and the structure of the scolex of their cestodes. It was then suggested that the structure of the gut was a possible factor contributing towards host-specificity in the Tetraphyllidea, and since so little was known of the morphology of the intestine it was decided to investigate this organ in greater detail. It has been confirmed that many genera and species of the Tetraphyllidea, in particular those found in British rays, show a remarkable adaptation to their environment. It is possible that these species can establish themselves successfully in a particular host only if the scolex is suitable for the habitat. This is supported by the literature on the Tetraphyllidea, which suggests that the main features of the scolex are laid down in an early stage of development of the cestode. In addition, preliminary observations on some species of the genus *Echeneibothrium* indicate that young immature individuals possess a scolex which is almost identical in size and structure with that of the adult.

There is also some evidence that the different genera and species of cestodes which are found in the same species of elasmobranch select particular regions of the intestine, and that in many cases different kinds of scolices show a relationship to the depths of the villi, crypts or reticulations of the mucosa as well as to the volume of their intervening spaces.

The above comments are interesting in view of the remarks made by Shulman[3] and Llewellyn[4] on morphological factors affecting the host-specificity of some helminth parasites. The results so far obtained indicate a similar phenomenon in the Tetraphyllidea, but it is assumed that other factors must operate in stimulating these cestodes to settle where optimum conditions occur for protection, nourishment, growth and reproduction. For example, physiological factors, in particular the carbohydrate, fat and protein metabolism of the Tetraphyllidea, are probably very

important for determining their host and habitat specificity.

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External Sexual Differences and their Significance in *Mormyrus kannume* Forskal.1775

Mormyrus kannume is distributed in the Nile system from the five major lakes of Uganda to the delta, and probably also in the Athi River system in Kenya[1]. The present communication was compiled from observations on specimens from the shallow waters of northern Lake Victoria.

There are external sexual differences in *M. kannume*. The base of the anal fin of the female is inclined at an angle of between 17 and 28° to an arbitrary axis between eye and tail fork, whereas in the male this angle lies between 32 and 33°. In the female or immature male, the anal fin is angular in outline, and the slender rays diverge from the base to the periphery of the fin. The anal fin of the mature male is rounded in outline, and the thickened, tapered rays converge to the periphery from the fin base, and due to the constriction at the periphery, when the fin is spread, a depression appears in the centre. Every immature male has an anal fin similar to that of a female, except for the angle at which it is attached to the body. As the testis ripens, the anal fin becomes modified to the form found in the mature male, and after breeding, the testis regresses and the anal fin gradually assumes its original form.

The significance of the modified anal fin cannot be conclusively demonstrated, since the breeding behaviour of *M. kannume* has not been observed. The simultaneous maturation of the gonad and modification of the anal fin in the male, however, indicate that the anal fin has an important function during breeding. If recently killed male and female are placed side by side with their anal fins spread and in contact at the peripheries, a chamber is formed between their anal fins in the manner illustrated in Fig. 1. If this chamber is used to surround the eggs during fertilization, fewer spermatazoa might need to be produced than if the gametes were dissipated into the surrounding water before fertilization. Therefore the use of a fertilization chamber in *M. kannume* during spawning might account for the relatively minute testis of the mature male. In every mature male fish with a total weight of less than 600 gm., the testis never weighed more than 3 gm., and a specimen weighing more than 4 kgm. had a ripe testis which weighed only 7 gm. In a variety of experiments in which macerated testis material and eggs taken from ovulated ovaries were mixed in small volumes of water, effective fertilization was never more than 25 per cent, and frequently less than 10 per cent. This may indicate that the gametes of this species are viable for only a limited period after contact with water, and that fertilization is possible only where immediate intimacy between ovum and sperm occurs. Immediate contact between ovum and sperm may be possible within the fertilization chamber.

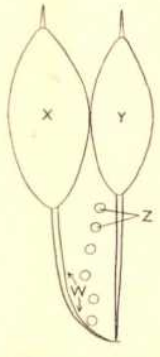

Fig. 1. Diagrammatic transverse section of a pair of fish in lateral contact in the region of their anal fins. (× ½). *W*, Depression in centre of male anal fin; *X*, mature male (34 cm.); *Y*, female (33 cm.); *Z*, extruded ova within the fertilization chamber

M. kannume is a very active gregarious species which probably has the co-ordinative ability to form a fertilization chamber. I have observed that, after being frightened, individuals of *Marcusenius nigricans*, another very active gregarious Mormyrid, form an unusually compact shoal which swims as a single unit through rocky crevices. Individuals of *M. kannume* may also be able to maintain close contact with each other while swimming, and as an extension of this type of behaviour, pairs may be able to form a fertilization chamber during spawning.

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Isolation of Liver Nuclei

A METHOD of isolating pure nuclei from rat liver has been elaborated from those described by Alfrey[1], Schneider and Hogeboom[2], Chauveau[3] and Zbarskij[4].

A rat was fasted for 24 hr. and then killed by decapitation. The liver was perfused with 0·25 *M* saccharose containing 0·0018 *M* calcium chloride and homogenized in a Teflon Potter–Elvehjem homogenizer for 2–3 min. at 1,000 r.p.m. in 0·25 *M* saccharose (+ 0·0018 *M* calcium chloride) at 1:10 dilution. The homogenate was filtered through four sheets of cotton gauze or through Jena *G O* glass filter. The filtrate was afterwards centrifuged for 5 min. at 500 r.p.m. in the horizontal head at 0–2° C. Thereafter we pipetted out the supernatant, which was not sharply separated from the precipitate, and put it on the surface of 0·34 *M* saccharose (+ 0·0018 *M* calcium chloride) and then centrifuged for 10 min. at 2,000 r.p.m. and 0–2° C. in the horizontal head. The supernatant was rejected and the precipitate, composed mainly of nuclei, was resuspended in 0·25 saccharose (+ 0·0018 *M* calcium chloride) and again put on the surface of 2·2 *M* saccharose, the density of which was exactly 1·272 gm./ml. This density, according to Zbarskij[4], allows the sedimentation of pure nuclei only, and at the same time it prevents the sedimentation of smaller cellular structures and of whole cells.

The distance from phase border, that is, from the boundary layer, of 2·2 *M* saccharose and 0·25 *M* saccharose with suspended nuclei to the bottom of tube was 1·5 cm., and the time of centrifuging was 30 min. at 30,000*g* (as calculated for the bottom of tube). The diameter of the tube was 16 mm. The last centrifuging was performed on a super-speed attachment of an MSE refrigerator centrifuge at 0–2° C. The nuclear fraction appears as a light yellow precipitate. When this method is used special attention must be paid in order to attain suitable thickness of the layer of 2·2 *M* saccharose solution and also to the diameter of the tube.

The smear of the nuclear fraction suspended in 0·25 *M* saccharose showed no whole cells, and only few very small fragments of cells were observed. The appearance of the nuclei was like this in living cells. The nuclei have clearly visible nucleoli and normally distributed intranuclear constituents; this is evidence of their normal status. We did not observe any deformation or agglutination of nuclei prepared by this method.

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Case of Apparent Resistance of *Rattus norvegicus* Berkenhout to Anticoagulant Poisons

OVER a period of two months, a heavy rat population on a farm in the west of Scotland was treated with two anticoagulant poisons, 'Diphacinone' and 'Warfarin'. Although the treatments were properly conducted, and the rats ate the poison bait freely, little impression was made on the size of the population. There was no evidence of recruitment from outside, and the conclusion drawn was that this population was more than normally resistant to these anticoagulants. Cage tests on 28 animals trapped on the farm to confirm this gave the results shown in Table 1.

Table 1

	Poison	Concentration (per cent)	No. of days feeding	Mortality
Farm rats	'Diphacinone'	0·0025	5	2/9
	'Warfarin'	0·005	5	1/9
	Nil	—	—	0/10
Controls	'Warfarin'	0·005	5	12/15

The remaining 25 rats were further tested at the Ministry of Agriculture, Fisheries and Food laboratories at Tolworth with similar results. More work on the survivors and their progeny is in progress.

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Ophiuroids feeding on Phytoplankton

RECENTLY, Nagabhushanam and Colman[1] have described carrion-eating by some species of ophiuroids including *Ophiocomina nigra* (Abild.) and *Ophiothrix fragilis* (Abild.), from observations both in the laboratory and in the sea, a phenomenon which has been recorded previously[2,3]. The two species mentioned as well as *Ophiopholis aculeata* (L.) have, however, been reported to feed on a wide range of food from seston and plankton to bottom invertebrates[2,3]. In particular, *Ophiothrix fragilis* and *Ophiopholis aculeata* are considered to be mainly suspension feeders[4,5] (using strong ciliary currents[6] in catching detritus), being also facultatively carnivorous. Of the species mentioned, *Ophiocomina* is anatomically well adapted for a carnivorous habit[3]. Nevertheless, all the species mentioned are considered to feed in essentially the same way[2,3].

In order to evaluate the efficiency as suspension feeders of the three species mentioned, we have fed them with phytoplankton labelled with carbon-14. The animals were starved for 1–2 weeks. Two or three individuals of the same species were placed in each of a series of jars containing 400 ml. membrane-filtered sea water to which identical concentrations of carbon-14 labelled plankton algae (natural phytoplankton populations) were added. In every experiment mentioned, constant stirring in 'plunger jars'[7] prevented settling of phytoplankton. The animals were kept in the dark and at a constant temperature.

Two different substrata for the ophiuroids were used; stones and empty shells as one, and the octocoral *Alcyonium digitatum* L. as the other. The latter was used because *Ophiothrix* is often found clinging to it, a phenomenon which is in accordance with the view that *Ophiothrix* is a reophile animal[8]. After 18 hr. the radioactivity of the stomach contents of the ophiuroids was measured.

Table 1. RADIOACTIVITY (c./min.) OF STOMACH CONTENTS OF OPHIUROIDS AND TISSUE HOMOGENATE OF *Alcyonium*

Species	Substratum: Stones and empty shells (c./min.)	Substratum: *Alcyonium digitatum* (c./min.)
Ophiothrix	186	326
	226	120
Ophiopholis	57	5·5
	162	59
	79	20·3
Ophiocomina	0	0
	0	0·9
	0	1·3
Alcyonium	—	110

On the dead substrates, no uptake of phytoplankton by *Ophiocomina* was found. The faint traces of radioactivity measured in specimens of *Ophiocomina* using *Alcyonium* as a substrate is a secondary phenomenon as the octocoral has *a priori* filtered the algae. *Ophiocomina* accordingly cannot be regarded as a suspension feeder, in contrast to the two other species which are extremely efficient suspension feeders, *Ophiothrix* being the superior one.

To measure the rate of removal of plankton algae by starved *Ophiothrix* and *Ophiopholis*, these species were fed with carbon-14 labelled strains of *Sceletonema costatum*. In both species three different concentrations of *Sceletonema* were used (10 : 5 : 1), but the starting activity in the same concentrations was identical. In each of the 2 × 3 jars, three animals were placed in 400 ml. membrane-filtered sea water. The radioactivity in subsamples of 10 ml. water was measured at increasing time-intervals starting with 1 hr.

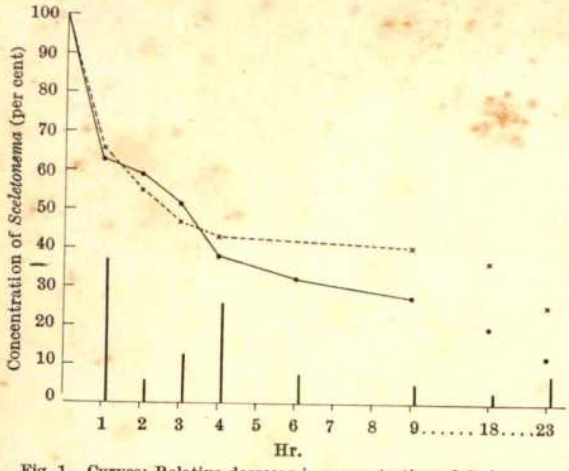

Fig. 1. Curves: Relative decrease in concentration of *Sceletonema* caused by filtration of *Ophiothrix fragilis* and *Ophiopholis aculeata*. ●—● *Ophiothrix fragilis*; ×---×, *Ophiopholis aculeata*. Columns: Relative rate of removal per hr. of *Sceletonema* by *Ophiothrix fragilis*

As the feeding-rates (relative) of the ophiuroids in the three concentrations of algae were almost of the same order of size, the relative average rate of removal of algae is shown in Fig. 1.

Obviously due to hunger, the filtering-rate is always greatest during the first hour and of about the same intensity in both *Ophiothrix* and *Ophiopholis* (respectively 37 per cent and 34 per cent of the algae present were removed). After 4 hr., however, *Ophiothrix* had surpassed *Ophiopholis*, and after 23 hr. *Ophiothrix* had removed 88 per cent of the algae, *Ophiopholis* only 75 per cent.

In all our experiments *Ophiothrix* has proved to be the most efficient filterer of phytoplankton. The highest efficiency was found in three specimens which removed about 50 per cent of the *Sceletonema* present in 400 ml. sea water in 1 hr. This ability probably explains the mass occurrences of this species (> 340 individuals per m.^{2}) in the English Channel[5], where strong tidal currents carry considerable amounts of suspended matter over the food-collecting net of tangled *Ophiothrix* arms. Our demonstration of the absence of filtering in *Ophiocomina nigra* also helps to explain the low ratio of only about 0·6 of this species for every 100 *Ophiothrix fragilis* in the English Channel[5].

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SOIL SCIENCE

Changes with Time in the Availability of Strontium-90 in Soil

DETAILED knowledge of the behaviour of strontium-90 in soil is of particular importance in assessing the long-term consequences of its deposition on agricultural land. Experiments have been carried out to determine whether strontium-90 becomes progressively fixed and therefore less available to plants. The majority of the more recent evidence suggests that the availability is decreased to only a small extent, if at all, by changes in the physico-chemical state of strontium-90 in the soil[1]. Deeper penetration through the soil or a more thorough mixing may, however, reduce the quantity of strontium-90 which is absorbed by plants[2].

Further information on this subject is being obtained from a long-term experiment now in progress in this laboratory. The experiment was designed to investigate both the rate at which strontium-90 moves down the soil profile under natural conditions and the manner in which the absorption of strontium-90 by plants changes with time, either as a result of penetration in the soil or because of chemical changes over long periods. Concrete cylinders, 1 yd. wide and 1 yd. deep, were filled with five different soils (Table 1) and left in the open to consolidate for nine months. In the summer of 1956, 1 mc. of carrier-free strontium-90 in aqueous solution was applied to the surface soil of each. Some cylinders were left bare and others were planted with rye grass which was sampled and assayed at regular intervals. In the four seasons for which results are now available, the ratio of strontium-90 to calcium in the grass grown on all soils has decreased by some 20–30 per cent. This reduction could be attributed to either or both of the causes; namely, to slow chemical changes which have reduced the availability of strontium-90 in the soil or to the increasing penetration of strontium-90 down the soil profile. The work here described was undertaken to obtain more direct information on possible changes with time in the physico-chemical form of strontium-90 in the soil; the manner in which it is redistributed down the soil profile will be described elsewhere.

Table 1. DATA ON SOILS

Soil	*p*H	Total exchange capacity	Exchangeable calcium
		m.equiv./100 gm.	
I	6·4	10·2	5·1
II	6·7	10·4	6·3
III	5·7	12·2	6·6
IV	7·6	26·2	23·1
V	7·8	28·7	28·0

It is known that chemical extraction procedures do not necessarily give adequate information on the relative availability to plants of strontium and calcium in the soil; difficulties arise owing to the fact that the chemical composition of the soil is to a greater or lesser extent modified by such treatments. An improved procedure which depends on measuring the relative concentration (or potential) of the two ions in a solution with which the soil is in true equilibrium was devised by Schofield and preliminary results have been published[3]. The same principle can be used to compare the availability of strontium ions which have been present in a soil for different periods of time. Dilute calcium chloride solution (0·01 *M*) has been found a suitable medium in which to equilibrate

soil for this purpose; changes in the availability of strontium can be inferred from the relative extent to which material which has been present in the soil for different periods passes into this solution.

This method has been used to compare the availability of the strontium-90 which had been incorporated in the soils for 3½ years, from the cylinders referred to above, with that of strontium-89 which was freshly added to the soil. Small aliquots of air-dry soil from the experimental cylinders were moistened with water or with a solution of carrier-free strontium-89. Seven days later they were shaken for 24 hr. with 0·01 *M* calcium chloride solution (soil/solution ratio of 1 : 8); three replicates of each treatment were employed. After centrifuging, the clear supernatant solutions were decanted and the quantities of strontium-89 or -90 which had passed into solution were determined. The soils were then boiled with 8 *M* nitric acid for 5 min. Repeated extractions with hot concentrated acid were carried out on some samples. The residual activity in the soil was determined with a calibrated beta scintillation counter; it was ascertained that the strontium-89 extracted from the soil, together with that estimated as remaining therein, did not differ significantly from that originally added.

The results in Table 2 show that the amount of freshly added strontium-89 which became equilibrated with the calcium chloride solution ranged from 55·5 per cent in soil I to 26·5 per cent in soil IV. The corresponding values for strontium-90, which had been in the soil for 3½ years, were some 10–3 per cent lower. This difference was significant ($P > 0·01$) for all soils except soil V. The nitric acid extraction removed almost all the strontium-89 from the soils but about 1 per cent of the strontium-90 remained. Even after repeated extractions with concentrated acid, the amount of strontium-90 remaining in the soil was not greatly reduced.

Table 2. THE EXTRACTION OF FRESHLY ADDED STRONTIUM-89, OR STRONTIUM-90 WHICH HAD BEEN PRESENT FOR 3½ YEARS, FROM VARIOUS SOILS

Soil	I	I+Ca*	II	III	IV	V
% removed from the soil by equilibration with 0·01 *M* calcium chloride solution						
^{89}Sr	55·5	46·3	49·1	49·9	26·5	27·9
^{90}Sr	50·7	41·7	44·7	45·6	24·5	27·2
$^{90}Sr/^{89}Sr$	0·91	0·90	0·91	0·91	0·92	0·97
% which remained in the soil after boiling for 5 min. with 8 *M* nitric acid						
^{89}Sr	0·05	—	0·06	0·10	0·05	0·30
^{90}Sr	1·6	1·4	1·0	1·8	1·5	0·9
$^{90}Sr/^{89}Sr$	32	—	17	18	30	3
% which remained in the soil after repeated extractions with nitric acid						
^{89}Sr	0·03	—	0·01	0·03	0·03	0·01
^{90}Sr	1·2	1·0	0·5	1·1	0·6	0·3
$^{90}Sr/^{89}Sr$	40	—	50	37	20	30

* Lime (at the rate of 10 tons/acre) was applied to the soil surface 1 year after the strontium-90.

The result of equilibrating the soils with dilute calcium chloride solution suggests that the availability of the strontium-90 has been reduced by a small amount over the period of 3½ years. Further evidence that some strontium is slowly converted into less-accessible forms is provided by the fact that rigorous extraction with acid displaced less of the strontium-90 which had been present for 3½ years than of the recently added strontium-89.

The mechanism whereby tracer amounts of strontium become firmly bound in soils is of theoretical interest, although these results suggest that the effect of such physico-chemical changes on the absorption of strontium-90 by plants is too small to be of great significance in the assessment of the passage of strontium-90 through food chains. The present experiment will be repeated after the strontium-90 has been in the soils for a longer period.

I am indebted to the late Dr. R. K. Schofield for his advice during the progress of this work.

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VIROLOGY

Mechanical Transmission of the Infectious Variegation Virus of Citrus

INFECTIOUS variegation was described as a possible virus disease of citrus in 1931 by Petri[1]. His description of symptoms and his illustrations are similar to those reported by Fawcett and Klotz[2], who transmitted the causal agent by bud-grafting from variegated lemon to sour orange. They noticed that some of the symptoms were similar to those associated with psorosis and suggested that the diseases might possibly be related. Klotz and Fawcett[3] noted that crinkly leaf of lemon is sometimes associated with infectious variegation. Fawcett and Bitancourt[4] were uncertain whether infectious variegation differed sufficiently from crinkly leaf to be considered a separate disease. From cross-protection studies, Wallace[5] concluded that infectious variegation is caused by a strain of the psorosis virus. Grant and Smith[6] reported infectious variegation in Florida and transmitted the causal agent by bud and leaf-piece grafts to several different species of citrus.

Many unsuccessful attempts have been made to transmit mechanically the viruses responsible for tristeza, psorosis, xyloporosis, and exocortis. To date these failures have been explained on the basis of insufficient virus concentration in the inocula, inhibitors, intrinsic properties of the virus, or the susceptibility of the test plant. In 1959, Holmes[7] reported the mechanical transmission of potato mottle virus to three species of citrus. The virus induced only one local lesion on one plant of each species, and was recovered to plants of *Nicotiana tabacum*. The virus was not recovered from non-inoculated leaves of citrus. Holmes[7] concluded that failures to transmit citrus viruses mechanically may have been due to the use of insusceptible or insufficiently susceptible test plants rather than to the presence of inhibitors in citrus foliage.

In the present investigations, leaves of Eureka lemon plants with typical symptoms of infectious variegation—such as vein banding, veinlet banding, speckle, blotch, and crinkle—were frozen (−10° to −20° C.) in a mortar with 1 ml. of 20 per cent sucrose

per gm. of leaf material and with a small amount of activated charcoal. The material was thawed and triturated with a mortar and pestle. The pulp was squeezed through cheese-cloth, and expressed juice obtained in this way was used for subsequent inoculations. Leaves to be inoculated were dusted with 500-mesh 'Carborundum' and inoculated by rubbing with a gauze pad saturated with inoculum or by brushing with a nylon-bristle brush that had been dipped in the inoculum. Inoculated leaves were rinsed with tap water immediately after inoculation. The tests were conducted during January–March. The test plants were either very young seedlings (2- to 4-leaf stage) or older seedlings approximately 12–14 in. high. Controls were comparable test plants that were treated as described except that leaves from healthy Eureka lemon plants provided the source of 'inoculum'.

Table 1. NUMBERS OF CITRUS SEEDLINGS INFECTED BY INFECTIOUS VARIEGATION VIRUS MECHANICALLY TRANSMITTED FROM EUREKA LEMON

Exp.	Test species	Relative age of test plants	Transmission	
			Test plants*	Controls
1	Eureka lemon	Young†	7/7	0/7
2	Eureka lemon	Young	5/5	0/5
3	Sour orange	Young	5/5	0/5
4	Eureka lemon	Old‡	3/3	0/3
5	Eureka lemon	Old	0/3	0/3
6	Sour orange	Old	1/3	0/3

* Numerator is number of plants infected after a five-week period and the denominator the number inoculated.
† Seedlings in 2- to 4-leaf stage.
‡ Seedlings 12–14 in. tall.

In three experiments in which the test plants were young when mechanically inoculated, all inoculated plants became infected (Table 1). Some transmission to older plants was obtained, but the results were erratic. Fifteen to twenty-five days after inoculation, some Eureka lemon plants exhibited systemic symptoms identical with those on the source plant. The sour-orange seedlings exhibited vein banding and, later, chlorotic blotches in young leaves, and leaf crinkle and cupping. Some inoculated leaves of Eureka lemon 8–10 days after inoculation exhibited slight chlorotic blotches that afterwards enlarged. When such leaves were cleared in alcohol and stained with iodine, they showed typical starch lesions[8] (Fig. 1).

Both inoculated and non-inoculated leaves of the test plants were examined for virus in two ways. Mechanical inoculations were attempted by the methods described, and leaf pieces were grafted to lemon and sour-orange seedlings. Virus was recovered from young systemically infected leaves as well as from inoculated leaves of experimentally infected plants by leaf piece-graft inoculations. Virus was transmitted by mechanical means from young systemically infected leaves but not from inoculated leaves. The failure to recover the virus by mechanical means from the inoculated leaves may be due to the age of leaf or to low concentration of virus. Old leaves are difficult to triturate with a mortar and pestle, and the virus concentration may be low because of the type of local virus multiplication.

It seems unlikely that use of insufficiently susceptible test plants could account for the previous failures of mechanical transmission of citrus viruses. The results reported here show that the failure of mechanical transmission of at least one citrus virus is not due to low concentration or intrinsic nature of the virus. Earlier attempts may have failed because inhibitors were not removed.

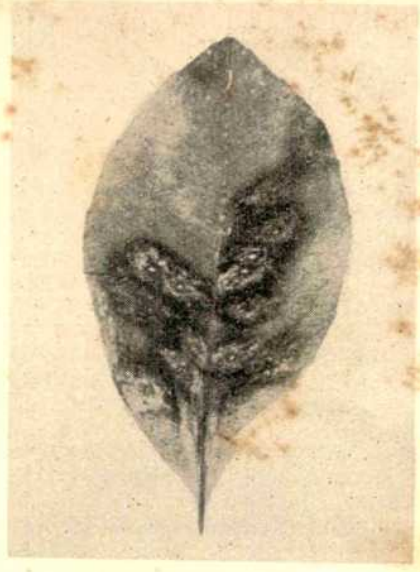

Fig. 1. Leaf of Eureka lemon 14 days after mechanical inoculation with infectious variegation virus, showing expansion of initial local lesions and starch-retention pattern. Leaf was cleared in alcohol and stained with iodine

The effect of sucrose and activated charcoal on the successful transmission of infectious variegation from citrus to citrus is unknown. Possibly enzyme-inhibiting properties of sucrose are somehow related to a mechanism by which sucrose might negate the effects of viral inhibitors in juice of citrus leaves. Moreover, viral inhibitors may be adsorbed by the activated charcoal, thus reducing their interference with infection and multiplication.

The beneficial effects of sucrose and activated charcoal may be elucidated after further study. The important fact at present is that a citrus virus has for the first time been transmitted mechanically from citrus to citrus. Mechanical transmission of any citrus virus immediately facilitates work on the properties of the virus, host-range, test plants, symptomatology, purification, serology, indexing methods, and eventually morphology of the virus particle associated with the disease. Further work on mechanical transmission of variegation and other citrus viruses from the point of view of inhibitors, hosts, and virus concentration is in progress.

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FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, November 7

BRITISH SOCIETY FOR THE PHILOSOPHY OF SCIENCE (in the Joint Staff Common Room, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. S. Vajda: "The Building of Models and the Theory of Games".

INSTITUTION OF ELECTRICAL ENGINEERS (at Savoy Place, London, W.C.2), at 5.30 p.m.—Discussion on "The Impact of Television on Society" opened by Lord James of Rusholme.

SOCIETY OF ENGINEERS (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Miss M. V. Griffith. "The Heat Pump in Great Britain".

SOCIETY OF CHEMICAL INDUSTRY, LONDON SECTION (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Dr. W. Idris Jones: "The Future of Chemicals from Coal".

ROYAL INSTITUTE OF CHEMISTRY, LONDON SECTION (joint meeting with the WOOLWICH POLYTECHNIC SCIENTIFIC SOCIETY, at the Woolwich Polytechnic, Thomas Street, London, S.E.18), at 7 p.m.—Dr. W. Davies: "Some Aspects of the Chemistry of Cancer".

ROYAL GEOGRAPHICAL SOCIETY (joint meeting with the BRITISH SCHOOL OF ARCHAEOLOGY IN IRAQ, at 1 Kensington Gore, London, S.W.7), at 8.30 p.m.—Prof. M. E. L. Mallowan: "Discoveries at Ur".

Monday, November 7—Tuesday, November 22

ROYAL PHOTOGRAPHIC SOCIETY OF GREAT BRITAIN, MEDICAL GROUP (at 16 Princes Gate, London, S.W.7)—Exhibition of Medical Photography.

Tuesday, November 8

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C.1), at 1.15 p.m.—Mr. B. C. Brookes: "A Philosophy of Applied Science".*

INSTITUTION OF MECHANICAL ENGINEERS, AUTOMOBILE DIVISION (at 1 Birdcage Walk, Westminster, London, S.W.1), at 4.30 p.m.—Dr. A. E. W. Austen, Mr. B. E. Knight, Dr. W. T. Lyn and Dr. T. Priede: "Fuel Injection, Combustion and Noise".

ZOOLOGICAL SOCIETY OF LONDON (at the Zoological Gardens, Regent's park, London, N.W.1), at 5 p.m.—Scientific Papers.

INSTITUTION OF CHEMICAL ENGINEERS (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Mr. W. D. Armstrong and Mr. R. M. Wood. "The Dynamic Response of a Distillation Column".

PARLIAMENTARY AND SCIENTIFIC COMMITTEE, GENERAL COMMITTEE (in Committee Room 11, House of Commons, Westminster, London, S.W.1), at 5.30 p.m.—Discussion on "Recent Developments and Problems Connected with Supersonic Flight" initiated by Mr. P. A. Hufton and Dr. A. E. Russell, C.B.E.

UNIVERSITY OF LONDON (at Senate House, London, W.C.1), at 5.30 p.m.—Prof. M. G. Kendall: "New Prospects in Economic Analysis" (Stamp Memorial Lecture).*

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. W. M. Court Brown: "Chromosome Analysis and Clinical Medicine".* (Sixth of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

ILLUMINATING ENGINEERING SOCIETY (at the Federation of British Industries, Tothill Street, London, S.W.1), at 6 p.m.—Mr. F. P. Bentham. "25 Years of Stage Lighting".

INSTITUTION OF THE RUBBER INDUSTRY (at the Royal Society of Tropical Medicine and Hygiene, Manson House, 26 Portland Place, London, W.1), at 5.30 p.m.—Mr. P. B. Lindley "Rubber in Engineering". 7 p.m.—Dr. A. N. Gent and Mr. M. Braden: "Mechanics of Attack of Rubber by Ozone".

ROYAL SOCIETY OF MEDICINE, PSYCHIATRY SECTION (at 1 Wimpole Street, London, W.1), at 8 p.m.—Discussion on "The Use of Psychiatric Skills in Industrial Organizations". Opening Speakers. Dr. J. J. O'Dwyer and Dr. Elliott Jaques.

Wednesday, November 9

ZOOLOGICAL SOCIETY OF LONDON (at the Zoological Gardens, Regent's Park, London, N.W.1), at 10.30 a.m.—Symposium on "Vertebrate Locomotion".

UNIVERSITY OF LONDON (at the Postgraduate Medical School of London, Ducane Road, London, W.12), at 2 p.m.—Dr. P. J. Rendle "Regulation of Carbohydrate Metabolism by Hormones and Other Factors".*

INSTITUTE OF PHYSICS AND THE PHYSICAL SOCIETY, COLOUR GROUP (in Lecture Theatre No. 3, Physics Department, Imperial College, London, S.W.7), at 3 p.m.—Mr. L. B. Happé: "Some Problems of Colour Reproduction in the Cinema"; Mr. J. Vickers: "Problems in Printing Colour Negatives"

PALÆONTOLOGICAL ASSOCIATION (at the Geological Society of London, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Prof. Dorothy Hill (University of Queensland): "The Fine Structure of the Coral Skeleton and its Application in Classification".

UNIVERSITY OF LONDON (at King's College, Strand, London, W.C.2), at 5.30 p.m.—Dr. H. E. Rose: "Vibration Mills and Vibration Milling".* (First of three lectures. Further lectures on November 16 and 23).

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. Charles Wilcocks: "Aspects of Medical Investigation in Africa—Trypanosomiasis".* (Third of four Heath Clark Lectures. Further lecture on November 10.)

ROYAL INSTITUTE OF CHEMISTRY (at the Royal Institution, 21 Albemarle Street, London, W.1), at 5.45 p.m.—Dr. T. C. Waddington: "Liquid Hydrogen Halides as Ionizing Solvents" (Meldola Medal Lecture).

INSTITUTE OF INFORMATION SCIENTISTS (at the College of Preceptors, 2 Bloomsbury Square, London, W.C.1), at 6.15 p.m.—Mr. C. A. Ronan: "Problems in Transliteration of Cyrillic".*

BRITISH INSTITUTION OF RADIO ENGINEERS, MEDICAL AND BIOLOGICAL ELECTRONICS GROUP (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6.30 p.m.—Mr. T. G. Brown: "Diagnostic Applications of Ultrasonics".

SOCIETY OF CHEMICAL INDUSTRY, FOOD GROUP (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Meeting on "Food Technology in Italy". Speakers: Mr. A. E. Billington, Mr. R. D. Mason, Dr. J. R. Nicholls and Dr. J. Tramer.

SOCIETY FOR PSYCHICAL RESEARCH (at Kensington Town Hall, Kensington High Street, London, W.8), at 7 p.m.—Mr. Christopher Scott "The Douglas Johnson T.V. Sitting".

WOMEN'S ENGINEERING SOCIETY (at "Hope House", 45 Great Peter Street, Westminster, London, S.W.1), at 7 p.m.—Mr. E. C. Cookson and Mr. A. H. Emerson: "Railway Modernisation and Electrification".

Thursday, November 10

LINNEAN SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Mr. A. Bogdan. "Grass Pollination by Bees in Kenya"; Dr. J. B. Free: "The Pollination of Fruit Trees by Honeybees".

INSTITUTION OF ELECTRICAL ENGINEERS, UTILIZATION SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Prof. F. C. Williams, F.R.S., Dr. E. R. Laithwaite, Mr. J. F. Eastham and Mr. L. S. Piggott: "The Logmotor—a Cylindrical Brushless Variable-Speed Induction Motor"; Prof. F. C. Williams, F.R.S., Dr. E. R. Laithwaite, Mr. J. F. Eastham and Mr. W. Farrer: "Brushless Variable-Speed Induction Motors using Phase-Shift Control".

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. M. R. Pollock: "Physiological Adaptation in Microorganisms".* (Seventh of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

OIL AND COLOUR CHEMISTS' ASSOCIATION (at the Royal Society of Tropical Medicine and Hygiene, Manson House, 26 Portland Place, London, W.1), at 7 p.m.—Mr. A. G. North: "Water-Thinnable Stoving Finishes".

CHEMICAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 7.30 p.m.—Prof. R. S. Nyholm, F.R.S.: "Electron Configuration and Structure of Transition-metal Complexes" (Tilden Lecture).

RADAR AND ELECTRONICS ASSOCIATION (at the Royal Society of Arts, John Adam Street, Adelphi, London, W.C.2), at 7.30 p.m.—Mr. C. A. Burgess: "V.H.F. Aerial Techniques".*

ROYAL INSTITUTE OF CHEMISTRY (at Croydon Technical College, Fairfield, Croydon), at 7.30 p.m.—Dr. H. J. Barber "Some Aspects of Chemotherapy".

Thursday, November 10—Friday, November 11

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 10.30 a.m. daily—Discussion on "Progress and Needs of Marine Science" led by Dr. G. E. R. Deacon, F.R.S., and Dr. F. S. Russell, F.R.S.

Friday, November 11

ASSOCIATION OF APPLIED BIOLOGISTS (at the British Museum (Natural History), South Kensington, London, S.W.7), at 10.50 a.m.—Meeting on "Applications of Radiation in Biology".

INSTITUTION OF ELECTRICAL ENGINEERS (joint meeting with the Royal Aeronautical Society, at Savoy Place, London, W.C.2), at 5.30 p.m.—The Rt. Hon. The Viscount Caldecote, D.S.C.: "The Future of 'Electrics' and 'Electronics' in Aircraft and Guided Missiles".

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 9 p.m.—Prof. R. J. Harrison: "Experiments with Diving Seals".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned.

LECTURER or ASSISTANT LECTURER (preferably with experience in chemical or biochemical aspects of pharmacology) IN THE DEPARTMENT OF PHARMACOLOGY—The Registrar, The University, Leeds 2 (November 14).

BIOCHEMIST (honours graduate with some research experience), to assist Dr. R. M. C. Dawson on isotopic studies on lipid metabolism in rumen micro-organisms and in the ruminant digestive tract—The Secretary, Institute of Animal Physiology, Babraham, Cambridge (November 15).

FISHERIES ADVISER (with a university degree in biology and a minimum of five years experience on both research and development) in the Ministry of Animal Resources, Sudan, for duties which will include the biological and technological investigations leading to the establishment of a profitable inland fisheries industry, and also the training of Sudanese assistants—The Appointments Secretary, Sudan Embassy, 3 Cleveland Row, St. James's, London, S.W.1 (November 15).

LECTURER IN THEORETICAL PHYSICS—Prof. A. Salam, Physics Department, Imperial College of Science and Technology, London, S.W.7 (November 15).

ASSISTANT EXPERIMENTAL OFFICER (with a degree or equivalent qualifications in chemistry) IN THE DEPARTMENT OF PEDOLOGY, for duties mainly concerned with the chemical analysis of peat and herbage—The Secretary, The Macaulay Institute for Soil Research, Craigiebuckler, Aberdeen (November 19).

RESEARCH ASSISTANT (graduate in medicine, and preferably some physiological knowledge and experience in simpler biochemical estimations) IN THE DEPARTMENT OF ANÆSTHETICS—The Registrar, King's College (University of Durham), Newcastle upon Tyne (November 19).

READER (with high academic qualifications and good experience in teaching and research) IN CIVIL ENGINEERING—The Clerk to the Governing Body, Battersea College of Technology, London, S.W.11 (November 28).

CHAIR OF PURE MATHEMATICS—The Registrar, University College, Singleton Park, Swansea (November 30).

LECTURER IN EDUCATION at the University of New England, Armidale, N.S.W., Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, November 30).

LECTURER IN THE DEPARTMENT OF STATISTICS, University of the Witwatersrand, Johannesburg, South Africa—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (South Africa and London, November 30).

LIBRARIAN—The Secretary, The Queen's University, Belfast (November 30).

RESEARCH FELLOW IN BOTANY at the University College of Rhodesia and Nyasaland for research into the autocology of *Salvinia auriculata*, to be conducted partly at Lake Kariba and partly at the College—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (November 30).

SENIOR LECTURER or LECTURER IN CHEMICAL ENGINEERING at the University of Natal, Durban—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (South Africa and London, November 30).

SENIOR LECTURER or LECTURER IN MECHANICAL ENGINEERING at the University of Auckland, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand and London, November 30).

UNIVERSITY LIBRARIAN—The Registrar, The University, Leicester (November 30).

LECTURER (with an honours degree and preferably some operating or research experience in some aspect of mining engineering) IN MINING ENGINEERING in the School of Mining Engineering and Applied Geology, University of New South Wales, Kensington, N.S.W.—The Agent-General for New South Wales, 56–57 Strand, London, W.C.2 (Australia and London, December 2).

LECTURER IN ORGANIC CHEMISTRY at Makerere College (The University College of East Africa)—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (December 10).

CHAIR OF PURE MATHEMATICS—The Registrar, University College of Wales, Aberystwyth (December 31).

PIG INDUSTRY DEVELOPMENT AUTHORITY FELLOW, for research in pig health—The Secretary, Royal College of Veterinary Surgeons Trust, 9 Red Lion Square, London, W.C.1 (February 25).

ASSISTANT, Grade B (with an honours degree in physics, and research or industrial experience in some branch of applied physics), IN THE DEPARTMENT OF PHYSICS—The Registrar, Bristol College of Science and Technology, Ashley Down, Bristol 7.

CHEMIST (with a first- or good second-class honours degree in chemistry or an equivalent qualification, and preferably experience in the inorganic analytical field and a knowledge of geochemical techniques) in Nyasaland, to take charge of the Geological Survey Departments, chemical laboratory, and to undertake assaying and chemical testing of rocks, including full silicate rock analyses—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.105/4/04.

CHEMIST (with an honours degree in chemistry, veterinary/agricultural or medical experience, and some experience in biochemistry) with the Government of Tanganyika, to supervise the Chemical Section of the Veterinary Research Laboratory (duties will include frequent safaris for experiments in the field)—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/8/020.

LECTURER (graduate in physics, preferably with teaching and research experience); and an ASSISTANT LECTURER (preferably with teaching or industrial experience) IN PHYSICS—The Principal, National College of Food Technology, St. George's Avenue, Weybridge, Surrey.

LECTURER IN PSYCHOLOGY—The Principal, West End Hospital Speech Therapy Training School, 59 Portland Place, London, W.1.

OFFICIAL FELLOW AND TUTOR (preferably with interests in pure mathematics) IN MATHEMATICS—The College Secretary, Balliol College, Oxford.

RESEARCH ASSISTANT (with a first- or second-class honours degree in mathematics or science) IN THE SUB-DEPARTMENT OF COMPUTATION, for duties which will include the preparation of programmes for the Ferranti "Pegasus" computer, and the provision of assistance to other users of the machine—The Registrar, The University, Southampton.

TECHNICIAN (with experience of microbiological techniques and preferably some knowledge of biochemical or brewing procedures), to take charge of large-scale growth of micro-organisms by continuous fermentation methods and to be concerned with growth and purification of bacterial viruses—The Deputy Director, Medical Research Council Biophysics Research Unit, King's College, Strand, London, W.C.2.

WHOLE-TIME BIOCHEMIST (non-resident), for hospital biochemical work in the Mansfield Area Pathology Service—The Hospital Secretary, King's Mill Hospital, Sutton-in-Ashfield, Notts.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Ministry of Agriculture, Fisheries and Food. Report of the Working Party on a Welsh Agricultural College, 1960. Pp. ii+32. (London: H.M. Stationery Office, 1960.) 1*s*. 9*d*. net. [38

British Broadcasting Corporation. B.B.C. Engineering Monograph No. 31: The Power Gain of Multi-Tiered V.H.F. Transmitting Aerials. By P. Knight and G. D. Monteath. Pp. 38. (London: British Broadcasting Corporation, 1960.) 5*s*. [48

Durham University Appointments Board. Second published Annual Report, 1958–1959. Pp. 7. (Durham: The University Appointments Board, 1960.) [48

Bulletin of the British Museum (Natural History). Entomology. Vol. 9, No. 4: A Review of the African Species of the Genus *Cheumatopsyche* (Trichoptera, Hydropsychidae), with special reference to those of Southern Africa, and the Ephemeroptera Types of Species described by A. E. Eaton, R. McLachlan and F. Walker, with particular reference to those in the British Museum (Natural History). By D. E. Kimmins. Pp. 253–318. 20*s*. Vol. 9, No. 5: The *Jamides euchylas* Complex (Lepidoptera: Lycaenidae). By G. E. Tite. Pp. 319–336+plate 21. 8*s*. Zoology. Vol. 6, No. 7: The Ecology and Taxonomy of some Angola Birds (Based on a collection made in 1957). By B. P. Hall. Pp. 367–453+plates 5 and 6. 40*s*. (London: British Museum (Natural History), 1960.) [48

Other Countries

Canada: Department of Northern Affairs and National Resources. National Museum of Canada. Bulletin No. 162: Contributions to Anthropology, 1957. Pp. iii+208 (28 plates). 2 dollars. Bulletin No. 168: List of the Marine Fishes of Canada. By D. E. McAllister. Pp. ix+76. 1.25 dollars. (Ottawa: Queen's Printer, 1960.) [28

Metropolitan Life Insurance Company. Statistical Bulletin, Vol. 41 (June 1960): Recent and Future Mortality Trends. Blood Pressures in Men and Women. Longevity of Industrial Policyholders in 1959. Many Women Killed in Accidents. Pp. 12. (New York: Metropolitan Life Insurance Company, 1960.) [28

University of California Publications in Geological Sciences. Vol. 37, No. 1: Fossil Mammalia from the Early Wasatchian Four Mile Fauna, Eocene of Northwest Colorado. By Malcolm C. McKenna. Pp. 1–130. (Berkeley and Los Angeles: University of California Press: London: Cambridge University Press, 1960.) 2.50 dollars. [28

Proceedings of the California Academy of Sciences. Fourth Series. Vol. 31, No. 1: The Wasps of the Genus *Plenoculus* (Hymenoptera Sphecidae, Larrinae). By Francis X. Williams. Pp. 1–49. Vol. 31, No. 2: Interpopulation Variation in the Colubrid Snake *Natrix pryeri* from the Riukiu Islands, with description of a New Subspecies. By E. V. Malnate and Harold E. Munsterman. Pp. 51–67. Vol. 31, No. 3: Further Records of Neotropical Tabanidae (Diptera) Mostly from Peru. By Cornelius B. Philip. Pp. 69–102. (San Francisco: California Academy of Sciences, 1960.) [28

Abridged Scientific Publications from the Kodak Research Laboratories, Vol. 34, 1952. Pp. 253+xvi. (Rochester, New York: Eastman Kodak Company, 1960.) [28

Food and Agriculture Organization of the United Nations. World Forest Inventory, 1959. Pp. xii+137. (Rome: Food and Agriculture Organization of the United Nations; London: H.M. Stationery Office, 1960.) 12*s*. 6*d*.; 2.50 dollars. [28

Western Australia. Geological Survey—Mineral Resources of Western Australia. Bulletin No. 7: Iron Ores in Western Australia. Collated by R. R. Connolly. Pp. 103. Bulletin No. 113: Miscellaneous Reports for 1956. Pp. 206+35 plans in separate atlas. (Perth: Government Printer, 1959.) [28

Transactions of the American Philosophical Society. New Series, Vol. 50, Part 6. The Paleocene Pantodonta. By Elwyn L. Simons. Pp. 99. (Philadelphia: American Philosophical Society, 1960.) 2.50 dollars. [28

Atomic Energy of Canada Limited. Annual Report, 1959–60. Pp. 36. (Ottawa: Queen's Printer, 1960.) 25 cents. [38

New Zealand Forest Service: Forest Research Institute. Technical Paper No. 28: A Root and Stem Canker of Exotic Conifers in New Zealand. By J. W. Gilmour. Pp. 19+8 plates. (Wellington: Government Printer, 1959.) [38

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A COMMONWEALTH ADVISORY AND TECHNICAL SERVICE

THE fourth report of the Select Committee on Estimates for the session 1959–60, which deals with the Colonial Office, is of considerable interest to many scientists and technologists for its section dealing with the Overseas Civil Service*. Of equal scientific interest, however, is the section which examines generally the provision of aid and advice on administrative and technical problems to dependent territories and independent countries in the Commonwealth, and which leads the Select Committee to recommend that a committee of inquiry be set up to consider the establishment of a Commonwealth Advisory and Technical Service. A sub-committee of the Select Committee regarded this as an indispensable instrument of future assistance to such countries inside and outside the Commonwealth. Besides this, the Committee's examination of financial relations with the dependent territories touches on the mechanism by which grants are made for research and development purposes, and finally the Committee's consideration of proposals for some form of merger of the Colonial Office and of the Commonwealth Relations Office are of wide general interest as well as closely affecting the future of the Overseas Civil Service.

Consideration of the arguments for and against such a merger led the Committee to accept the arguments in favour. The Committee believes that it is desirable from the point of view of efficiency in Whitehall, and that it offers the best way of preserving, for the benefit of independent and dependent territories alike, knowledge and experience that might otherwise be lost. The continued existence of two separate Departments of State to deal with the affairs of a rapidly developing and changing Commonwealth leads to a dichotomy of thought and approach that militates against the unity of the Commonwealth; and the Committee does not regard as well founded the argument that such a merger would not be acceptable to the rest of the Commonwealth. On the contrary, it believes that with the right presentation and given sufficient thought and care, the concurrence of the other independent members of the Commonwealth can be secured, and that the benefits to be gained are so substantial that no effort should be spared to achieve it. In particular, the merger would ease many economic and technical problems during the transition to independence and afterwards.

The Select Committee recommends accordingly that the two Offices should be merged on the lines of a tripartite organization outlined in evidence by Sir Hilton Poynton, the Permanent Under-Secretary of State for the Colonies, in which one of the three sections would be organized functionally with no distinction between independent and dependent countries, particularly in the field of technical aid, social services and the like. If the full advantages are to be obtained, this step should be taken at once; and the Select Committee recommends further that the new Department should be known as the Commonwealth Office and should be administered by a single Secretary of State, assisted by three or more departmental ministers. These views appear to be shared by Mr. Kenneth Younger, director-general of the Royal Institute of International Affairs, who gave evidence before the Committee, and from time to time such a merger has already been suggested in Parliament.

If such a merger of the two Offices takes place, the establishment of a Commonwealth Advisory and Technical Service will be no less necessary, in the Committee's view, in order to reach the objectives of planning overseas assistance. Moreover, Sir Hilton Poynton also pointed out that economic, educational and research problems do not really differ according to whether a territory is an independent country or whether it is still a dependent territory, and the disadvantages of the present system are likely to become more obvious as less-developed territories such as Tanganyika attain independence. The proposed Service would establish on a rational and more comprehensive basis the present provision for new forms of technical assistance in the shape of the services of experts, and the Select Committee emphasizes that only if aid for new States is granted in an ordered programme can it be properly effective and hence economical to the taxpayers of the United Kingdom.

Establishment of such a Service will enable the maximum benefit to be gained from assistance given to new States during their dependent days, and it would secure for these countries the experience and knowledge of Overseas Civil Service officers who, on retirement from that Service, could continue in the new Service to employ their talents for the benefit of overseas governments rather than take other employment. Finally, this Commonwealth Service should strengthen the links between Commonwealth countries. Recruitment from the Commonwealth, and especially the older countries, and provision by this means of aid by them to young countries, would broaden the basis of the Service and further understanding between Commonwealth countries. These solid advantages are regarded as outweighing the disadvantages of such a scheme, which would not offer a comprehensive solution to the intractable problem of redundancy which already confronts the Overseas Civil Service, though the Committee believes that the difficulty of ensuring graduated promotion for officers in such a Service could be overcome. It emphasizes, however, that it is essential

* Fourth Report from the Select Committee on Estimates, together with part of the Minutes of Evidence taken before Sub-Committee D and an Appendix, Session 1959–60, Colonial Office. Pp. xxxvii+280. (London: H.M. Stationery Office, 1960.) 14s. net.

to safeguard the flexibility and informality of Commonwealth relationships, and it suggests that the administration of the proposed Service in the United Kingdom would require to be entrusted either to a Commonwealth institution, such as the Commonwealth Economic Consultative Council, or to the proposed new Commonwealth Office.

In considering the financial aspects of relations with the dependent territories, the Select Committee directs attention to the urgent need for devising some system to enable Colonial development and welfare programmes to be brought to completion after the expiry of the period for which expenditure was originally authorized. It also comments on Colonial information services and criticizes the refusal of the Colonial Office to accord information officers in the Colonial territories right of direct correspondence on technical matters with the Central Office of Information. Such rights, it recommends, should be granted, especially in territories approaching independence; and it also recommends that, especially in emergent territories, the British Council should seek to enlist local financial support, as such co-operative effort would enhance local appreciation of the services of the Council.

It is against this background, and especially the two major recommendations for the establishment of a Commonwealth Office and a Commonwealth Advisory and Technical Service, that the Committee's discussion of the problems presented by the Colonial Office staff and the Overseas Civil Service is best considered. Despite the present uncertainty of careers in the Colonial Service, the number of candidates expressing a preference for service in the Colonial Office still exceeds the number accepted, partly because of a decline in the standard of candidates. Nevertheless, the Office at present finds it difficult to guarantee careers with proper expectation of promotion, both to its new recruits and to those more senior officers whose careers can only be continued for a full term of years by transfer to other Departments. While there is less reluctance among its staff than three years ago to spend half their time abroad instead of only the two years early in their service to which officers of the Administrative and Executive Class are normally liable, the Select Committee recommends firmly that only staff prepared to serve at home and overseas should be recruited to the Colonial Office in future. Further, to assist in planning the future establishments, the present staff should be asked immediately to state whether they would be prepared to serve abroad, in the event of their being transferred to the Commonwealth Relations Office. The recommendation that Colonial Office staff should spend longer periods on secondment abroad in order to acquire a fuller understanding of the governments and peoples of Colonial territories is clearly intended to apply to the staff of the proposed Commonwealth Office also.

The examination of the Overseas Civil Services emphasizes further some of the points made by Sir Kenneth Younger in his recent book, "The Public ervice in the New States", and is based partly on a memorandum on the Colonial Office and the Overseas Civil Service submitted on behalf of the Colonial Secretary. The numbers of the Overseas Civil Service decreased in 1959 by at least 10,000–14,000, most of whom were employed by the East Africa High Commission and the Governments of Hong Kong, Kenya, Tanganyika and Uganda; but although 1,067 officers were recruited in 1959, at the end of the year there were still 866 vacancies. The main drawback to recruitment is the inability of the Colonial Office to offer a guaranteed career for 25–30 years, owing to the decreasing numbers of posts in territories under the control of the Secretary of State. The suggested Commonwealth Advisory and Technical Service should help to overcome this difficulty, but the Committee is critical of the present conduct of recruitment to the Overseas Civil Service, and it suggests that the Colonial Office should take the initiative among recruiting agencies by revising and modernizing its recruiting methods for such appointments, particularly so as to provide more direct and imaginative forms of contact with university students. It also considers that the Office has not been active enough in seeking recruits from Commonwealth countries, and recommends that the Colonial Office should take immediate steps to promote recruitment from Commonwealth countries to the Overseas Civil Service, both on pensionable and on contract terms. A new approach to the problem of local recruitment is also needed.

The importance of these measures is underlined by events in the Congo and elsewhere during the past year, and it is clear enough that the countries now emerging are likely to have a greater need of the services of overseas officers, because they are less developed than such countries as Ghana and Malaya, the Federation of Nigeria, Cyprus, or the West Indies Federation. Despite the seriousness of the problem of redundancy, which the Committee believes might have been largely solved had the foundation of the Overseas Civil Service in 1954 been more than just a change of name, and would have been alleviated had the Special List *A* and proposed secondment schemes of 1956 succeeded, it is thought that there is a future for the Overseas Civil Service in a much-reduced form, employed in some territories on terms and in an atmosphere difficult to foresee at this time of rapid change. It is essential, in the view of the Committee, for the United Kingdom to shoulder part of the burden of paying differentials between the salary and allowances of an overseas officer and those of a local officer, and this principle has since been accepted.

Such a measure should help to improve the morale and so to staunch the wastage of overseas officers, while retaining the links between the United Kingdom and the Commonwealth and assisting to ensure the stability and forward the development of emergent countries. Of itself, however, it will scarcely do more than alleviate temporarily the uncertainty clouding the future career of every overseas officer in an emergent country, and the Committee recommends further an urgent and comprehensive examination of the organization and terms of service of the Overseas

Civil Service, taken in conjunction with its recommendation for the establishment of a Commonwealth Advisory and Technical Service.

Though the Select Committee presents the case for a single Commonwealth Office cogently and persuasively, if not altogether conclusively, taken by itself it is unlikely to meet the most urgent needs. Far more important than the elimination of overlapping and the financial savings which a new administrative arrangement might permit is the question of outlook and the whole tempo of administration. This is indeed recognized by the Committee, which noted, moreover, that some increase in staff in consequence of the greater need for technical services in the dependent territories might be unavoidable, and again that there was likely to be increasing need for officers with technical rather than purely administrative qualifications. The evidence submitted points clearly to the danger that, without some merger, the existing Colonial Office advisory staff of 58 dealing with such questions as agriculture, animal health, education, fisheries, flora and fauna, medical research, etc., may be dispersed, and also that the important research programmes now maintained from Colonial Development and Welfare Funds may be interrupted when territories come to independence.

The essential recommendations of the Committee are those relating to the Overseas Civil Service and to the establishment of a Commonwealth Advisory and Technical Service, and they have the prior claim on the Government's attention. They are more important than financing the projected scheme of technical aid to which Mr. Iain Macleod referred on October 12 during the Conservative Party meeting at Scarborough, and which is unlikely to be effective unless prior attention is given to the means by which such aid is to be channelled and the conditions of service to be offered to those who are expected to provide such assistance. Unless those conditions are reasonable and appropriate, it may prove impossible to recruit staff of the high quality required, still less to expect from them the standards in which enthusiasm and efficiency are fostered. Like Mr. Kenneth Younger in "The Public Service in New States", the Select Committee puts the emphasis in the right place—on the human factor, on the men and women who will provide the required services, and on the conditions under which they will be expected to work. With this report before it, the Government cannot just leave the problem to such bodies as the newly formed Overseas Development Institute; and in view of the demand that technical assistance makes on the services of scientists and technologists of all kinds, it is to be hoped that the Overseas Research Council, with the full support of the Minister for Science and the Advisory Council for Scientific Policy, will lend the full weight of its influence in the establishment of satisfactory conditions for overseas service, and the urgent and thorough examination of the desirability of establishing a Commonwealth Advisory and Technical Service as the Select Committee recommends.

A CENTURY OF PROGRESS IN EVOLUTIONARY BIOLOGY

Darwin's Biological Work

Some Aspects Reconsidered. By P. R. Bell, J. Challoner, J. B. S. Haldane, P. Marler, H. L. K. Whitehouse and J. S. Wilkie. Edited by P. R. Bell. Pp. xiii+343+5 plates. (Cambridge: At the University Press, 1959.) 40*s*. net.

THIS valuable book consists of six excellent chapters on the present position of a number of the biological topics on which Darwin himself worked. Unfortunately the inept title, which suggests a work of purely historical interest, is likely greatly to hinder sales. This is a pity because it deserves to be in every scientific library and widely read among senior students.

The opening chapter by P. R. Bell, who edits the volume, summarizes a century of research on the movement of plants in response to light. Among the many important conclusions emphasized is the fact that the study of phototropism has become intimately connected with the basic problems of cell physiology—a conclusion which would certainly have astonished Darwin, who at least in his theorizing on natural selection was inclined to regard the animal or plant as 'given', and who was not much attracted to physiology. Bell points out that among the implications of modern views as to phototropism is the conclusion that the current division of botany into two more or less independent disciplines—morphology and physiology—is neither sound nor likely to be profitable. The other botanical chapter also takes the form of a most able review, by H. L. K. Whitehouse, of a hundred years progress in the study of cross- and self-fertilization of plants. One of the most topical subjects which emerges from this discussion is that of cytoplasmic inheritance and the respective parts played by nucleus and cytoplasm in hereditary transmission.

Perhaps the two zoological chapters constitute the most outstanding feature of the book. The first is by J. B. S. Haldane and is entitled "Natural Selection". In a little less than fifty pages Haldane contributes a review of the subject which is masterly in its simplicity and lucidity and yet at the same time profound. It is hard to imagine how it could have been better done. However, the last two-and-a-half pages, which deal with philosophical difficulties and implications of Darwinian theory, are open to some criticism. Here the writing is too condensed, and statements are made without sufficient explanation and support; although it is probable that if he had given himself more space the writer might well have been able to provide these. Thus he states that the difficulty in assuming mind to be a product of evolution does not arise for a consistent idealist, nor for a consistent materialist. Whatever may be the idealist position, this is certainly not true for what is normally understood by the term 'materialist'. Although Haldane has a few words to say as to what he himself means by this term in relation to some Chinese and Hindu philosophical concepts, he does not say enough to make the matter clear. Another idea which it would have been good to have further developed arises from the suggestion that Darwin may have started a revolution in philosophy as great as that initiated by Aristotle, whose logic is mainly based on his efforts to classify animals. Darwin, in comparing species,

pointed out that in studying any two forms we shall be led to weigh more carefully and to value higher the actual amount of difference between them. Haldane suggests that some future philosophy will be based on differences whereas to-day's common-sense philosophy, Aristotelian in origin, is based on similarities. He considers that this may in due course have a profound effect on the outlook both of scientists and philosophers on the natural world.

Among all Darwin's writing "The Expression of the Emotions in Man and Animal" (1872) was perhaps exceeded in originality only by "The Origin" and "The Descent of Man". Its impact was long delayed, but none the less great when it came. P. Marler provides an admirable chapter on subsequent developments in the study of animal communication. He deals with chemical, visual and auditory communication in both invertebrates and vertebrates, and summarizes for the first time in this connexion a great deal of the modern ethological literature. His chapter is profusely illustrated, and the sections on the evolution of bird song, on the origins of communication and on animal and human language are of particular interest. The book is completed by a valuable account of palæontology and evolution by J. Challoner, who pays particular attention to the imperfections of the geological record, the question of group evolution and evolutionary series.

Finally, a chapter by J. S. Wilkie on the originality of Darwin's theory of evolution shows him to be an expert on the work of Buffon and Lamarck, and consequently he is able—in contrast to many modern writers on this subject who take their views second-hand—to give an authoritative assessment of the scattered suggestions as to the possibility of evolution in the works of the former. In regard to Lamarck, he points out that it was his deistic assumptions which gave his theory its peculiar structure. Lamarck supposed that God, in directing the process of evolution, was aiming directly at the production of man and that for this reason linearity should be empirically discoverable in the evolutionary series. It is characteristic of deism to assert that the mind of God is infinite yet to suppose that we can see things from God's point of view. Believing this, Lamarck was unable to tolerate the idea that any species should be 'wasted' on the way towards the production of man so he is unwilling to admit the possibility of extinction. It was these presuppositions and their consequences which made the Lamarckian theory unable to adapt itself readily to the data of comparative anatomy, and even less able to assimilate the fossil record, which of course shows no simple upward trend of organization. Wilkie's chapter brings to a conclusion a valuable and distinguished book.

W. H. THORPE

RADAR IN WEATHER RESEARCH

Radar Meteorology

By Louis J. Battan. Pp. xi + 161. (Chicago: University of Chicago Press; London: Cambridge University Press, 1959.) 45*s*. net.

WHEN it was discovered that centimetric radar could detect precipitation, the meteorologist found himself in the possession of an almost embarrassingly powerful tool for weather research. Since the end of the War, meteorologists in many countries have used the spare military radars which became available to make great advances in precipitation physics. There is a use, too, for radar in weather forecasting, and now that State meteorological services are acquiring their own weather-radar sets, increasing numbers of meteorologists are being introduced to this technique.

There have been few general surveys of progress in this field, or accounts of radar theory from a meteorological aspect, and the newcomer to the subject has been faced with the task of acquiring the basic physical principles from text-books, of finding out the workings of his radar equipment from the technicians and of abstracting past research work from a mass of published papers. This slim volume by one of the foremost radar meteorologists in the United States is written for these, and for others with a more superficial interest in radar meteorology. Although more than one-third of the book is devoted to radar theory, they will learn little physics and less electronics from it. After an all too brief chapter on the fundamentals of radar and the types of indicator units normally encountered, and a sketchy introduction to the theory of propagation of electromagnetic waves, the standard equations for the detection of spherical and non-spherical water and ice particles are produced. While the Rayleigh approximation can be used at centimetric wave-lengths for rain, hailstones exist in sizes well outside the Rayleigh region. It is surprising therefore that no reference is made to Ryde's war-time work showing the very high back-scattering cross-sections of larger ice spheres (recently confirmed by the author's own calculations).

The difficulties encountered in the quantitative use of radar are perhaps too well brought out in the chapter on precipitation measurements. The power received back by the radar is proportional to the sum of the sixth powers of the drop diameters. In order to deduce rates of rainfall or other meteorological data, it is necessary to make assumptions about the drop-size distribution law, and it is encouraging that reasonable results can be obtained when this is done. No attempt is made to explain the large discrepancy between observed and calculated values of echo power which has been found by all those attempting to obtain quantitative values from signal intensity measurements.

The greater and more useful part of the book is devoted to a discussion of the use made by meteorologists of centimetric, and more recently of millimetric, radars. Here the author, being a meteorologist, is on happier ground, and has produced a valuable and concise account of research in this field during the past 10–15 years. Inevitably there is emphasis on American investigations into severe weather, both from thunderstorms and hurricanes, which in themselves are of little interest to some readers. Nevertheless every country has its own weather problems, and their analysis by radar techniques will lead, as this book indicates, to a better understanding of cloud and precipitation physics.

There are two notable omissions in the list of chapter headings on the uses of radar. No specific mention is made of the value of radar to the synoptic meteorologist. While it may be true that the forecaster has no use for radar information, an appraisal of the value of the data for forecasting research would have been of great interest. Neither is there mention of the allied problem of the analysis and dissemination of radar data, a problem which will increase in magni-

tude as radar sets are made to produce more and more data required for use operationally.

A chapter on 'angels' shows that argument is still strong on the causes of echoes received from apparently clear air. The book concludes with a chapter on special instrumental techniques, which might well have come at the end of the theoretical section, since some of the techniques are referred to thereafter. There is no doubt that the meteorologist is now developing radar sets to meet his special needs, and we can expect progress to become even more rapid than over the initial fifteen years of radar meteorology covered by this book.

The book is well produced and there are adequate references, although the method of giving references as footnotes, liberally sprinkled with *op. cit.* and *ibid.*, is at times irritating. The small circle of prospective buyers presumably necessitates the high price.

J. R. PROBERT-JONES

DELINQUENT BOYS AND THEIR PARENTS

On the Threshold of Delinquency

By John Barron Mays. (Social Research Series.) Pp. x+243. (Liverpool: Liverpool University Press, 1959.) 25*s*. net.

Delinquency and Parental Pathology

A Study in Forensic and Clinical Psychology. By Dr. Robert G. Andry. Pp. xv+173. (London: Methuen and Co., Ltd., 1960.) 21*s*. net.

EACH of these books is a study of a small group of delinquent boys—but they have little else in common. Mr. Mays has written an engaging account of an attempt to deal with a particularly difficult bunch of youngsters by setting up a youth club in a delinquent area. No systematic description is given of what actually went on inside the Dolphin Club and one has only a vague picture, for example, of the number of staff engaged, of the use and misuse of equipment, and what a normal week's programme looked like. But a much more important point is made and illustrated with a wealth of detail, that the Club succeeded in keeping boys off the streets and enlisted the co-operation of otherwise indifferent parents in achieving this and possibly other aims.

There are three main strands running through the work: (*a*) an account of incidents and activities in and around the club; (*b*) pen pictures and case-histories of the club members; (*c*) many observations on the social patterns of the district and on the nature of delinquency in general.

The book is somewhat discursive, and the author moves rather too freely from one topic to another. But the observation is shrewd, the descriptions are vivid, and the commentary is uncommonly penetrating. The reader's interest is held, and at the end one has a clear picture of a courageous experiment carried out by people who had no illusions but who were not thereby discouraged. Their achievement is clear and the book is both informative and encouraging.

In a particularly discerning passage (pp. 26–28), Mr. Mays gives an overall estimate of the major factors underlying delinquent behaviour in adolescents. He brings out clearly the difficulties of "boys approaching adolescence who require a strong father figure with whom they can identify themselves". This is, to a large extent, the text of Dr. Andry's remarkable study. Here eighty delinquent boys in a remand home are compared with eighty non-delinquent boys from a reasonably matched group. Following a systematic interview of each of these boys and of thirty sets of parents in each group, he examines parental roles as perceived by the boys and also the parents' perception of their own roles. He concludes that delinquent boys "tend to perceive greater defects in their fathers' roles than in their mothers' roles, whereas non-delinquents tend to perceive the roles of both parents as being adequate. (Further, this seems confirmed in the main by both parents)". This general conclusion is followed up by detailed investigation on specific points, and the differential response of the delinquent and non-delinquent is subjected throughout to a statistical test of significance. For the most part the differences between the responses of the delinquent and the non-delinquent group are most impressive.

In his introduction to Dr. Andry's book, Dr. Mannheim implies that some special interest in fathers is a not unexpected reaction to Bowlby's now classic theory of the effects of early maternal deprivation. This may be so, but Dr. Andry's study and Dr. Bowlby's work are not strictly comparable. Andry specifically excludes neurotic cases (though he does not define the term) and his technique is confined to questioning adolescent boys (between the ages of 11 and 15 years) and some of their parents. Since he excludes (for perfectly good reasons) children with an *I.Q.* below 80 and also children from broken homes, his sample is by no means representative of the delinquent population. He might, quite probably, obtain similar results from a wider sample. Bowlby claims to have shown a clear connexion between early traumatic maternal deprivation and subsequent maladjustment (not necessarily delinquent). Moreover, a high proportion of the cases in which he is interested could properly be called neurotic or psychopathic. This is not inconsistent with, but is quite different from, assessing the respective roles of father and mother during the adolescent period.

Dr. Andry's book is somewhat repetitive and his language is occasionally obscure (for example, "a research worker may use a set of data to derive a maximal system of control with respect to the end object via the possible decision"). But the experiment which he describes is rigorously planned and his use of statistical methods is judicious. A short review of the literature and an extremely interesting bibliography are included. This is a study which will certainly have a considerable effect on future thinking and its direct implications so far as case work is concerned are obvious.

One striking fact is mentioned by both Mays and Andry. The delinquent boy is often keenly aware of his father's defects, and particularly of the poor relationship between boy and father. Father and mother are equally aware of the situation; and all the parties concerned would like to see it improved (though their thoughts and feelings may be vague and confused). Experience strongly confirms this, and it seems that actual teaching of the basic techniques of father–son relationships—and particularly the overcoming of embarrassment on both sides—is often surprisingly effective.

JOHN GITTINS

THE NEW RADIO ASTRONOMY CENTRE OF THE UNIVERSITY OF SYDNEY

By PROF. H. MESSEL

THE Chatterton Astronomy Department of the School of Physics, and the School of Electrical Engineering, have established a Radio Astronomy Centre in the University of Sydney.

Radio astronomy is concerned with observations of the heavens at radio wave-lengths rather than with light waves. It is a relatively new and vigorously growing branch of one of the oldest of the sciences, and Australia has taken a leading part in its development. Almost all the Australian work, so far, has been carried out by the radio astronomy group in the Radiophysics Division of the Commonwealth Scientific and Industrial Research Organization.

Recently, however, several members of this group have joined the staff of the University of Sydney, and, in addition, several outstanding English radio astronomers have already joined, or will soon join, them. Most of these are in the Chatterton Astronomy Department of the School of Physics under Prof. Harry Messel. One group, led by Dr. B. Y. Mills, who was previously with the Commonwealth Scientific and Industrial Research Organization, will engage immediately in radio astronomy work. Another, in which Dr. R. Q. Twiss of the School of Physics and Prof. Hanbury Brown of the University of Manchester will join forces, will work with the giant stellar interferometer in the optical field of astronomy.

Radio astronomy, however, is the meeting point of astronomy, physics and all the most advanced techniques of electronics and electrical engineering. The appointment of a group of leading radio astronomers, including Dr. B. Y. Mills, to the Chatterton Astronomy Department and the recent appointment of Prof. W. N. Christiansen, formerly of the Commonwealth Scientific and Industrial Research Organization radio astronomy group, to the chair of electrical engineering at the University of Sydney, has made possible the establishment of the new Radio Astronomy Centre. The Centre will mean the pooling of resources, intellectual and material, of the Schools of Physics and Electrical Engineering for an attack on some of the major fundamental problems of radio astronomy. The basic interest in the School of Electrical Engineering in solid-state devices and low-noise receivers will contribute a great deal to this joint action.

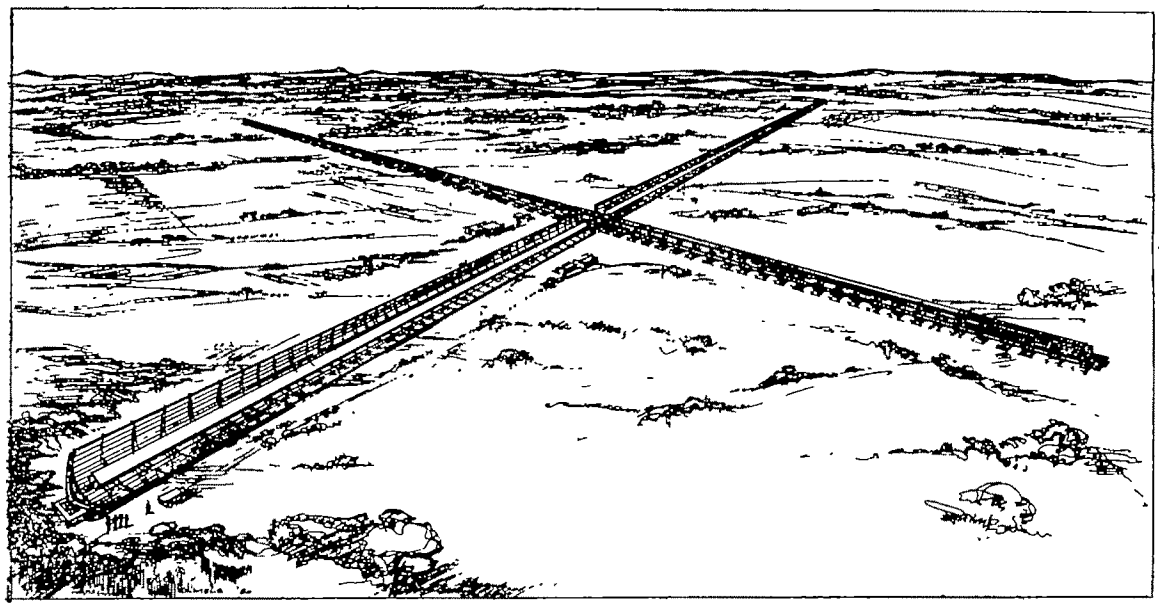

Fig. 1. Artist's sketch of the giant Mills' cross for the University of Sydney Radio Astronomy Centre

One of the first problems to be considered by the Radio Astronomy Centre is that on which Dr. Mills has been engaged for some years: the detailed observations of sources of radio emission, both in our own Galaxy and in the very distant regions of space. Such observations are very important for a study of the physics of the rare gaseous medium, lying around and between the stars, which probably holds the key to the problem of the formation and evolution of galaxies such as our own, the Milky Way system. These observations are of particular importance to the School of Physics, which is already established as a leading centre of cosmic-ray research, because it has been shown that there is a very close connexion between cosmic rays and the cosmic radio emissions observed at wave-lengths of 1 m. or longer. It is hoped also that a study of the weakest radio-sources

will yield valuable information about the distribution and state of matter in the most distant regions of the universe and perhaps help to answer the age-old question as to its origin.

For the new studies a very large radio telescope will be needed, far too large to be built in a completely steerable form, such as the large paraboloid being constructed by the Commonwealth Scientific and Industrial Research Organization at Parkes. The radio telescope needed for this work must have dimensions of about one mile, and the most suitable form for this is a cross-like structure invented by Dr. Mills and called a Mills cross. The cost of a radio telescope of this type and size will be about £300,000.

The Chatterton Astronomy Department, supported by the Nuclear Research Foundation, has set aside £100,000 for the first stage of this telescope. The rest of the cost to complete the instrument to its full size must be raised elsewhere by the Schools of Physics and Electrical Engineering of the University. During the next year, when the first stage of the telescope is being designed and construction commenced by Dr. Mills and his collaborators, Prof. Christiansen will be in Holland engaged in a design study for a similar instrument for a Benelux research foundation. Because of the different conditions it is probable that the details of the two instruments will be very different. This close international collaboration is typical of many astronomical projects and should be of great benefit to astronomy in both countries.

Although the design of the Sydney radio telescope has not been completed, the broad specifications are already decided (Fig. 1). It is intended to operate at two different wave-lengths, near 75 cm. and near 3 m. The shorter wave-length is the basic one, and will give the higher sensitivity and resolution; the beam-width will be less than 3 min. of arc with the planned size of 1 mile. The longer wave-length will be used to obtain spectral information, particularly of optical emission nebulæ for which observations in the neighbourhood of this wave-length are most important.

The arms of the cross will be in the form of cylindrical parabolas with 'line' feeds for the two wave-lengths at their foci. It will be possible to direct the instrument in the meridian plane, partly by mechanical and partly by electrical means, rotation of the Earth bringing all parts of the sky, within the coverage of the instrument, into view. Emphasis is being placed on rapid alteration of the setting of the radio telescope so that many selected objects can be studied in a single night's observation; at the same time a number of simultaneous records at closely spaced elevations produces the analogue of a photograph taken with an optical telescope. Because of the vast amount of data which will be produced by the instrument, the principal output will be in digital form on paper tape, and for analysis will be fed directly into *Silliac*, the electronic computer of the School of Physics.

This instrument will combine very well with the 210-ft. steerable radio telescope of the Division of Radiophysics, which is designed primarily for operation at shorter wave-lengths, down to 10 cm., including the *H*-line wave-length of 21 cm. The conjunction of these two very powerful instruments in studies of the southern skies, particularly of the central regions of the Milky Way and the closest of the external galaxies, the Clouds of Magellan, is an exciting prospect for Australian radio astronomers.

The joint effort of the Schools of Physics and Electrical Engineering in this ambitious undertaking is without parallel in the University of Sydney, or indeed in any Australian university, and may help substantially in setting a pattern for the more effective introduction of advanced research into the universities of Australia.

THE INTERNATIONAL GEOPHYSICAL YEAR

A SYMPOSIUM on the "International Geophysical Year", arranged by Section A (Mathematics and Physics) of the British Association, was held in Cardiff on September 1.

Dr. R. Stoneley opened the symposium with a reminder that the idea of international co-operation in scientific matters is by no means a modern one. Sir Graham Sutton has pointed out that in 1861 the American meteorologist Commander F. M. Maury, in an article in the *British Association Notices and Abstracts*, strongly advocated international co-operation in the scientific exploration of the Antarctic. However, the suggestion was not followed up, and it was not until 1882–83 that the First International Polar Year marked the commencement of scientific collaboration in polar research: observations were made in arctic regions of auroræ, geomagnetic and meteorological phenomena. Fifty years later, 1932–33, the Second International Polar Year included as new features the observation of weather conditions above ground-level by means of radio-balloons, and the investigation of the ionosphere by radio.

It was too much to expect scientists to wait until 1982 for another Polar Year, and in 1950, Louis V. Berkner and Sydney Chapman suggested to the Mixed Commission on the Ionosphere that the Third International Polar Year be held only 25 years after the second, with the advantage that 1957–58 would coincide with the expected sunspot maximum. This project was recommended by that Commission to the three parent Unions (Union Géodésique et Géophysique Internationale, International Astronomical Union, Union Radio Scientifique Internationale) and was approved in 1951 by the International Council of Scientific Unions, which appointed a special committee, to be known later as the Comité Spécial de l'Année Géophysique Internationale, with Prof. S. Chapman as president; the name of the project was changed to 'International Geophysical Year', embracing the whole Earth, and not merely the polar regions. The duration of the International Geophysical Year was extended to the eighteen months July 1, 1957–December 31, 1958. By the commencement of the Year the number of nations participating had grown to 67.

The scientific activity was divided among 14 'disciplines': (1) World Days and Communications; (2) Meteorology; (3) Geomagnetism; (4) Aurora and Airglow; (5) Ionosphere; (6) Solar Activity; (7) Cosmic Rays; (8) Longitudes and Latitudes;

(9) Glaciology; (10) Oceanography; (11) Rockets and Satellites; (12) Seismology; (13) Gravity Measurements; (14) Nuclear Radiation. Each of these was represented on the Comité Spécial de l'Année Géophysique Internationale by a reporter. Correspondingly, national committees were set up in the participating countries, with reporters for each discipline. In all, five conferences of the Comité were held, in addition to conferences of special groups. The general plan was that all observational data were to be collected and sent as promptly as possible to the three appropriate World Data Centres, of which the first was in Washington, D.C., the second in Moscow, and the third in centres different for various disciplines. Thus, there should be in existence a triplicate centralized record of the observations relating to each discipline: notification of each despatch of data to the Centres was sent to the co-ordinator of the International Geophysical Year (Vice-Admiral Sir Archibald Day) at Brussels. To co-ordinate more efficiently the taking of observations a calendar of World-Days was drawn up, indicating the days on which there should be a special concentration of observational work. In addition, provision was made for a world-wide distribution of warnings of special events, such as outbreaks of solar activity.

All this central organization, however economically managed, involved considerable expenditure. The earlier expenses were borne by the International Council of Scientific Unions, which by the end of the International Geophysical Year contributed some £14,000 to the project. More than double this amount, about £30,000. was paid by Unesco during the same period, during which the participating nations themselves contributed some £60,000. But this total sum of about £100,000 is small compared with the total expenditure, principally by the participants, of a sum of the estimated order of £300,000,000—a tribute indeed to the efficiency of the central organization.

The task of publishing the results of the International Geophysical Year is an onerous one. A scheme of publication of the *Annals of the International Geophysical Year* was approved by the Comité Spécial de l'Année Géophysique Internationale with the help of an advisory committee presided over by Gen. Laclavère and later by Dr. D. C. Martin, with Sir Harold Spencer Jones as general editor until May 1958, when this task was transferred to the secretariat of the International Geophysical Year. To secure co-ordination of observational work, a series of four "Instruction Manuals" was published well ahead of the Year. The complete series of the *Annals* will deal with the history and planning, as well as national programmes, lists of International Geophysical Year stations, summaries of results with their analysis, interpretation and discussion, bibliographies and catalogues of material available at World Data Centres. Evidently some procedures, such as access to data at these Centres, will need to be developed or modified according to needs and experience. Analogous problems, such as publication and storage of data, will fall to the lot of individual countries. In Great Britain, for example, the Royal Society has well in hand the publication of the Halley Bay Observations, under the editorship of Dr. D. C. Martin.

Something should be said about the continuation of the International Geophysical Year effort after the end of 1958. The manifest success of the plan led to the proposal at the fifth conference of the Comité Spécial de l'Année Géophysique Internationale at Moscow in the late summer of 1958 that the International Geophysical Year period should be extended to the end of 1959, making 2½ years in all. Not all the nations involved could assent to this scheme, since in some cases the national commitment was explicitly limited to the original 18 months. It was, however, unanimously agreed that, so far as practicable, observations should be continued throughout 1959 under the title of "International Geophysical Co-operation", with the central organization bridging the gap until a smaller special committee could take over the functions of the Comité Spécial de l'Année Géophysique Internationale. Some of the International Géophysical Year disciplines that are otherwise catered for have been dropped, and two new disciplines, aeronomy and palæogeophysics, have been included*.

The Antarctic claimed special attention. As H. Wexler pointed out, essentially for seven reasons: (1) It is a large part of our planet; (2) it contains 86 per cent of the world's glacial ice; (3) it is the most efficient cold air factory, and contains the South Pole; (4) the melting ice generates the antarctic bottom current; (5) it is the region of the aurora australis; (6) it contains the south magnetic pole; (7) it presents a stable platform for the investigation of the thermal and electrical properties of an atmosphere cut off from sunlight for many months of the year. Thus, it is not surprising that 12 nations sent expeditions to Antarctica.

During 1954 the Vahsel Bay region of the Weddell Sea was recommended by the Comité Spécial de l'Année Géophysique Internationale at a conference in Rome as a suitable place for a station on the Antarctic continent, and the Royal Society decided to send an expedition there. An advance party late in 1955 erected the base hut at Halley Bay; the main party arrived on January 4, 1957. The leader of the expedition was Col. R. A. Smart, who later was succeeded by Mr. J. MacDowall.

Taking part in the symposium held by the British Association were: Prof. W. J. G. Beynon, who was reporter for the ionosphere, both on the Comité Spécial de l'Année Géophysique Internationale and on the U.K. National Committee for the International Geophysical Year; Mr. J. MacDowall, who, as mentioned, had for part of the time the leadership of the Halley Bay Expedition, in addition to his heavy responsibilities for observations in meteorology, glaciology, seismology and geomagnetism; Dr. G. E. R. Deacon, chairman of the U.K. National Committee for Geodesy and Geophysics, and national correspondent for oceanography.

Ionospheric Observations

Ionospheric studies formed a major part of the overall programme of the International Geophysical Year, and some of the early results of these studies were described by Prof. W. J. G. Beynon of the University College of Wales, Aberystwyth. The most important type of study—vertical radio soundings—was carried out at more than 160 stations. Work on radio-wave absorption by the ionosphere was carried out at some 40 stations by the conventional ground-based method and at a further 30 stations by a method

* The writer wishes to express his indebtedness to Prof. S. Chapman's article, "The International Geophysical Year", published in Vol. 1 of the I.C.S.U. Review, January 1959.

which employs radiation from radio stars. Movements in the ionosphere formed a special investigation at a further 36 stations. This radio work on the ionosphere was supplemented by other investigations, including rocket and satellite experiments.

In siting the ground-based stations, high priority was given to the equatorial zone since earlier work had indicated that the ionosphere exhibits a number of anomalies in the locality of the magnetic equator. These investigations have confirmed that in the uppermost layer of the ionosphere (the $F2$ layer) there is a belt of low electron density centred on the magnetic equator, with maxima located some 15°–20° of latitude away on each side. At times the densities at these maxima are as much as three or four times that in the equatorial trough. Theoretical work suggests that these maxima north and south of the magnetic equator result from a movement of high-level equatorial ionization outwards along the magnetic field, and the results now available from the close network of ionospheric stations tend to confirm this suggestion.

A second equatorial problem, for which the results obtained during the International Geophysical Year have already been published, concerns the 'equatorial electro-jet'—an intense but narrow current system, postulated by magneticians to account for abnormally large magnetic variations observed at equatorial magnetic observatories and notably at Huancayo. A series of rockets launched during the International Geophysical Year by U.S. workers from a ship-borne launcher, at latitudes between 4° N. and 2½° S., show that the equatorial electro-jet is limited to a zone of only about 3–4 degrees of latitude around the magnetic equator, and that it flows in one or more current sheets of thickness about 10 km. at levels of 95–125 km. above the ground.

It has long been appreciated that disturbances in the Earth's magnetic field, and associated disturbances in high latitudes in the form of aurorse, are very probably caused by electrically charged particles entering the Earth's atmosphere from outside and being guided towards high latitudes by the terrestrial magnetic field. More than 50 years ago the Norwegian physicist Störmer made an extensive analysis of the trajectories of solar electrically charged particles as they approach the Earth, and published theoretical curves of particle precipitation in high latitudes. Investigations during the International Geophysical Year, by British workers, of two distinctive polar ionospheric phenomena (the 'radio black-out' and polar sporadic-E ionization) have shown that the incidence of these two phenomena and their variations with latitude are of the general form predicted by Störmer's 'precipitation curves'.

The incidence of streams of charged particles at high latitudes might be expected to give rise to an increase in the temperature of the upper atmosphere. Strong evidence that this is in fact the case has come from rocket soundings at Fort Churchill (latitude 59° N.) and at White Sands (latitude 33° N.). Above about 200 km. the average temperature at Churchill is some 1,200 degrees higher than at the lower-latitude station.

Geomagnetic and Seismic Observations

Mr. J. MacDowall gave an account of the Royal Society's expedition to Halley Bay. A suitable site 1¾ miles from the sea on a floating ice-shelf had been found by a ten-man advance party in January 1956, and a living hut 130-ft. long was erected. This was then the largest building in Antarctica, a record which will now undoubtedly be claimed elsewhere. With this advance party in the field during 1956 the main party in Great Britain were able to plan their preparations with a good appreciation of some of the practical problems facing the establishment of the scientific programme. One of the most serious problems was the mutual electrical interference; fortunately this did not greatly affect the carrying out of seismic and geomagnetic observations. The main problem was perhaps the situation of the observatory on what is now called the Brunt Ice-Shelf, which was about 50 km. long and 140 m. thick, floating in about 190 m. of sea water; the relative dimensions can be represented by a board of wood ½ in. thick and 10 ft. long overlying ¼ in. of water.

Such a situation was not considered ideal for seismic and geomagnetic recorders, which are ordinarily built on a firm subsoil-rock if possible. The advance party, the Building Research Station and the Scott Polar Research Institute contributed to the eventual solution of the problem of the geomagnetic instrument foundations, which were formed by driving 13 wooden telegraph-poles 20 ft. into the compacted snow of the ice-shelf; these reduced differential movement and formed a satisfactory vibration-free foundation. Snow accumulated on the flat upper surface of the ice-shelf at the average rate of 3 ft. per year (density 0·36 gm. cm.$^{-3}$); it afterwards became compacted and spread out, with the result that the ice-front, or coast-line, moved outwards, taking the Base with it at about 400 m./year. At the same time the Base rotated by about 0·5° a year, so that regular astronomical observations were needed in order to find the true orientation of the recording magnets.

The seismic recorders were tried in several situations, and were eventually installed at the bottom of a 30-ft. pit, the floor of which was sufficiently firm, and free from local vibration due to the nearby Base: at that depth the compacted snow has the consistency of soft sandstone. In this site the arrivals of longitudinal waves originating in any part of the world were well recorded; secondary phases and shear waves, however, were not well recorded, even from nearby earthquakes in the South Shetland Islands about 1,200 km. away. In seismological work, the first arrivals are undoubtedly the most important and to this extent the seismological readings were quite satisfactory.

On the question of the continuation of observations at Halley Bay, Mr. MacDowall considered that on the observational side the issue is clear cut, as much is now known that was unknown in 1956. In view of the unique situation of the Base it would be highly desirable to bring the Base up to the ideal geomagnetic observatory standard by making quick-run recordings and measurements of space gradients; tests should be made of other and better types of seismic instruments.

Oceanography

Dr. G. E. R. Deacon remarked that the main idea of the International Geophysical Year was to co-operate in work that needs world-wide networks of observations. Oceanographers exploited the idea by studying changes in mean sea-level, long waves

propagated across the oceans, and the general circulation of the oceans.

Mean sea-level, he said, is not the unalterable datum often implied in everyday usage; at the very first meeting of the British Association, indeed, Sir John Lubbock emphasized the importance of studying the effect of barometric changes on the height of the tide. Sir James Clark Ross in the 1840's found that the ocean behaved like a vast water-barometer; variations of temperature and density of course have to be taken into account.

From data compiled by the International Association of Physical Oceanography it was shown by Patullo, Munk, Revelle and Strong that the sea-level is usually lower in spring than in autumn, the range varying from a few cm. at island stations in low latitudes to 165 cm. in the Bay of Bengal. Near the British Isles the mean sea-level is 15–20 cm. higher in autumn than in spring; most of this can be accounted for by differences of temperature and pressure, but part may be due to the storage of water on the land during the winter months. Some of the fluctuations from year to year are attributable to changes in climate, but the actual rise and fall of the land seems to play a part in it. Variations of mean sea-level become of practical importance in coastal defence against inundation.

Another matter of practical importance arises when a seismic surge or tsunami (popularly called a 'tidal wave') travels across an ocean from the seat of a submarine earthquake in the form of waves which cause considerable damage and loss of life when they impinge on the sea shore. Since the wave-length is in practice many times the depth of the ocean, the waves travel with speeds $(gh)^{\frac{1}{2}}$, corresponding to the usual theory of long waves in shallow water, where g is the acceleration due to gravity and h is the depth of the water. Thus, the ordinary speed of travel is 400–550 miles per hour. On April 1, 1946, for example, a submarine earthquake near the Aleutian Is. gave rise to waves which reached Hawaii 4½ hr. later, causing great loss of life and much damage. At Valparaiso these waves were still 5 ft. high, and in the Antarctic were large enough to wash away an old hut left by the British Graham Land Expedition. Since that disaster a warning system, based on the recordings of earthquakes, has been instituted in the Pacific; during the International Geophysical Year long-wave recorders were installed on many oceanic islands as well as on continental margins, and their records have added much to the knowledge and development of the subject.

After 150 years of ocean exploration there are sufficient observations of temperature and salinity at all depths to give a general idea of the large-scale movements of oceanic waters. Dr. Deacon gave as an example the deep current starting between Greenland and Labrador, where cold water with a fairly high content of salt sinks and spreads southwards at depths of 2,000–3,000 metres. The flow is continued, with a reinforcement of water of high salinity from the Mediterranean, as far south as 50° S., where it rises and forms a stratum between a large wedge of Antarctic bottom water and a shallow layer of Antarctic surface water. This current has been traced round the Cape of Good Hope into the Indian Ocean and south of Australia into the Pacific Ocean. These bodies of water, though moving slowly, transport large quantities of heat and considerably affect the mechanics and productivity of the oceans. During the International Geophysical Year a notable advance was made in the direct determination of the velocity of flow by using a simple form of float devised by Dr. J. C. Swallow. This could be arranged to float at a predetermined depth and give out sound signals by means of a simple circuit and a magneto-striction oscillator. The results have been surprising: for example, a southward counter-current below the Gulf Stream was observed to flow at 1/3 knot, water at a depth of 2½ miles north-east of Bermuda moved northward for several days at nearly 1 knot, while U.S. scientists have found an equatorial subsurface current in the Pacific flowing at 2½ knots.

In all, Dr. Deacon considered the oceanographic work carried out during the International Geophysical Year to be an undoubted success. It brought to light more problems than it solved, and has led to other co-operative schemes.

Conclusions

Summing up the symposium, Dr. Stoneley remarked that while some of the discoveries have been spectacular, such as the van Allen belts, only the lapse of time will permit an adequate appraisal of all the results of the International Geophysical Year. The geophysical conclusions will gradually fall into their place in this rapidly developing science, but, as with the explosion of Krakatoa in 1883, some of the observations will undoubtedly be of value in lines of research as yet quite unforeseen. Many of the benefits are already clear, even if it is premature to assess their relative importance. However, Dr. Stoneley mentioned in particular the following:

(*a*) Support has been forthcoming for large-scale and expensive projects which, without the stimulus of the International Geophysical Year, would not have been undertaken. This is particularly true of Antarctic expeditions.

(*b*) There has been a great stimulus to research in geophysics. In seismology, for example, it has resulted in the setting-up of a number of new stations, of re-equipping and modernizing some of the older ones, and in planning new large-scale lines of research. Likewise, a new magnetic survey of the Earth has been planned.

(*c*) The general public has become much more aware of the background and the development of geophysics. Radio and television broadcasts have been extremely effective.

(*d*) The interrelationship of different disciplines has been emphasized. For example, the determination of the inertial constants of the Earth from observations of artificial satellites, linking up with the gravitational field of the Earth and its internal constitution; the world-wide programme of micro-seismic observations, linking oceanography, meteorology and seismology.

(*e*) The closer association of scientists, whether of the same or of different nationalities, by correspondence, interchange of publications and personal discussion.

Finally, Dr. Stoneley raised the question of the next International Geophysical Year. His own view was that the rapid advances in geophysics would call for another such project sooner than 1985. However, such occasions of international co-operation while stimulating are expensive. It is also conceivable that an overdose of stimulants may not be in the best interests of geophysics.

R. STONELEY

EFFECT OF NOISE AND VIBRATION ON MAN

THE prefix, bio-, attached to the names of various disciplines among the physical sciences, is becoming increasingly familiar to workers outside the biological field as the specialties in applied biology increase and multiply. One of the sessions in Section G (Engineering) of the recent British Association Cardiff meeting was entitled "Bio-mechanics" and was devoted to two topics in the field of what the Americans are now calling 'bio-acoustics'. Prof. E. J. Richards, of the Department of Aeronautics and Astronautics, University of Southampton, spoke on "Noise Annoyance and its Assessment", and Flight-Lieut. J. C. Guignard, Royal Air Force Institute of Aviation Medicine, delivered a paper on "Some Effects of Low-Frequency Vibration on Man" under the co-authorship of himself and Mr. A. Irving, who holds a research fellowship at the same Institute. Both papers dealt specifically with aircraft noise and vibration.

Prof. Richards began by emphasizing that the primary function of the human ear is communication, and he defined 'noise' as everything which is heard and which hinders communication. He allowed a fairly wide definition of communication and illustrated with several amusing examples how the labelling of a given sound pattern as 'noise' (that is, 'annoying') depends very largely on circumstances and will vary greatly from one individual or community to another. The annoyance caused by jet aircraft noise is, he said, virtually impossible to establish in scientific units and can only be assessed by the reactions of the population in areas irradiated by the noise. He described the establishment of empirical limits of acceptable noise around airports, based on the incidence of complaints by individuals and organized groups living nearby, and cited American surveys of aircraft noise and public reaction to it during operation of piston-engined aircraft from Idlewild Airport, New York (before the introduction of jet traffic). These surveys were used to establish a figure of 107 decibels as the maximum tolerable overall noise-level, measured at ground-level in the open air.

However, Prof. Richards continued, when jet aeroplanes began to fly overhead producing 107 decibels of noise on the ground, it was soon obvious that this figure was no longer acceptable—owing to the different quality of the noise from jet engines. Prof. Richards then digressed to explain the decibel scale of sound pressure measurement—related to the logarithmic response of the human ear to mean square sound pressure—and went on to stress the fact that the disturbance produced by noise depends very much on the frequency distribution of the sound. This is partly due to the non-linear frequency-response of the human ear, and, in practice, it is found that noises of high pitch are considerably more annoying than equally intense noises of relatively low pitch. Prof. Richards showed the meeting curves of equal subjective loudness, together with curves of equal 'noisiness' (annoyance) for pure tones, obtained by American workers in laboratory studies, and he pointed out that the latter curves were, in effect, weighted against the higher frequencies.

The reason for the greater annoyance produced by the jet aircraft (at a given overall sound pressure-level) lies in its emitting a higher proportion of its total noise at high frequencies. For example, jet aircraft noise spectra show the highest levels in the frequency-band 600–2,400 c./sec., as against the band 75–300 c./sec. for the propeller aircraft. Prof. Richards described the concept of the 'perceived noise-level' (quoted in *PN* decibels) and its derivation using the subjective 'equal noisiness' data to transform physical sound pressure measurements. The determination of perceived noise-level allows comparisons between noises of differing spectral quality. A criterion of acceptability can therefore be established for jet noise, based on information regarding other types of noise from industrial sources and piston-engined aircraft. It turns out that the acceptable 107 decibels for propeller aircraft at Idlewild is equivalent to 111 *PN* decibels, which is now the standard accepted by the American authorities and to which jet aircraft must conform in populated areas around that aerodrome.

Prof. Richards then described the probable need for revision and modification of currently accepted *PN*-levels as jet operations became more extensive and the characteristics of jet aircraft and their flight envelopes altered. Present methods of minimizing jet noise include the fitting of noise suppressors and the practice of throttling back the engines when passing over built-up areas during the climb. This of course lengthens the climb and, while reducing the intensity of the local noise nuisance, spreads it over a wider area. Prof. Richards recalled that the current standards of acceptable noise were based on reactions to the worst quartile of propeller aircraft operating over a fairly narrow zone, and that jets would cause a more widespread disturbance. (At the present time, however, the worst annoyance is caused by jet airliners frequently breaking the rules for noise reduction on take-off.)

It is anticipated that the number of jet aeroplane movements at London Airport will increase some eight-fold over the next decade or so, involving not only a very high frequency of take-off during the day but also the introduction of more night operations. Prof. Richards considered some of the implications of these trends for the 111 *PN* decibels-limit. It has been found that, when the incidence of complaints from the surrounding population is related to the number of take-offs at different times of day, proportionally more annoyance is caused by noise during the evening hours of wireless and television entertainment and bed-going. It has been suggested, therefore, that a 10 *PN* decibels reduction in allowable noise must be specified for night operations. It will also be necessary to consider the duration and frequency of occurrence of aircraft noises, and some further reduction in the day-time standard may become obligatory as jet traffic grows heavier.

It appears that quite a high proportion of complaints arise from the landing of jet airliners rather than their taking-off and that in many cases (80 per cent in one survey) people who expressed annoyance revealed, directly or indirectly, some element of fear of aircraft crashes. The pattern of noise on landing is different from that on take-off and is probably more alarming, since the aircraft passes lower over the house-tops, the onset of noise is sharper and the sound spectrum often contains discrete

frequency spikes due to compressor whine. A typical jet aircraft throttled back for landing might show a spike of some 15 *PN* decibels amplitude superimposed on the random noise spectrum at about 2,000 c./sec. It is found that noise containing discrete frequency spikes is more disturbing and would require a lower *PN* decibel figure as the maximum acceptable. The 'annoyance penalty' in the example cited would be of the order of 6 *PN* decibels; but Prof. Richards recommended caution in interpreting such figures, since the estimates of penalty due to discrete frequencies are based on laboratory experiments using 'white' noise, whereas the practical *PN* decibel limit is based on studies of propeller aircraft noise which is itself made up of discrete frequency sounds.

Prof. Richards amplified some of the above points in replying to questions asked in discussion, during which a number of speakers expressed alarm at the prospect of the worsening noise nuisance brought about by jet operations. He agreed that what is urgently needed are extensive and well-controlled social surveys of the noise problem. Speaking on the threat of sonic bangs produced by supersonic transport aircraft, Prof. Richards said that, during a typical supersonic flight, free air pressure jumps of the order of 1 lb./sq. ft. must occur over the majority of the flight path. The nuisance value of such bangs was not at all certain but may be great, affecting large populations if supersonic airliners were to fly overland as well as oversea routes. The problem, again, was one of annoyance and its assessment. Individual reactions to impulsive noise were likely to be very variable. The approach was to determine experimentally the limiting tolerable amplitudes of pressure jump, using realistic samples of people in rather the same way that thresholds of annoyance by continuous noise can be determined in the laboratory and in the field. Prof. Richards felt that, while the aeronautical engineer and the acoustician can do much to minimize aircraft noise at source and in transmission, there is still an urgent need for human data which must be provided by the experimental psychologist and the social scientist.

Aircraft noise disturbs a large population outside the aircraft, whereas mechanical vibration as an environmental factor concerns only the people inside it. Published work on the physiological actions of vibration is accordingly much smaller in quantity, less well known, and of less general interest than that on noise and hearing. The paper by Flight-Lieut. J. C. Guignard and Mr. A. Irving described current research at the Royal Air Force Institute of Aviation Medicine, Farnborough, on the effects of very low-frequency vibrations on man. This is, in the first instance, a problem of military aviation. Aircrew can be violently jostled in high-speed flight through turbulence and, again, disturbing intensities of more or less periodic vibration can occur in some types of aircraft—notably helicopters. In civil aviation, it has been predicted that vibration will be a potential nuisance to the passengers and crew in supersonic airliners. These aircraft may have natural modes of oscillation at very low frequencies, easily excited by gusts and being poorly damped at the great altitudes at which supersonic flight is to be made.

After reviewing briefly the biological actions of mechanical vibration (which are in many cases fairly narrowly frequency-dependent), the authors went on to explain the approach they have adopted in their present field. Although in-flight studies of reactions to turbulence and experiments using dynamic flight simulation have their attractions, the authors favoured the study of human frequency-response to simple sinusoidal vibration. Some reasons were given for this approach, including ease of interpretation and generality of application of the results. The frequency band selected for study was the infra-sonic region (that is, below about 20 c./sec.) in which are excited major aircraft structural modes of vibration, as well as physical resonances in the human body. The lower limit of the band studied was 2 c./sec.

A method of conducting resonance search tests on the human body was described in some detail. One feature which had not been adopted in previous work was careful standardization and control of the subjects' posture (as well as other conditions of vibration) during the tests. Acceleration resonance was measured in seated men at forcing frequencies of approximately 2·4, 4·8 (the dominant response) and 13 c./sec., the latter being detected only as a phase resonance between seat and head. So far, the results showed fair agreement with those of other workers, but the investigation was taken a step further by examining the influence of some physical variables in the conditions of vibration on the resonant response of the body. The influence on resonance of body size, force of vibration (that is, acceleration-amplitude) and muscular tensing were examined and it was found that, while the effects of the first two named were small, tensing modified considerably the man's dynamic response. The tensing manœuvre, in effect, increased both the damping and the stiffness of the body, reducing the dynamic amplification at resonance and increasing the dominant resonant frequency to nearly 6 c./sec.

The paper ended with an account of a simple experiment of more direct practical interest concerning the degradation of visual and visuo-motor performance by whole-body vibration. Performance was measured in four subjects doing two simple tasks during vertical sinusoidal vibration applied through the seat, the test material remaining at rest. The measure of performance used was the time taken to complete a number of replicates of each task. Five frequencies of vibration were applied, in half-octave increments from 2·4 to 9·5 c./sec. at a constant acceleration-amplitude of 0·25*g*. The presentation of conditions was randomized and performance during vibration was compared with that at rest. Vibration hindered the subjects, and the worst performance in each task was measured at 3·4 c./sec. (which is a rather lower frequency than that of the dominant physical resonance in the body). The authors concluded—very tentatively—that the degradation of visual performance in this experiment was related to the velocity-amplitude of vibration at the subject's head. It was incidentally pointed out that breaking down of fixation of a static target by the eyes during whole-body vibration occurs at about 2 c./sec.

Flight-Lieut. Guignard agreed with comments made in discussion to the effect that vertical vibration was only one component of the acceleration pattern of an aircraft in flight, and also stated that different patterns of resonance could be elicited in the body by, for example, transverse excitation. Most work has been done on vertical vibrators as a matter of custom and convenience, and because the vertical components of low-frequency aircraft vibration were considered to be particularly important.

J. C. GUIGNARD

OBITUARIES

Prof. E. M. Killick

PROF. ESTHER MARGARET KILLICK died on May 31. Her sudden death ended an active and productive professional life, during which she made significant contributions to physiological knowledge, participated widely in academic administration, and was held in high esteem by students and colleagues alike.

Esther Killick came of a medical family, and after her education at Leeds Girls' High School, proceeded to the University of Leeds. Having obtained her medical qualifications, she began her professional career as an investigator to the Safety in Mines Research Board. During this appointment she demonstrated her clinical ability by obtaining the membership of the Royal College of Physicians at the first attempt, without having previously held a house appointment. During her association with the Mines Research Board she came into contact with J. S. Haldane and his work, and her interest in respiratory problems persisted up to the time of her death, when she was still actively engaged in research in respiratory physiology. This interest had a basis in the feeling that her best contribution to medicine would be in the study of the etiology of human respiratory disease, especially in mining and other industries.

Following the work in Leeds, she was appointed lecturer in industrial medicine and hygiene in the University of Birmingham in 1935. Three years later she was appointed lecturer in applied physiology in the London School of Hygiene and Tropical Medicine, and at the same time married Prof. A. St. G. Huggett, professor of physiology at St. Mary's Hospital Medical School. She had two daughters, born in 1940 and 1945. After spending four years at the London School of Hygiene, on the retirement of Prof. Winifred Cullis from the Sophia Jex-Blake chair of physiology in the Royal Free Hospital School of Medicine, she was appointed to this professorship. She thus came to control a department in a school which has a notable record of pioneering educational achievements, and which has, in the past, fostered the cause of education in the sciences for women, when other schools maintained an attitude of indifference, or even of open hostility.

Prof. Killick entered into the problems of her professional appointment with great energy and evolved a well-balanced and highly efficient department, at the same time actively pursuing her own research interests and entering very fully into administrative work. In the course of these activities she contributed, over a long period, research work of high quality, particularly on the effects of carbon monoxide on man and animals. This particular aspect of respiratory physiology and pathology became more and more her special interest in medicine. She was the first to show that the mouse and man acclimatize to carbon monoxide differently, and that the latter does so by the pulmonary epithelium developing the power of actively inhibiting the passage of carbon monoxide from the lungs into the blood, thereby allowing more oxygen to be taken up than would occur if both gases entered by diffusion. This active intervention by the epithelium of the lung explained in an unexpected way the phenomenon which Haldane some years previously had attributed to active secretion of oxygen into the blood. In fact, as Esther Killick showed, Haldane was right in attributing an active role to the pulmonary epithelium, but it was not active transport of oxygen. Her special knowledge in this field was sought widely, both in Great Britain and in the United States, particularly by the U.S. Air Force. She served on various committees concerned with this aspect of physiology, both during and after the War, with the Royal Navy and the Medical Research Council.

In 1953 she worked as a visiting professor in the Department of Medicine at Johns Hopkins Medical School with Dr. R. L. Riley and Dr. Joseph Lilienthal.

She took an active and exceedingly useful part in the administrative work of the University of London. In this she showed exceptional powers of quick and logical thought, and the ability to eliminate the irrelevant and the redundant. She was, in consequence, a most effective chairman, and occupied this position on the Board of Studies in Physiology, and the Board of Pre-Clinical Studies. She was a member of the Board of the Faculty of Medicine, and her advice and opinion were particularly valued on the Senate Committee on Colleges Overseas in Special Relation. Perhaps her work on the latter was her most outstanding contribution to the University, since she participated in the establishment of the Preclinical Departments in the Colleges of Ibadan and the West Indies, and on various occasions served as examiner or visiting representative of the University of London. She also served on the Committee of the Central Research Funds of the University and on the Special Advisory Board on Biophysics.

These various activities illustrate her energetic participation over the whole field of academic work, but they cannot convey the outstanding characteristic of Esther Killick. This was the possession of a quiet manner and a kindly and pleasant disposition which accompanied a keen and quick intelligence and a character of exceptional resolution and determination. These characteristics were discernible in all she did and, in addition, those of her colleagues who have participated in university examinations with her will always remember her quiet approach to the candidates, the kindly appreciation of their problems, and the scrupulous accuracy of assessment of their work.

Esther Killick was guided by certain principles, and one of these was the belief that women, just as well as men, could contribute to society and to a profession by reason of their intrinsic worth; and that they could pursue an active career and simultaneously bring up a family. In both of these she achieved success.

In her work she upheld the traditions of the Royal Free Hospital School of Medicine, the School which appointed in the person of her predecessor the first woman professor of physiology in the University of London. Over the period of nearly twenty years during which Esther Killick worked at the Royal Free, she was held in esteem and affection by her students, her staff and by a wide circle of colleagues.

W. BURNS

Mr. L. J. Goldsworthy

LEONARD JAMES GOLDSWORTHY was head boy of Ripon Grammar School (1910) and won an Exhibition to Magdalen College, Oxford. Here he became a pupil of T. S. Moore and after graduation (1913) carried out research under the supervision of W. H. Perkin, jun. He took part in College laboratory teaching at Christ Church and Queen's College.

At the early age of twenty-four he became professor of chemistry at the Victoria College of Science, Nagpur, but his scientific work and teaching naturally suffered in the early years of the First World War because of his keen attention to military duties. During 1917–20 he saw active service in Egypt and Palestine as an officer of the Deccan Horse, 16th Cavalry, and held several administrative posts. In later years he continued military activities and during 1933–35 was commanding officer of the 6 (Burma) Batt., U.T.C. Still later he served in the Second World War in the Home Guard in Oxford.

During 1917–22 Goldsworthy held various posts as inspector of schools and deputy or assistant director of public instruction, but in 1923 returned to chemical teaching and research as lecturer at University College, Rangoon; he became officiating professor of chemistry in 1931, retiring in 1935.

While in Burma, Goldsworthy held many official advisory posts and, as was ever his wont, did all that was possible to promote the welfare of his students. He was a warden of one of the university halls of residence and a member of the governing bodies of several university colleges in Burma.

After leaving Rangoon he returned to Oxford and undertook research on intermediates in contemplated synthesis of penicillin and other topics related to natural products, as well as more general fields such as the Leuchs synthesis of polypeptides, orientation of substitutions in benzene derivatives and certain molecular re-arrangements of interest in relation to the chemistry of quinamine. Some of this work was unfinished. In 1937 he found that the Leuchs reaction applied to *d*- or *l*-alanine gave a polypeptide similar to that from glycine, very sparingly soluble and of high molecular weight. But *dl*-alanine under the same conditions gave a water-soluble product of a quite different type. The analyses of ester end-groups indicated a low molecular weight, but it was felt that this required confirmation and other interests supervened.

Later he received a University appointment as senior research assistant to the Waynflete Professor. In this capacity his long experience in the East was turned to very good account, and with characteristic unselfishness and generosity he gave invaluable personal help to many beginners in research and to others who encountered special difficulties. Goldsworthy's own technique at the bench was very neat and his practical example most effective. To overseas students in particular he was not only guide and philosopher, but also friend. Many of them enjoyed his hospitality and that of his wife.

After 1955, one of his major interests was the development of gas-liquid chromatography and, though he retired in 1958, he continued to assist the teaching work at the Dyson Perrins Laboratory and delivered lectures in the academic year 1959–60.

He was a man of great personal charm, a most sincere scientist and a devoted teacher. In 1927, he married Rose Cawthorn and there are two sons.

ROBERT ROBINSON

NEWS and VIEWS

Royal Society: Medal Awards

THE following awards of medals have been made by the President and the Council of the Royal Society: *Copley Medal* to Sir Harold Jeffreys, formerly Plumian professor of astronomy in the University of Cambridge, for his distinguished work in many branches of geophysics, and also in the theory of probability and astronomy; *Rumford Medal* to Dr. A. G. Gaydon, Warren Research Fellow, for his distinguished work in the field of molecular spectroscopy and particularly its application to the study of flame phenomena; *Davy Medal* to Prof. J. M. Robertson, Gardiner professor of chemistry and administrative head of the Chemical Laboratories in the University of Glasgow, for his distinguished pioneering work on analysis of crystal structure, especially of organic compounds; *Darwin Medal* to Mr. E. J. H. Corner, reader in plant taxonomy in the University of Cambridge, for his distinguished and strikingly original botanical work in tropical forests; *Hughes Medal* to Dr. J. L. Pawsey, assistant chief of the Division of Radiophysics of the Commonwealth Scientific and Industrial Research Organization, Australia, for his distinguished contributions to radio astronomy both in the study of solar and of cosmic radio emission.

National Institute of Sciences of India: Awards

AT the annual general meeting of the National Institute of Sciences of India held on October 7, the following awards were announced: *Shanti Swarup Bhatnagar Gold Medal* 1959 (for applied sciences), to Dr. Atma Ram, director of the Central Glass and Ceramic Research Institute, Calcutta, for his outstanding contributions to the development of technology and creating a science consciousness in the glass and ceramics industry in the country; *Chandra Kala Hora Memorial Medal* 1960 (for contributions to the development of fisheries in India), to Sri Hiralal Chaudhuri, research officer (fish breeding), Central Inland Fisheries Research Station, Barrackpore, for his contributions towards induced breeding in carp.

Mining at Leeds: Prof. J. T. Whetton, O.B.E.

PROF. J. T. WHETTON, who has recently retired from the chair of mining in the University of Leeds, has had a distinguished academic and military career. After gaining early mining experience in the Yorkshire coalfield he served in the First World War in France and the U.S.S.R.; in 1919 he was awarded the Military Cross and the Russian Order of St. Stanislav. He resumed his mining studies at the University of

Leeds and after graduation was appointed research assistant in the Department of Mining at King's College, University of Durham, where he remained on the academic staff until 1939, becoming lecturer and then reader. During this period he was awarded the degree of M.Sc. by the Universities of Leeds and of Durham. During 1937–48 he commanded the 4th Survey Regiment, R.A.T.A., and was on active service during 1939–45 in the Balkans, the Middle East, North Africa and north-west Europe. He received the Distinguished Service Order, the Order of the British Empire, the Belgian Order of the Crown with Palm and the Belgian Croix de Guerre. Since his appointment in 1945 to the chair, the Department at Leeds has expanded steadily both in undergraduate numbers and research activities. Under his direction work in several fields, but particularly in geophysics, coal preparation, ground movement and pneumatic and hydraulic flow, has been carried out and he has contributed to nearly a hundred papers in these and other mining subjects. He was chairman of convocation for three years and was pro-vice-chancellor of the University of Leeds during 1955–57. He has been chairman of the Committee of Mining Professors of Great Britain for some years, and is at present president of the Midland Institute of Mining Engineers.

Prof. H. J. King

DR. H. J. KING, who is to succeed Prof. Whetton, had several years experience in mining and mine surveying in the South Wales coalfield before 1936 when he was awarded the David Davies Mining Scholarship and other scholarships for studies at the Treforest School of Mines and University College, Cardiff. Before he completed the course he joined H. M. Forces as a Territorial and served with the Royal Artillery and then with the Royal Engineers, specializing in tunnelling, at home and in north-west Europe. For a time before demobilization in 1945 he was staff captain at 21 Army Group with special responsibilities for establishing educational facilities for troops in preparation for their return to civilian life. On demobilization he returned to complete the mining course at Cardiff and in 1946 was awarded the joint diploma of the University College, Cardiff, and the Treforest School of Mines; in the same year he obtained the degree of B.Sc. (Eng.), London, as an external candidate and was awarded first-class honours. He was lecturer in mining in Whitwood Technical College for a year and was then appointed lecturer in mining and surveying at the University of Leeds, becoming senior lecturer in 1956, in which year he obtained the degree of Ph.D. of the University of London. In 1960 he was appointed reader in mining at Leeds. Prof. King is well known for his special interest in mine surveying and particularly for his research work in the laboratory and in the field on ground movement and mining subsidence, in which he has achieved a world-wide reputation.

C.S.I.R.O. Division of Entomology: Mr. F. N. Ratcliffe, O.B.E.

ON January 1, 1961, Mr. F. N. Ratcliffe will relinquish his position as officer-in-charge of the Commonwealth Scientific and Industrial Research Organization Wildlife Survey Section to become assistant chief of the Division of Entomology in Canberra. He will be mainly concerned with the ecological and biological control investigations that comprise a substantial part of the Division's activities. Mr. Ratcliffe was a member of the Division of Entomology during 1937–49, working first on termites and later on stored wheat pests. Between 1941 and 1946 he served with the Australian Army Medical Corps, and was actively associated with the work of the Malaria Control Units in northern Australia and New Guinea, and with investigations on mosquito control techniques. On returning to the Division after the War, until the establishment of the Wildlife Survey Section, of which he was the first officer-in-charge, Mr. Ratcliffe acted as assistant to the chief, Dr. A. J. Nicholson, who was succeeded on his retirement this year by Dr. D. F. Waterhouse.

United Kingdom Atomic Energy Authority: Appointments

SENIOR appointments in the Development and Engineering Group have been announced by the United Kingdom Atomic Energy Authority. Mr. P. T. Fletcher will be deputy managing director (General Management); Mr. R. V. Moore, formerly director of reactor design, will be deputy managing director (Projects); and Dr. H. Kronberger, formerly director of research and development, will be deputy managing director (Development). Mr. S. Fawcett, formerly deputy director, has succeeded Mr. Moore as director of reactor design. The Research and Development Directorate at Risley has been divided into two executive directorates. Dr. H. K. Hardy and Mr. F. W. Fenning have been appointed respectively as director of fuel element development and director of reactor technology.

Solid State Physics at Harwell

THE newly formed Solid State Physics Division at the Atomic Energy Research Establishment at Harwell, under Dr. W. M. Lomer (see *Nature*, 188, 21; 1960), is to be organized into four research groups. One group, under Dr. G. E. Bacon, will be concerned with neutron crystallography, for magnetic and structural investigations and studies in crystal chemistry. Another group, under Dr. R. D. Lowde, will use a variety of techniques, such as time-of-flight measurement and the scattering of cold neutrons, to investigate the dynamics of crystals and of spin systems. Magnetic investigations with polarized neutrons and work on various physical properties employing radioactive tracers, resonance and other techniques will form the work of a third group under Mr. A. D. Le Claire. Later a further group will be added to investigate defects in crystals. There will be opportunity for university participation in the programme.

British Shipbuilding and Research

A STATEMENT regarding the replacement of the *Queen Mary* was made on November 3 by the Minister of Transport, Mr. E. Marples, in the House of Commons and by the Paymaster-General, Lord Mills, in the House of Lords. The size, speed, accommodation and physical characteristics of the new ship will be as recommended by the Chandos Committee, and the Government also agrees with the Committee's advice that the capital cost should not exceed £30 million: up to that figure the Government and the Cunard Line will contribute in the proportion of 3 to 2, any excess being met by the Cunard Line. The ship will be owned by a separate subsidiary company of Cunard with provision to ensure that the ship and company

remain under British control. The Chandos Committee proposed that the Government's 25-year loan should carry 4·5 per cent interest, but the Government has decided that interest on the loan should be at the rate for 25-year loans which is being charged by the Public Works Loan Board when the agreement is signed. At the present interest rate of 6·25 per cent, and assuming a total cost of £30 million, the grant would amount to some £3·25 million and the loan to £14·75 million. The statement met with some criticism in both Houses. In the House of Commons, Mr. Marples maintained that the Government was not putting up much risk capital, and that according to estimates of travel for the next ten years, by the end of ten years the taxpayer would be very well covered.

Lord Alexander of Hillsborough again asked for access to the report of the Chandos Committee and Lord Mills referred to an agreement to keep confidential the mass of technical and financial information contained in the report. Lord Lucas of Chilworth, however, while agreeing that there might perhaps be good technical reasons for not producing the report, suggested that the economic survey of the prospects of trans-Atlantic travel which enabled the Chandos Committee to formulate some of its proposals could be made available, and Lord Mills undertook to look into this possibility. The proposal is to be discussed further in both Houses, but dissatisfaction with the Government decision has already been expressed on the grounds that the decision appears to have been undertaken independently of the inquiry by the Council for Scientific and Industrial Research into the shipbuilding industry, and that the report on that inquiry is also being kept secret. Incidentally, when speaking at the launching of the 9,000-ton *Clan Fergusson* on November 3, Mr. A. Cayzer, deputy chairman of the British and Commonwealth Shipping Company, suggested more research by British shipbuilders is necessary, and for that purpose smaller firms might need to amalgamate. A few large substantial companies could carry out research more easily and efficiently than a number of small units, and this applied particularly to the engine-makers.

Children's Interests in Science

To find out children's interests so that the content of a science syllabus could be devised, 141 boys and 142 girls aged eleven in St. Helens were asked to write down a list of questions in science which would interest them and which they would like to know more about. The director of education, N. F. Newbury, has summarized and analysed their replies in the summer edition of *Teaching Science*. Grouped under general headings, the topics dealt with most frequently were natural phenomena (1,186); the human body (753); how things work (718); animals other than humans (393); and in more specialized fields, floating (130); chemistry (130); light (85); inventors (48); magnetism (43). The questions occurring most frequently were of the type "How does an aeroplane fly ?"(100), and "What is electricity and how is it made ?"; while questions such as "Why do people die ?" (27), and "What is gravity ?" (29), were at the other end of the scale. There was only a limited interest on questions on space: 29 questions on rockets, 10 on satellites and flying saucers and 9 on space. Some questions quoted without comment were "How far up does gravity reach ? A candle wants air, so why does it go out when you blow it ? Why does heat make things expand ?" By their replies the children show clearly that, at this stage, they have little enthusiasm for orthodox Nature study, but are mainly concerned with themselves and their surroundings. At this age they tend also to ask similar questions.

Historic Books on Mining and Kindred Subjects

A COLLECTION of rare and historic books owned by Mr. Robert Annan is being exhibited during November 15–December 31 at the Science Museum, South Kensington. These books deal with mining, assaying and metallurgy, mining law and mineralogy. Although mining has a long history, written records are extremely scanty, and it was not until the early and mid-sixteenth century when the works of Agricola and others were published that technical records of mining and ancillary practices became generally available. In medieval times the German miner was pre-eminent, his methods of working the ore deposits and the later treatment of the ore being much superior to those employed elsewhere. It is not surprising, therefore, that many of the rare books in the exhibition are of German origin. Books published in other countries are also to be shown: of particular interest is Gabriel Plattes' "Discovery of Subterraneall Treasure" of 1639, which, although having little technical merit, was the first work devoted entirely to mining to be printed in English. The oldest work on exhibition is "De Mineralibus" by Albertus Magnus (written about 1260) in the version printed at Padua about 1476 and later at Venice in 1495.

The Perkin Centenary Trust: Awards

THE Perkin Centenary Trust was established to commemorate William Henry Perkin's discovery of 'Mauveine' in 1856 and to promote technical education in all aspects of the manufacture and application of colouring matters. The Trustees offer the following awards for the academic year 1961–62: (1) *The Perkin Centenary Fellowship*, for one or two years for the purpose of higher study of any subject approved by the Trustees. Its value is £750 per annum with an additional grant of up to £100 per annum towards certain designated expenses, and is tenable, from October 1961, at any university, technical college or other institution approved by the Trustees. (2) *Two Perkin Centenary Scholarships*, each for two years, renewable at the discretion of the Trustees for one further year, to enable candidates employed in an industrial firm or other institution concerned with the manufacture or the application of colouring matters to receive an education at a university or technical college. Each award will have a value of £350 per annum. There is no means test, and a successful candidate is not debarred from receiving the whole or a part of his normal salary from his employers during his tenure of the scholarship. (3) *Perkin Centenary Trust Travel Grants*. Applications are invited from teachers concerned with the study of any aspect of the manufacture or the application of colouring matters at a university, technical college, or other institution. Preference will be given to applications from lecturers, senior lecturers and readers, or the equivalent grades in other institutions, wishing to gain experience at a similar institution or in industry overseas. Grants will be available towards the cost of travel and maintenance for periods, related to the purpose of

the visit, of from one to three months. Further information can be obtained from the Secretary, The Perkin Centenary Trust, c/o The Chemical Society, Burlington House, London, W.1. Applications for the awards must be made by May 1, 1961.

University News :

Birmingham

THE following have been appointed lecturers: Dr. P. Swinbank, C. P. Van Zyl and Dr. J. D. Dowell (physics); Dr. F. J. Emery (mathematical physics); Dr. T. S. M. Maclean and Dr. E. F. Stack-Forsyth (electrical engineering); K. Foster (mechanical engineering); Dr. G. W. Rowe (industrial metallurgy); Dr. G. M. Bennison (geology); Dr. D. A. Wilkins (botany); Dr. J. M. Webber (chemistry). The appointments to fellowships are as follows: B. W. Petley (physics); H. R. Shaylor (Staff Fellow in nuclear physics); T. W. Preist and T. F. Tuan (mathematical physics); B. Cockayne and Dr. N. Pessall (physical metallurgy); D. J. White (engineering production); D. G. Parsons (S. C. Johnson Research Fellow in the Department of Chemistry). The above appointments took effect on, or before, October 1.

Edinburgh

THE following appointments to lectureships have been announced: B. I. Davies (bacteriology); Dr. P. C. Jocelyn (senior lecturer in biochemistry); Dr. L. G. Plaskett (biochemistry); M. Jacobson (physiology); Dr. A. L. Bartlet (veterinary pharmacology).

Hull

RECENT appointments to lectureships included: Dr. D. W. G. Ballentyne (physics); Dr. J. Friend (botany); S. C. Kapoor (philosophy). Research fellowships have been given to Dr. P. Bruck (chemistry) and Dr. A. Richmond (chemistry).

Leeds

AMONG the recent appointments to lectureships are the following: Mr. P. Kelly (metallurgy), Mr. C. Mack (textile engineering) and Mr. J. R. Proud (agriculture). Dr. D. F. Horler has been appointed as Research Fellow in the Department of Leather Industries and Dr. W. E. Seeds in the Department of Biomolecular Structure. The titles of emeritus professor have been conferred on Prof. P. J. Moir, on his retirement from the chair of surgery, Prof. E. A. Spaul, on his retirement from the chair of zoology, and Prof. J. T. Whetton, on his retirement from the chair of mining.

London

DR. B. J. MASON, Warren Research Fellow of the Royal Society, has been appointed to the University chair of cloud physics tenable at the Imperial College of Science and Technology from October 1, 1961. Dr. S. Cohen, of the National Institute for Medical Research, has been appointed to the University readership in immunology tenable at St. Mary's Hospital Medical School.

Dr. D. R. Laurence, senior lecturer at University College and University College Hospital Medical School, has been appointed to the readership in pharmacology and therapeutics tenable at the College and School; the title of reader in tropical hygiene in the University of London has been conferred on Dr. B. B. Waddy in respect of his post at the London School of Hygiene and Tropical Medicine.

Announcements

THE Keith Prize for the period 1957–59 of the Royal Society of Edinburgh has been awarded to Dr. J. B. Tait, Department of Agriculture and Fisheries for Scotland Marine Laboratory, Aberdeen, for his paper entitled "Recent Investigations in the Faroe–Shetland Channel", published in the *Proceedings* of the Society during the period of the award and for his work in the general field of oceanography.

SIR RICHARD RAMAGE has been appointed Commissioner to examine the present arrangements for localization in the East African Posts and Telecommunications Administration and certain other services of the East Africa High Commission, and to make arrangements for accelerating the process. In particular, he is to consider an extension of the 'in-service training scheme' and qualifications at present required in all grades in which posts are held by expatriate officers.

DR. FRED LESTER, head of the Department of Science at Hatfield Technical College, has been appointed principal of the College of Further Education, Loughborough, and will take up his duties on January 1. Dr. R. F. Robbins, formerly of Nottingham Technical College, and at present senior lecturer in organic chemistry at Hatfield, has been appointed head of the Department of Science as from January 1, 1961.

BESIDES a list of members, with an alphabetical index, and a list of members elected on May 11, the Records of the American Academy of Arts and Sciences, 1959–60, includes lists of officers and committees for 1960–61, the statutes, records of meetings, 1959–60, and the reports presented at the annual meeting on May 11, 1960 (Pp. 128. Boston, Mass.: American Academy of Arts and Sciences, 1960).

THE Institute of Physics and the Physical Society is organizing a conference on "Physics of Polymers" at the University of Bristol during January 10–12. Further information can be obtained from the Secretary, Institute of Physics and Physical Society, 47 Belgrave Square, London, S.W.1.

THE Department of Chemistry, Purdue University, in co-operation with the Office of Naval Research, is organizing a symposium on "Nitro Aliphatic Chemistry", to be held at Lafayette, Indiana, during May 25–26, 1961. Emphasis will be placed on polynitro aliphatic compounds. Those wishing to contribute papers should send abstracts to Prof. Henry Feuer, Department of Chemistry, Purdue University, Lafayette, Indiana, from whom further information can be obtained. Abstracts must be received not later than February 1.

A SYMPOSIUM on "Plant Resources of the Middle East and South Asia for the Pharmaceutical Industry and Rauwolfia", organized jointly by the Government of Pakistan, the Unesco Middle East Science Co-operation Office and the Unesco South Asia Science Co-operation Office, will be held at the North Regional Laboratories of the Pakistan Council of Scientific and Industrial Research, Peshawar (Pakistan), during December 6–14. Further information can be obtained from the Unesco South Asia Science Co-operation Office, 21 Curzon Road, New Delhi, or the Indian National Commission for Unesco, Ministry of Education, Government of India, New Delhi.

THE INSTITUTE OF BIOLOGY

THE tenth anniversary of the foundation of the Institute of Biology was celebrated by a dinner held in the restaurant of the Zoological Society of London on January 8, 1960.

It may be recalled that the first general meeting of the Institute was held at King's College, London, on January 5, 1950, when more than 150 biologists were present, representing most branches of the subject. This meeting, however, was only a culmination of more than three years activity (see *Nature*, 168, 131; 1951). A council of fourteen members was elected, with Dr. E. Hindle as president, Prof. J. F. Danielli as honorary secretary, and Dr. R. J. C. Harris as honorary treasurer. Rules of membership were drawn up, and an office was established in the British Medical Association House, Tavistock Square, with a general secretary and staff. The membership reached about 500 by the end of the year and has steadily increased so that by the end of 1959 it numbered 2,250, with 260 overseas members.

Each year the Institute has held a symposium on some subject of general biological interest and published the papers and discussions. The first symposium in 1950 was on "Biological Hazards of Atomic Energy", and the topic for 1960 was "Biology of Space Travel". Freezing and drying, biology of deserts, biology of the sea, numbers of man and animals, biological aspects of the transmission of disease, the biology of ageing, the biological productivity of Britain, the effects of pollution on living material, and problems arising from the control of pests and diseases indicate the wide range of topics which have been discussed at successive meetings; and the records of these symposia are of considerable value to students in these respective fields.

The Institute's widening activities necessitated larger premises, and in 1955 a move was made to the present quarters at 41 Queen's Gate, London, S.W.7. At the same time, nine local branches have been founded: six in Britain, one in Northern Ireland, another in Eire, and one in Malaya. These local branches hold meetings independently of the central organization.

The Institute represents the views of biologists on various national and local bodies concerned with technical education, and played an active part in promoting the scheme for endorsed certificates, which is now firmly established with courses in some dozen centres. The Ministry of Education has now joined the Institute in endorsing certificates; and the Scottish Education Department, with the co-operation of the Institute of Biology, has instituted a National Certificate in Biology.

The Institute publishes a quarterly journal containing news of general interest to biologists, as well as articles on broad topics and book reviews. One of its publications, "Biology as a Career", is now in its third edition; in addition, advice on this subject is given to student members, parents, youth advisory officers and teachers. Also two surveys on salaries were undertaken, during 1953 and 1956.

The Institute maintains an appointments register for the use of members seeking advice on potential employers and vacancies, a service of especial value to overseas members. It also publishes a list of full-time consultants on biological subjects, including a list of topics for which the services of occasional consultants can be obtained. The Institute also maintains an information service for the use of members, Government departments, firms and the general public, and is consulted on a wide range of biological subjects.

On various occasions the Council of the Institute has made representations of their views to various Ministers of State on matters affecting the development of biological research. Through the medium of the Parliamentary and Scientific Committee, assistance is given to keep members of Parliament informed of the biological background to such problems as food supplies, ageing, Colonial research, pollution, etc.

The officers of the Institute have been selected with the object of obtaining as wide a representation as possible of the various branches of the subject. The office of president, restricted to two years duration, has been held successively by Dr. E. Hindle, Prof. F. E. Fritsch, Sir James Gray, Prof. W. H. Pearsall and Dr. A. S. Parkes. The honorary secretaries have been Prof. J. F. Danielli, Dr. G. E. Fogg and Mr. H. J. Bunker; and honorary treasurers, Dr. R. J. C. Harris, Dr. N. E. Hickin and Mr. W. V. Harris. The general secretary, Mr. D. J. B. Copp, has served the Institute since 1951, having previously been assistant-secretary of the British Association.

NUCLEAR SCIENCE IN THE MIDDLE EAST

IT might be thought a bold experiment to hold a nuclear science conference in an area which is only just beginning to make progress in this field; nevertheless, the symposium held in Hamadan during July 6–18 was an undoubted success.

The symposium was organized by the CENTO (Central Treaty Organization) Institute of Nuclear Science in Tehran (see *Nature*, 186, 513; 1960), and all ten of its scientific staff took part. The total number of participants was about sixty, as follows:

France	1
Iran	more than 30*
Pakistan	8*
Turkey	2
United Kingdom	12*
United States	2
United Nations observers	2

* Including CENTO Institute staff.

The French and United Nations participants were experts on various missions in Iran. Delegates' expenses were met from CENTO funds, from the

funds of the Governments concerned, and from other sources.

The symposium was opened by Dr. T. Ziai (Under-Secretary, Ministry of Industries and Mines) on behalf of the Iranian Government, and by the Governor of Hamadan. Thereafter there were nineteen working sessions, including four general discussions, on a wide range of nuclear science topics. The proceedings were informal, and no record was kept; this no doubt contributed to the freedom and liveliness of discussion.

Perhaps the most valuable feature of the symposium was its impact on the nuclear science policies of the CENTO countries. To this end, many of the papers took the form of surveys in which the authors assessed what lines of work might be profitable in their particular field, and what they might involve in facilities and training. For example, Dr. D. I. Page, of the CENTO Institute, considered the application of isotopes to water-flow problems, with special reference to conditions in Turkey. He listed ten problems which had been proposed by the Hydraulics Research Laboratories in Ankara. Of these, four appeared impracticable for such reasons as the large amount of radioactivity involved; two others appeared of doubtful feasibility; and four others, estimation of suspended matter in flood water, detection of seepage points in irrigation channels, movement of underground water, and analysis of cement by radioactivation, were worth pursuing.

Another paper providing useful guidance to countries considering new programmes was that on mutation-breeding in agriculture, by Dr. H. J. Curtis of the Brookhaven National Laboratory. He emphasized the necessity of growing very large numbers of plants in such work; the fact that the variations produced by radiation can also be produced by more conventional means; the need for a lengthy programme of orthodox plant-breeding before a commercially valuable variety can be derived from a radiation-produced mutant; and the meagre results to date in terms of new commercial varieties. Nevertheless, the fundamental aspects of the work fully justify continued effort.

Further papers in the same category were those on prospecting for radioactive minerals, on running a fall-out laboratory, on the use of carbon-14 in biochemistry, and on establishing a medical radioisotope clinic. There were also general discussions on the potentialities of radioisotope applications in the CENTO region, on their applications in the oil industry, and on atomic energy and public health.

Iran, as the host country, naturally sent the strongest delegation to the symposium, and this gave an opportunity for direct discussion of her nuclear science programme. Prof. A. A. Azad, who is in charge of the Tehran University Nuclear Centre, gave a general account of the programme, which includes a 5-MW. swimming-pool type reactor to be operating in 1962; and Dr. A. A. Sheibani described the Iranian radioactive prospecting project. The discussion which followed ranged over such fundamental issues as the possible uses of a large research reactor, and the value to the region of some of the larger nuclear instruments. The interest aroused was such that both the Pakistani and Turkish delegations expressed a desire for similar international discussions in their own countries.

Other topics at the symposium included reactor instrumentation, waste disposal and recent applications of radioisotopes in medicine, besides various research reports on nuclear physics and on applications of radioisotopes in botany and entomology.

The choice of Hamadan, a quiet, historic town, as the venue of the symposium, rather than Tehran, was something of a novelty to the Iranians, but was much appreciated by all the delegates on account of the relaxed atmosphere and opportunities for informal contacts that it provided. The local authorities contributed to this by their welcome and by their generosity in providing a meeting place, excursions and other amenities. As a final charming gift they gave each delegate a framed picture of a scientist of former days, Avicenna, whose home town was Hamadan.

H. A. C. McKay

CONVECTION IN METEOROLOGY

THE subject of "Convection" was chosen as the topic of the symposium for the first day of the Royal Meteorological Society's summer meeting held in the Electrical Engineering Department, Queen's College, Dundee, on June 30. This was the first meeting of the Society ever to be held in Dundee, and was to be followed on the next day by a symposium on "Agricultural Meteorology" (see *Nature*, 187, 995; 1960). The president of the Society, Dr. J. M. Stagg, took the chair.

The opening speaker was Dr. F. H. Ludlam of the Imperial College of Science and Technology who reviewed the subject of convection in the atmosphere. This is a phenomenon which ranges in scale from the currents associated with fair-weather cumulus to those in the large thunderstorms which result in extensive flooding. Whereas the dynamics of the smaller currents are broadly understood as circulations associated with rising bubbles or columns of warm air, the dynamics of thunderstorms, or for that matter, the precise physical processes involved, are not so well understood. The Bénard convection cell pattern, for which a theory exists, does not seem to occur frequently in the atmosphere, although recent photographic evidence from an American weather research rocket shows a regular pattern of 'groups' of cumulus. The most satisfactory method of forecasting the extent of cumulus development still seems to be that based on the old 'parcel' theory, where the air is assumed to form into bubbles or 'parcels', which break away from the surface and rise adiabatically through the environment until a layer sufficiently stable to prevent further penetration is reached. This method entirely neglects any modification of the environment, such as subsidence warming, and leads to little real understanding of the dynamics of the process.

The difference between a large cumulus extending to, say, 15,000 ft., and a cumulonimbus, with its associated characteristics of hail and lightning, seems

to be more than an enlargement of scale of the same process. A completely new physical factor seems to be involved resulting in up-currents which may be as large as 80 m.p.h. and horizontal currents of up to 60 m.p.h. Radar observations made by workers from the Imperial College of Science and Technology and the Meteorological Office have shown air to move into the base of such a storm at 60 m.p.h., and maintain this speed while passing vertically up through the storm, flowing horizontally out of the top at a height of 7 or 8 miles. The kinetic energy of such a system extending over a horizontal region of about 20 square miles is 100–1,000 times that of a typical large cumulus producing a moderate rain shower. The exceptional rate of growth to a thunderstorm of this size from the typical large cumulus usually occurs after rain has started falling. A physical feature of these thunderstorms which indicates the great energy of the up-draught is the exceptional size of hailstorms produced, which may be as large as golf balls. The latent heat of fusion released during their growth may be an additional source of energy, acting as a kind of booster to convection originated by surface heating.

Many of the vigorous thunderstorms affecting southern England have their origins over northern France and are propagated, rather than simply carried, in the upper-wind system. A strong-wind shear is always associated with these storms and they exhibit a well-defined anvil of cirrus cloud.

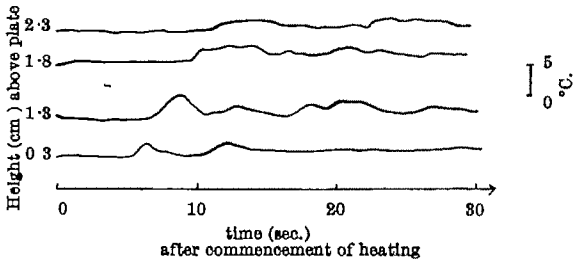

Fig. 1. Temperature fluctuations observed above a heat source in water. Rate of heating of plate = 40 W.

Dr. Ludlam was followed by Mr. C. Dixon of Queen's College, Dundee, who described an experiment he had performed on the initiation of convection currents in water. A semi-circular copper plate 5 cm. in diameter with an embedded electrical heating element was placed on the bottom of a tank of water with the straight edge adjacent to the 'Perspex' front of the tank. Thermocouples were set on to this face at intervals of $\frac{1}{2}$ cm. above the heater and temperature variations at these levels recorded on a Cambridge 6-channel oscillograph. A tracing of a typical recording is shown in Fig. 1. A period of about 10 sec. (depending on the rate of heating) elapsed before any temperature fluctuation was observed, and then an initial pulse travelled past the thermocouples in succession, followed by further pulses at fairly regular intervals of 2–3 sec. On switching the heater off, the pulses died away after a few seconds. It is hoped eventually to photograph tracers to determine the velocity distribution in these currents and associate this with the temperature variations.

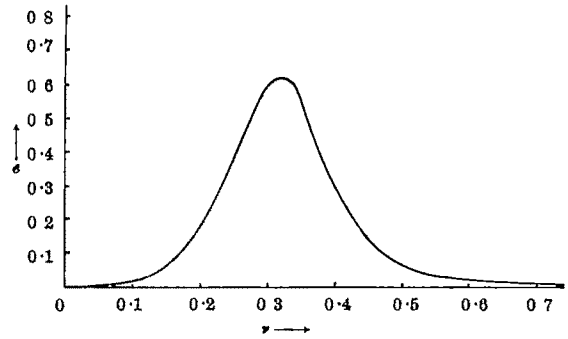

Fig. 2. Absorption of energy by gravity waves at an inversion.

$$\epsilon = E/r^4 g \Delta\rho, \quad \nu^2 = \frac{1}{2\pi^2} \cdot \frac{gr\Delta\rho}{w\rho}$$

E = energy absorbed by waves, ρ = density of lower laye, $\Delta\rho$ = density deficit of the upper layer, r = radius of bubble, w = velocity of rise

The third contributor to the symposium was Mr. F. W. G. Warren of the University of Sheffield, who explained a mathematical theory he had developed to determine what proportion of the kinetic energy of ascent of a thermal bubble or column was used in the production of gravity waves at an interface when the bubble or column penetrated a more stable layer. His results showed that such wave production was a maximum when the temperature of the rising column was about midway between those of the upper and lower layers near the interface, that is, such that the bubble was buoyant with respect to the lower layer, but not with respect to the upper. The dependence of the gravity wave-energy on the velocity of the bubble and its size is shown in Fig. 2.

The closing speaker was Dr. R. P. Pearce of Queen's College, Dundee, who explained a theory he had worked out for the development of sea-breezes and which also, with only slight modification, applied to the development of convection currents. The fundamental problem in both these cases is to solve the equations of heating and motion to give the velocity and temperature distributions at any time resulting from a given rate of heat-input. In the case of the sea-breeze this means predicting the time of onset of an onshore wind, and its strength, at any point inland from the coast, given the rate of heating well inland. In the convection problem it means being able to calculate the rates of growth of currents of various sizes from

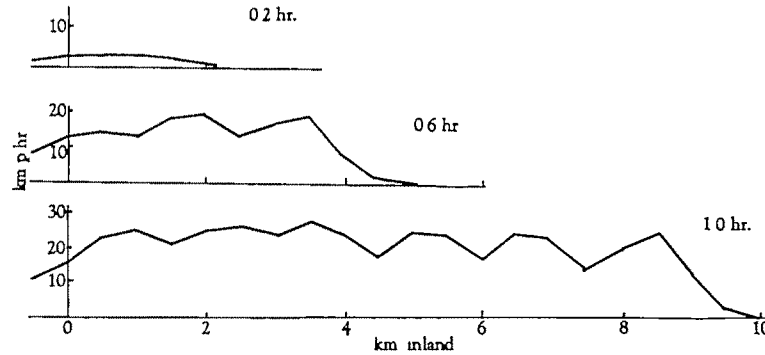

Fig. 3. Sea-breeze development. Surface velocity in km. per hr. Rate of heating 3° C. per hr. beyond 2 km. inland, decreasing towards the coast. Atmosphere initially static and isothermal

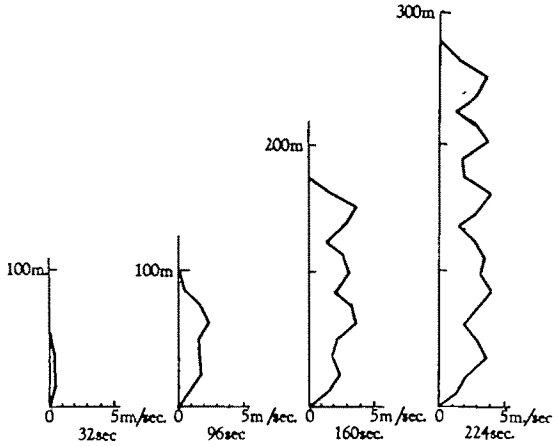

Fig. 4. Development of a thermal. Velocity in m. per sec. Atmosphere assumed initially static with dry adiabatic lapse-rate. Rate of heating approximately 1° C. per 3 min. up to 25 m., 1° C. per 6 min. at 37·5 m. and zero above 50 m.

the known rate of heating that produces them. In both problems the velocity and temperature distributions can be taken as two-dimensional, assuming no variations parallel to a long straight coastline in the case of the sea-breeze, and symmetry about a vertical axis in the case of a convection current. Nevertheless, the mathematical problem is still very complex, involving frequent integrations of Poisson's equation in two dimensions, a time-consuming process even for an electronic computer. A further simplification was therefore made assuming the form of the vertical distributions of velocity and temperature for the sea-breeze, and the radial distributions for the convection current. These assumptions are not unreasonable when the vorticity distribution is elongated, in this case horizontally for the sea-breeze and vertically for the convection current. The result, after introducing boundary conditions and integrating the equations to include the assumed distributions, is to eliminate one of the space variables, leading to a single partial differential equation to be solved for the surface (or axial) velocity u as a function of distance from the coast (or ground) x and the time t. This equation is of the form:

$$\frac{\partial^2 u}{\partial t^2} + a\frac{\partial^2(u^2)}{\partial x \partial t} + b\frac{\partial^2(u^2)}{\partial x^2} = F(x,t)$$

Here a and b are numerical constants with values depending on the assumed profiles of velocity and temperature. $F(x,t)$ is the horizontal *gradient* of the heating-rate in the case of the sea-breeze and can be taken as zero everywhere except near the coast. In the case of the convection current, it is the actual heating rate, and this can be taken as zero everywhere except near the ground. The equation is non-linear since no linearizing assumptions are made in the analysis. Some results of the numerical integration, using the Deuce computer at the University of Glasgow, are shown in Figs. 3 and 4.

The initial development of the sea-breeze near the coast and its subsequent penetration inland are features of the result illustrated by Fig. 3, and the analogous generation of the convection current at the surface and its penetration upwards is illustrated in Fig. 4. In both cases the onset at a point away from the origin is fairly sudden and 'frontal' in nature. Another interesting feature is the series of pulses behind the initial one. There is observational evidence for this occurring after the onset of a sea-breeze, and Mr. Dixon's observations described earlier show this property for a convection current in water. These fluctuations may, however, have been introduced into the computation as a result of truncation errors in the finite-difference approximations used in the integration of the equation. Further computations with different heating-rates show that smaller currents develop more rapidly than larger ones, as one observes on a typical convection day when the larger clouds usually develop during the late morning or afternoon.

The symposium ended with a general discussion. Dr. Ludlam's dynamical picture of a thunderstorm was discussed at some length and it became obvious that here was a useful field of study for the dynamical meteorologist, for no mathematical theory which can account for even the broadest features of these storms at present exists.

R. P. PEARCE

SAFETY OF FACTORY WORKERS

THE annual report of the Chief Inspector of Factories for 1959 reports a further decline in the number of fatal accidents, from 665 in 1958 to 598 in 1959, the lowest figures recorded this century*. While this figure continues the consistent downward trend in fatalities from the 828 in 1951, the downward trend in total accidents of the previous three years was checked, and the number of reported accidents rose from 167,697 in 1958 to 174,071, in spite of increased activities in the field of accident prevention, although it may be partly explained by the increase in the number of people employed and hours worked. The Chief Inspector, however, finds the increase in the number of accidents to young persons disturbing, and one of two chapters in the report dealing with subjects of interest without being necessarily restricted to the events of the year deals with the prevention of accidents to young persons. This has been discussed in *Nature* of November 5, p. 460; the other special chapter deals with designing machinery for safe operation. Besides directing attention to some of the more important safety principles, which, it is suggested, machine manufacturers should bear in mind, it urges that every opportunity should be taken to bring such considerations before the professional, research and teaching authorities concerned, and that industry as the user should insist on getting premises, plant and equipment with safety 'built in' by the suppliers.

As a result of a considerable number of changes made in the analysis and classification of information

* Ministry of Labour and National Service. Annual Report of the Chief Inspector of Factories for the year 1959. Pp. 128. (Cmnd. 1107.) (London: H.M. Stationery Office.) 7s. net.

about reported accidents, it should be possible to make greater use of the information already provided in the accident reports, and in addition to tables analysing accidents by industry, causation and process, there is included for the first time a table giving accident incidence rates for most of the industries under the manufacturing headings of the Standard Industrial Classification, as revised in 1958. In a number of industries, research associations and other bodies have continued to examine important problems of health and safety, such as dust and fumes and dangerous machinery, and the Chief Inspector believes that other industries could, with advantage, make wider use of their research associations in helping to solve their own special problems in this field. During the year, thirteen inspectors were appointed to the general inspectorate and at the end of the year eight more were awaiting appointment. Twelve inspectors were recruited to the specialist branches, and at the end of the year 409 inspectors of all grades were in posts, but there were twenty-four vacancies in the general inspectorate, one each in the Medical and the Electrical, and seven in the Chemical Branches.

At the end of 1959 there were 222,117 registered factories in Britain, compared with 223,085 in 1958, the decrease being almost entirely in the number of factories without mechanical power. An analysis in March showed that about one quarter of the factory population work in factories employing more than 1,000 people, but only four factories in every thousand are of this size, and on the other hand two-thirds of the number of factories employ fewer than ten people, but less than a thirtieth of the factory population. More than 26 per cent of reported accidents occurred in 'handling goods', 15·1 per cent were caused by falls of persons, and falls of all sorts accounted for 91 fatal accidents in factories, or 26 per cent of all fatalities. A chapter in the report reviewing the year mentions a number of industrial developments which have promoted greater safety in industry.

PHYTOGEOGRAPHY OF THE AUSTRALIAN REGION

DR. NANCY T. BURBIDGE has recently published a comprehensive account and analysis of the principal floristic regions of the vast Australian area, and of selected areas within it of special interest*; she has discussed the composition of the flora in relation to geological and geographical factors, and in a map of considerable interest she has indicated the probable paths of migration, chiefly by way of Sumatra, the Philippines and New Guinea, but including movements within the region, that have contributed to the contemporary phanerogamic vegetation. The phytogeographical region is regarded as including Australia and Tasmania, and can be divided into the tropical zone in the north and east, the temperate zone in the south and east, and the 'Eremæan' zone in the arid centre. While the demarcation of these zones is closely related to contemporary climatic conditions, the respective floras also show the results of selection by former climatic and geographical conditions.

Dr. Burbidge reports that although the flora of the South-West Province shows the highest proportion of endemism, there is a close relationship with the flora of the eastern part of the temperate zone. The Province, in fact, is not "the 'cradle' of the autochthonous elements of the Australian flora though it is apparently an asylum for many relict forms".

At the generic level the Tasmanian flora is not highly endemic, but it shows certain affinities with the flora of Malaysia and with genera found along the Malaysia–New Zealand arc or genera also occurring in South America. Some of the genera are unknown on the mainland, others are known from Australian Tertiary deposits. It appears that the Tasmanian flora includes relics from early Tertiary floras, survivors from the cold-climate regimes of the Pleistocene, and Australian elements which have mingled with the flora during periods of land continuity.

The high rainfall habitats of north-east Queensland are remarkable for the large number of families, genera, and species which are restricted to them, that is, within the Australian region. Thus, many genera have only a single representative which may also occur in Malaysia. Dr. Burbidge considers that some of these may be recent arrivals while others, known as fossils from southern deposits, have a more restricted distribution than in the past. While the close affinity with the flora of New Guinea is noted, Dr. Burbidge points out that there are certain affinities with the floras of New Caledonia and New Zealand which may be independent of those of other parts of the Australian region.

The composition of the Australian flora is primarily attributable to climatic selection within the region and from the biotypes which have become available as a result of migration—migration by communities rather than by chance dispersal of individuals being regarded as a major factor.

The study of Tertiary floras, though not extensive, indicates an affinity with the flora of South America which is "contrasted with the marked lack of data suggesting a similarly increased relationship with southern Africa. The relationship between fossil and modern representatives of such genera as *Podocarpus*, *Dacrydium*, and *Nothofagus* suggests that there has been a northward migration or a withdrawal to warmer latitudes since the Tertiary. All the main elements of the present-day flora are represented in the Tertiary assemblages. If current views on the 'Malaysian' or 'tropical' nature of some affinities and the 'Antarctic' nature of others be accepted then there is no indication that the major migration into the Australian Region came from one particular direction".

* *Australian J. Bot.*, 8, 75 (1960).

Also comprised in the Australian flora are temperate species with northern hemisphere affinities. Some of these occur in temperate communities in both hemispheres, but others are endemic to, and characteristic of, the 'Eremæan' zone. It is thought that the flora of this zone may have originated from a coastal sand dune and littoral type; and it is suggested that it developed from elements that migrated to the Australian region as early as the Cretaceous when there may have been a coastal continuity with the Tethys Sea. A further suggestion is that these plants remained in coastal habitats but moved inland, possibly along southern estuarine coasts, and became isolated under arid conditions during the Pleistocene or Recent times.

From Dr. Burbidge's analysis, it appears that eastern Australia "has been a very important migration route for a very long period, being linked with the northern hemisphere through Malaysia". The northward migration of Australian species has apparently been less successful than the southward migration of Malaysian ones, the ecological barrier afforded by dense tropical communities having inhibited the northward movement of the light-requiring Australian types: "The significance of such a barrier would be dependent on the climatic conditions during periods of land continuity between Australia and Malaysia and between Australia and New Guinea".

The view that Australia and New Zealand are constituent parts of a biogeographic region is regarded by Dr. Burbidge as unacceptable, unless such a region includes a portion of the island arc in the north-east.

THE WATER NET, *HYDRODICTYON*

THE water net, *Hydrodictyon reticulatum*, occurs only sporadically in Britain, but thanks to its ready growth in culture, the remarkable structure and unusual asexual reproduction of this rare alga have become familiar to many generations of students. Certain details of the life-history were hitherto obscure, however, and even less was known of other species of the genus. Our knowledge of the only three well-defined species, all occurring in South Africa, has now been greatly extended by the recent publication by Dr. M. A. Pocock (*J. South African Bot.*, 27, 167; 1960) of the results of detailed investigations which were in progress for a period of some twenty-five years. In addition to repeated examinations of materials collected in the field, extensive use was made of culture methods, the adoption of agar-plate cultures making it possible to follow the fate of individual cells and cœnocytes.

In all three species of *Hydrodictyon* the basic structure is a network of cœnocytes, each with many nuclei and conspicuous pyrenoids; but whereas in *H. reticulatum* (L.) Lagerheim the mature net is an elongated hollow cylinder, in the other two species (*H. africanum* Yamanouchi and *H. patenaeforme* Pocock) the cœnocytes form a flat typically one-layered plate. In *H. reticulatum* and *H. patenaeforme* the cœnocytes remain cylindrical, while in *H. africanum* they become spherical and dissociate, the individual cœnocytes developing independently for a considerable time.

In addition to these differences in the mature net, the three species differ in the details of their life-histories. It has long been known that in the asexual reproduction of *H. reticulatum* the protoplast of each cœnocyte divides into a large number of uninucleate zooids, which without being liberated rearrange themselves and unite to form a new net in the parent cœnocyte. There have been several differences of opinion as to certain details of this process, but the investigations of Dr. Pocock have clarified many points. In particular, it was found that at one stage in the process the zooids move freely among one another, all protoplasmic connexions between them having disappeared. Although the zooids are confined between the outer protoplasmic membrane and the vacuolar membrane, forming a single peripheral layer, they do not adhere to either membrane. The vacuolar membrane persists throughout net formation, finally disappearing when the young net is liberated by the rupture of the outer wall. There is no asexual reproduction of this type in the other species of *Hydrodictyon*, where daughter nets are never produced within mature cœnocytes.

In *H. patenaeforme* and *H. africanum* the mature cœnocytes produce swarmers which are always liberated into the water. The swarmers of *H. patenaeforme* may either behave as gametes, fusing in pairs to form first a planozygote which finally becomes a hypnospore, or may act as asexual spores producing hypnospores without previous fusion. As in the earlier known sexual process of *H. reticulatum*, the gametes are isogamous. In *H. africanum* the gametes are anisogamous and there is still some doubt as to whether they can act as asexual spores. The asexual production of hypnospores is found only occasionally in *H. reticulatum*.

The hypnospores of all species, whether sexually produced (zygospores) or asexually (azygospores), may enter a prolonged resting phase or may germinate at once following a period of growth. In *H. reticulatum* and *H. patenaeforme* the hypnospores on germination produce comparatively large zoospores, one from azygospores, typically four or eight from zygospores. After a period of motility, each zoospore settles down and gives rise to a polyhedron stage. Following a period of growth the polyhedron in turn divides to form zooids, which unite to produce the germ net. In *H. africanum*, although polyhedra are occasionally formed, the zoospore and polyhedral stages are usually cut out of the life-cycle. In this species the germ net is produced directly on germination of the hypnospore.

From the details of the life-history and from what is known of the cytology of *H. reticulatum*, it seems clear that in all three species the net is haploid, with the zygospore as the only diploid phase in the life-history, reduction division occurring on germination of the zygospore. The polyhedron is an interpolated vegetative phase, peculiar to the family Hydrodictyaceae.

A. ALLSOPP

ROLE OF THE GRAIN COAT IN WHEAT GRAIN DEVELOPMENT

By A. H. G. C. RIJVEN and C. A. BANBURY

Division of Plant Industry, Commonwealth Scientific and Industrial Research Organization, Canberra

THE mature grain of wheat has a thin coat consisting of several layers of dead and obliterated cells, and these layers are singularly low in content of various enzymes[1,2]. During the early development of the grain, however, such layers seem to be endowed with specific metabolic functions.

The first indication of this possibility arose from an attempt to correlate the ontogenetic pattern of glutamyl transferase content with the synthesis of gliadin in the developing wheat grain. A correlation was expected on the grounds that gliadin is particularly rich in glutamine[3] and that glutamyl transferase is believed to be identical with glutamine synthetase[4], and therefore responsible for glutamine synthesis. Moreover, it was considered possible that the transferase mediates the incorporation of glutamyl residues into the peptide chain of gliadin, which seems to contain *iso*glutamine[5]. However, when the determinations were carried out in 1958, with the variety Insignia, a rather different picture emerged (Fig. 1). The enzyme showed an early rise of activity, which began to fall 12 days after anthesis, that is, at a time when gliadin had scarcely begun to be produced. The peak of activity was not an artefact due to gradual accumulation of inhibitors or interfering enzymes. This was concluded from assays performed on deep-frozen material in which low activities of late harvests and high activities of early harvests appeared additive when the extracts were brought together.

In the 1959 season, closely similar observations were made on a different wheat variety, Festival, that is, a peak of activity of glutamyl transferase was found at 12 days after anthesis.

At this stage of the work it was realized that the different parts of the developing grain show a complex histogenetic pattern. Nutman[7] had directed attention to some of these phenomena and their possible physiological significance in rye. On macroscopic inspection, the most striking feature is the early growth of the grain coat, followed by its gradual decline and obliteration (Fig. 2); the endosperm shows a continuous growth in weight and volume. The peak in glutamyl transferase activity therefore seems to reflect changes in the coat rather than in the endosperm. This consideration led to investigations of the localization of the enzyme.

The complex composition and ontogeny of the outer layers of the wheat grain have been dealt with by Kudelka[8] and Percival[9]. It comprises the pericarp, integuments and nucellus. Lacking any precise term, the term 'grain coat' has been adopted here for the whole structure. During the earlier stages of development this can be easily separated from the endosperm. Also, from about 8 days after anthesis, the outer pericarp can be separated from the rest of the grain coat.

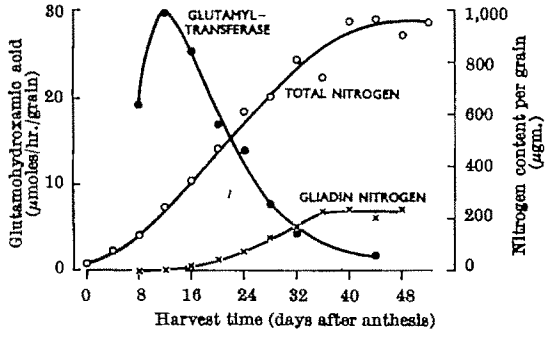

Fig. 1 Wheat, variety Insignia. Time-course of glutamyl transferase activity, and of total- and gliadin-nitrogen content on a grain basis.

From the ears of a particular harvest day the first grain out of a spikelet from the centre of the ear was used. The grains were ground in a cold mortar and three times extracted with water. After centrifugation at 500*g* the accumulated supernatants (1 grain per ml.) were used for the enzyme assay, in which the formation of glutamohydroxamic acid is measured under conditions similar to Stumpf *et al.*[6], the residue was extracted three times with 70 per cent ethanol, and gliadin was precipitated by adding 5 volumes of a mixture of 2 parts ethanol, 1 part ether and 0.01 per cent lithium chloride

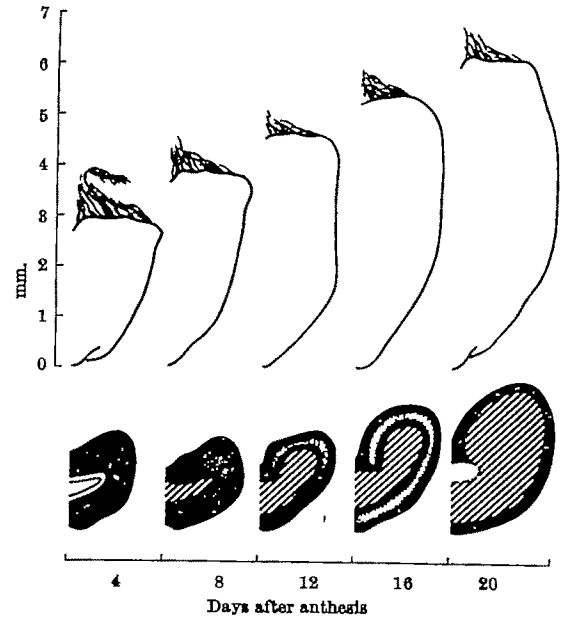

Fig. 2. Wheat, variety Festival. Right halves of abaxial and trans-sectional views of fixed grains harvested at 4-day intervals from anthesis. The blackened parts belong to the 'grain coat'; the gap (stippled) between outer pericarp and 'rest' of the grain coat, present from about 8 days after anthesis, is closed again at day 20. The endosperm (hatched) is at first only an acellular bag (see day 4)

Table 1. DISTRIBUTION OF SOME ENZYMES IN THE DEVELOPING GRAIN OF WHEAT

	Glutamyl transferase		Phosphatase		Leucine activating enzyme	
	$\Delta O.D.$ 540 mμ	%	$\Delta O.D.$ 400 mμ	%	Δ% exchange	%
Outer pericarp	0·303	60	0·149	50	nil	nil
Rest of coat	0·201	40	0·092	31	2·17	29
Endosperm	0·002	nil	0·058	19	5·39	71

Deep-frozen wheat grains, variety Festival, harvested 16 days after anthesis. Observed enzymatic activities of extracts of different parts of the grain, and the corresponding percentages of the total activity of the whole grain.

Glutamyl transferase: change in optical density (Δ *O.D.*) at 540 mμ (ref. 6) after incubation for 20 min. (30° C.) of extract equivalent of 0·5 grain.

Phosphatase: change in optical density at 400 mμ after incubation for 15 min. (30° C.) with disodium *p*-nitrophenol phosphate[10] of extract equivalent of 0·5 grain.

Leucine-activating enzyme: change in per cent exchange between pyrophosphate and adenosine triphosphate[11] after incubation for 15 min. (30° C.) of extract equivalent of 16 grains. Extracts were eluted phosphate gel purifications[12].

This 'rest' notably contains the chlorophyll layer, which is part of the pericarp. The outer pericarp of the earliest stages is opaque white, partly concealing the chlorophyll layer, but becomes more translucent as the grain starts to fill.

Glutamyl transferase activity was determined on extracts of outer pericarps, of 'rests' of grain coats and of isolated endosperms of deep-frozen 1959 material taken 16 days after anthesis. On a grain basis, 60 per cent of the activity appeared to be localized in the outer pericarp, 40 per cent in the rest of the grain coat and none was found in the endosperm. Neither was any activity found in isolated endosperms taken 32 days after anthesis. However, activity was found in concentrated extracts of endosperms, equivalent to 10 grains per ml., taken 12 days after anthesis. This amounted to 2 per cent of the activity of the grain coat. These results were confirmed using fresh material.

These observations suggest that the early peak in glutamyl transferase is associated with the early development of the grain coat and its gradual decline thereafter. They also suggest that the grain coat assumes a predominant role in the synthesis of the glutamine which is synthesized inside the grain. Admittedly this constitutes probably only part, and perhaps even a minor part, of all the glutamine which is ever present in the grain from anthesis to maturity, because the main source is presumably elsewhere in the plant.

The observations of Table 1 provide further examples of the differential distribution of enzymes within the grain and indicate the probable importance of the grain coat in wheat grain development.

The distribution of phosphatase, at 16 days after anthesis, was: outer pericarp 50 per cent, rest of grain coat 31 per cent and endosperm 19 per cent. These figures may be compared with those on phytase of the mature grain[2], where the coat contributes 7 per cent.

Leucine-activating enzyme appeared to reside mainly in the endosperm (71 per cent), none was found in the outer pericarp, but there was considerable activity in extracts of the 'rest' of the grain coat (29 per cent). This contrast between the parts of the coat is probably due to the chlorophyll layer in the 'rest' of the coat. This is full of chloroplasts, and these have been shown to harbour amino-acid activating enzymes[13,14].

These investigations are being continued.

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ANATOMICAL EVIDENCE FOR OLFACTORY FUNCTION IN SOME SPECIES OF BIRDS

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THERE is good morphological evidence that inherent responses to chemical sensory stimuli are of vital importance to some birds. It seems curious that the large olfactory organs of certain species[1] have so often been pointed out by anatomists, yet most olfactory learning studies have been done on feebly equipped birds such as pigeons, and have tended to keep alive in the text-books the idea that the chemical sense in birds is minimal or lacking. The maze type and conditioned reflex studies on microsomatic forms and the succession of uncontrolled field-tests initiated by those of Audubon[2] have kept dust from settling on the question, but have proved nothing about birds with superior receptors. There has been one recent, controlled, statistically significant laboratory experiment on olfactory learning in pigeons[3], and even in these weakly endowed birds the results were positive.

In dissecting the nasal tissues of birds for work on natural defences against respiratory disease[4], I have been repeatedly impressed by the size of some of the olfactory conchæ. Species were selected on the basis of the exposure of their nasal fossæ to extremes of environment, and not on the basis of olfactory behaviour. Of the species thus far dissected, by far the largest and most heavily innervated organs have been seen in the turkey vulture, *Cathartes aura*, the Trinidad oilbird, *Steatornis caripensis*, and the Laysan and black-footed albatrosses, *Diomedea immutabilis* and *D. nigripes*, each of which types represents a separate order with quite dissimilar feeding and nesting habits. Turkey vultures are diurnal carrion

feeders the solitary nests of which are found in sequestered hiding places; oilbirds feed nocturnally on fruits and nest colonially in total darkness in deep high caves in which they navigate by echo-location; the two pelagic albatross species feed mostly on marine crustaceans and nest colonially on islands, in the open, in shallow scrapes.

There is no question of degenerate or indifferent function of the olfactory organs of these birds. Other species seen in the course of this work have 1st nerve equipment varying from modest to considerable, but that of the three specified types is outstanding. In reviewing the literature on the habits of these particular birds, it is apparent that no definitive controlled experiments on the function or the sensitivity of the chemoreceptors have been done. It may be useful, however, to cite a few records of apparent olfactory behaviour in these species as clues to possible functions of the organs to be described.

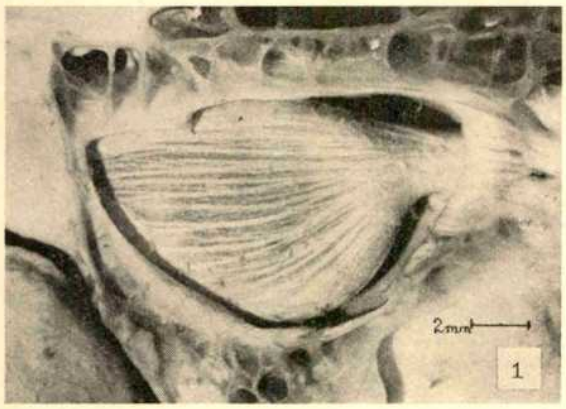

Fig. 1

Turkey vultures are high-altitude hunters. They apparently detect food odours which rise on the thermal updraughts on which they glide. They have been seen to pass over carrion upon which they would have spiralled straight down to feast if vision was the stimulus; having overshot the carrion until the scent was evidently carried up on the wind at an angle, they then turned suddenly and followed the scent beam to the prey[5]. A flock of 40–50 turkey vultures was seen to come in from a communal roost two miles away, sailing into the scent-laden trail of the first morning thermal to feed on offal which had been uncovered at dawn[6]. Fisher[7] has reported that a turkey vulture will not feed on newly discovered carrion so long as a human observer is upwind of it, no matter how well concealed he thinks himself to be.

From the many eye-witness accounts of keen olfactory perception in albatrosses, Loye Miller's is selected because his observation cruise was planned and the birds were marked[8]. Black-footed albatrosses were marked during movements of an oceanographic vessel to six stations 30 miles apart, with a 2-hr. stop at each point. Bacon drippings poured on to the surface of the sea attracted marked birds from at least 20 miles away within an hour. The birds discriminated by olfaction between paint scum and bacon drippings, refusing to approach the paint flux but going directly to the drippings.

The function of the chemoreceptor in *Steatornis* has not yet been determined. Dr. D. W. Snow, who has been studying the oilbirds of Trinidad for several

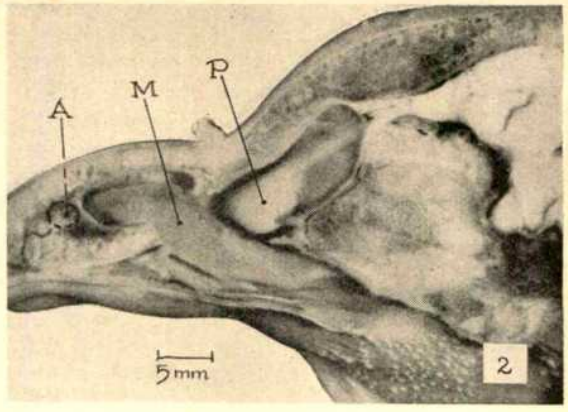

Fig. 2

years, writes in a personal communication that olfaction may be important in food finding: "Where the olfactory sense may come in, I think, is in locating trees that are in fruit". Some of their food trees are highly aromatic, and ripe and unripe fruits are mixed in the bunch. These nocturnal birds have large blue light-sensitive eyes, and it is not known whether they can distinguish ripe fruits by vision. Oilbirds not only nest colonially but also communally with bats, in absolute darkness, like the oriental swiftlet *Collocallia*. Novick[9] has recently suggested that the swiftlet may need a supplement to echo-location in discriminating its individual nest in a noisy crowded colony and that olfaction may serve this need. Many animals use musk secretions to mark territories, breeding sites, and family members for olfactory identification. Most species of bird secrete musk in their pygial glands, and these glands are known to be hyper-active in some species during nesting (hoopoes, wood-hoopoes, musk ducks, etc.). Turkey vulture nests smell of musk[10], and the musk secreted by albatrosses and other petrels clings to nest sites and even to dried skins for years[11].

The three species illustrated in Figs. 1–3 each has nasal fossæ precisely engineered to filter, warm, moisten, and sample inspired air chemically. Unfortunately, a sagittal view gives no concept of the airflow, nor does it demonstrate that the olfactory chamber is a cul-de-sac enclosed on three sides. The general arrangement of the structures in all the specimens is consistent with those of the oilbird

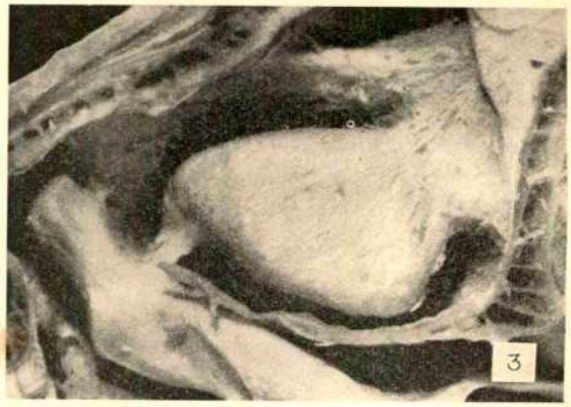

Fig. 3

(Fig. 2), though naturally the conchæ vary somewhat in relative size. The anterior concha, peculiar to birds, serves mostly as a baffle and thermo-regulator; the middle or respiratory one is covered with mucus-producing and ciliated cells; the posterior, olfactory, concha supports the free receptor fibrils of the 1st nerve and a quantity of serous glands peculiar to the olfactory organ. In each species the olfactory concha is conspicuously yellow in the fresh state. This concha is hollow in the albatrosses and the oilbird, the concavity being in communication with the cephalic air-sac system. The vulture concha is scrolled two and a half times, and has therefore a much greater surface area.

The mucosa of the conchæ was gently scraped away to reveal the underlying fibres of the olfactory nerve branches. As shown in Fig. 1, prominent branches are distributed over the entire convexity of the albatross concha. The network of end branches and fibrils was so thick in the turkey vulture that it was not possible to prepare a tidy dissection, and, as Fig. 3 shows, the entire surface was shaggy with torn nerves. The oilbird was photographed before the fibres were dissected out. The branches are somewhat closer together than those of the albatross but not so crowded as those of the vulture. In each species, strong branches of the 1st nerve also lie along the roof, posterior and ventro-lateral walls, and upper portion of the septum nasi of the olfactory chamber.

Though experimental results are wanting, it is suggested therefore that on the combined evidence of morphology and field-observation, it is probable that birds possessing large olfactory organs may respond instinctively to chemical stimuli, either alone or in complex interaction with auditory, visual, vibratory, and other organs of special sense.

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HYPOTHETICAL PATHWAY OF NITROGEN METABOLISM

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THE concept is widely accepted that nitrogen which enters the body of mammals as food ultimately is either stored in the form of body protein or eliminated. Elimination occurs chiefly through urine and fæces, in the form of urea, ammonia, creatine, creatinine, uric acid, amino-acids and other known nitrogen-containing katabolites. This concept represents the rationale for the technique of nitrogen balance studies, in which the nitrogen, recovered from urine, fæces, hair, and cage wash, and measured according to one of the many available modifications of Kjeldahl's method, is subtracted from the intake.

It is implicit in such a concept that positive nitrogen balance values must, within the limitations represented by concomitant variations in the amounts of other body constituents, particularly water and fat, be paralleled by a proportional increase in body-weight. A factor of 30 has repeatedly been found adequate in converting nitrogen weight into 'live' weight of the animal, provided unusually large deposits of adipose tissue are not present[1].

In the present article, results are presented which are not immediately consistent with the accepted postulate. Large and long-term nitrogen 'retentions' have been seen in our animals without proportionate increase in body-weight. Analogous results have already appeared in the literature[2–7] concerning several species, including man. My results, reached independently, confirm earlier observations and add

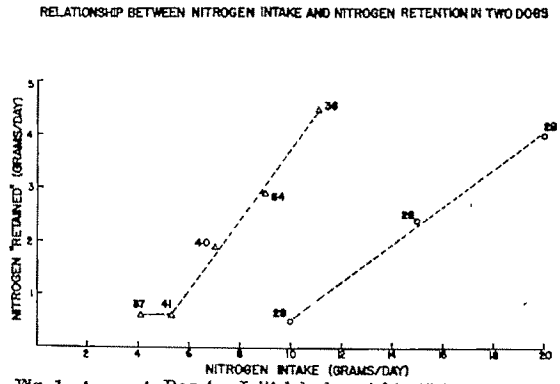


Fig. 1. △– – –△ Dog 4. Initial body-weight, 15·0 kgm.; final body-weight, 15·1 kgm. o– – –o Dog 9. Initial body-weight, 13·0 kgm.; final body-weight, 13·0 kgm. Numbers beside points indicate number of days observed.

Table 1. Nitrogen Balances and Variations in Body-weight in Male Mongrel Dogs

Dog	Status	Days observed	Daily intake Nitrogen (gm)	Daily intake Calories	Total nitrogen 'retained' (gm./dog)	Init. body-weight (kgm)	Weight gain (kgm.) Expected*	Weight gain (kgm.) Found
9	Normal	100	15·0	1,200	300	13	+ 9·0	0·0
4	Castrated	140	9·0	700	441	15	+13·2	0·0
2	Castr. and Depancreat	240	20·0	1,727	525	16	+15·7	+0·2
3	Castr. and Depancreat.	240	20·0	1,727	705	15	+21·0	+0·5

* Nitrogen 'retained' × 30

Table 2. RELATIONSHIP BETWEEN NITROGEN INTAKE, NITROGEN BALANCE AND BODY-WEIGHT IN DOG No. 4
(Initial body-weight 15 kgm.)

Period	Daily intake Calories	Daily intake Nitrogen (gm.)	Days observed	Average nit balance (gm./day)	Body-weight (kgm.) Init.	Body-weight (kgm.) Final
1	800	11 10	36	+4·48	15·0	15 0
2	700	8 98	64	+2 88	15 0	15 6
3	540	7 03	40	+2 35	15 6	15 6
4	400	5 30	41	+0 60	15 6	15·2
5	340	4 20	37	+0·62	15·2	14 5
6	396	4 20	22	+0 63	14 5	14 5
7	500	4 20	68	+0 70	14·5	15 1

new elements to this problem of impossibly high cumulative nitrogen 'retentions' without gain in weight. A hypothesis is advanced to explain the anomalous behaviour.

Dogs: Male mongrel dogs were kept in metabolic cages on a supplemented raw horse meat diet, and the nitrogen balance measured as described previously[8]. It was observed that animals, the body-weight of which remained practically constant throughout the experiment, were 'retaining' considerable amounts of nitrogen over long periods of time, as indicated in Table 1. The amount of nitrogen 'stored' by these animals is so large it could not have been retained at the expense of other body constituents. To explore this phenomenon further, the effect of varied nitrogen intakes was studied. Two dogs were observed, and the results are summarized in Table 2 and Fig. 1. Reasonable nitrogen equilibrium was obtained over a limited range of nitrogen intakes (periods 4–7). Above that range, a direct relationship existed between intake and 'retention'. No concomitant increase in body-weight was observed even when more than 4 gm. of nitrogen was 'retained' daily for 36 consecutive days.

Table 3. COMPOSITION OF THE DIETS USED IN THE RAT AND MOUSE EXPERIMENTS

Diet	*A*	*B*
Composition (per cent)		
Alphacel*	1·8	1 8
Sucrose	20 4	20 4
Corn starch†	40 7	20 4
Casein‡	16·7	37·0
Primex	7 4	7·4
Wessons Salt Mix*	3 7	3·7
Yeast§	9·2	9 2

Vitamins E and D were added to the feedings in the form of 10 per cent tocopherol in cod liver oil (2 drops three times a week). 1 gm. of either diet contains 3·75 cal.
* Nutritional Biochemical Corp.
† 'Argo'.
‡ Pure vegetable fat from Procter and Gamble.
§ Fleishmann 2019, obtained from Standard Brands, Inc, New York City, New York.

Rats: Experiment 1: Adult male Sprague–Dawley rats, weighing between 460 and 510 gm., were kept in standard metabolic cages at a constant temperature of 78° F. Regular periods of light and darkness were pre-set by an automatic switch. The animals were fed diet *A* of Table 3 once daily. Feeding consisted of adding new food to the cage after transferring the amount left over from the previous feeding to a separate compartment of the feeder. Animals were thus exposed to food at all times. Urines were preserved by addition of 50 ml. of 1 *N* sulphuric acid to the container placed under the funnel-shaped bottom of the cage. Urines and fæces were collected three times a week and analysed separately. Hair and whatever nitrogen could be recovered from the cages by careful washing with distilled water were collected together with stools. Nitrogen determinations were performed as described previously[8].

Rats were distributed among three groups, receiving different amounts of nitrogen. The results are presented in Table 4.

With the cages used in this experiment, separation of stools from urine was accomplished by means of a fine-mesh screen placed between the animal and the flask where urine was collected. It was thus possible that some urine might have been absorbed by the stools. Some urea could have been converted to ammonia gas and thus have escaped collection. To obviate this possibility, and to reduce experimental errors further, another experiment with rats was carried out.

Experiment 2: Special metabolic cages were constructed. They consisted of a 'Pyrex' animal jar divided, by means of a coarse (No. 3 mesh) stainless steel screen, into an upper compartment housing the animal and a lower compartment containing 450 ml. of 1 *N* sulphuric acid. Urine, fæces and other solid and liquid matter were thus immediately collected in the lower compartment under sulphuric acid. Food was offered in a special feeder, consisting of an outer stainless steel cup covered with a screen in which was set a smaller 'Pyrex' beaker. This permitted the food spilled by the animal to be safely collected on the bottom of the outer cup.

New food was offered once a day as described for Experiment 1. Cages, feeders and screens were copiously washed and urine, fæces, spilled food, food

Table 4. NITROGEN BALANCES AND VARIATIONS IN BODY-WEIGHT IN MALE SPRAGUE–DAWLEY RATS KEPT AT VARIOUS NITROGEN AND CALORIE INTAKES

Group	No of animals	Diet	Average daily intake/rat Nitrogen (mgm.)	Average daily intake/rat Calories	Consecutive days observed	Av. total nitrogen 'retention' (gm./rat)	Av. gain in body-weight (gm./rat) Init.	Av. gain in body-weight (gm./rat) Expected*	Av. gain in body-weight (gm./rat) Found
I	4	*A*	437	52 5	140	18 ± 3	465	+540	+5
II	7	*A*	374	45 0	140	17 ± 2	473	+510	−20
III	7	*A*	343	41 2	140	14 ± 2	468	+420	−90

* Nitrogen retained × 30

Table 5. NITROGEN BALANCES AND VARIATIONS IN BODY-WEIGHT IN MALE SPRAGUE-DAWLEY RATS (same rats used throughout)

No. of animals	Diet	Average weekly intake: Nitrogen (mgm.) Offered	Nitrogen (mgm.) Eaten	Calories Offered	Calories Eaten	Consecutive weeks observed	Av total nitrogen 'retention' (mgm./rat)	Av. body-weight (gm./rat): Init	Gain Expected*	Gain Found
6	*A*	6,654	5,118	787·5	615	3	+ 798	477	+23	+33
6	*B*	12,138	8,092	787·5	525	3	+1,119	510	+33	+23

* Nitrogen retained × 30.

left over and whatever could be collected by repeated washings, were pooled and analysed in a single weekly pool. Food left over was weighed before it was added to the 'cage content pool'. At the end of the washing, the cages appeared absolutely clean and no traces of solid matter could be seen.

Although this method gives no information concerning the partition of nitrogen between urine, fæces and other potential routes of elimination such as hair, nails, or saliva, it has the advantage of yielding the most accurate results concerning the nitrogen balance, because it eliminates multiple errors possible in the determination of several components rather than a single pool. Before analysis, the 'pool' was homogenized for 5 min. in a large blender and brought to volume with enough sulphuric acid to make the final concentration 30 per cent (v/v). Food was analysed in lots equal to the weekly offering, following a procedure identical to that used for the 'pool'.

In Table 5, the relationship between nitrogen intake, nitrogen 'retention' and changes in body-weight is shown for various diets and various nitrogen intakes. The results obtained with the less-critical method of collection (Table 4) are substantially confirmed. Unfortunately, the variations in body-weight are not as demonstrative as those presented in Table 4. It is clearly evident, nevertheless, that they are independent of the nitrogen retention, and most likely represent fat storage.

Mice: Experiments with mice were carried out exactly as in rat experiment 2 except for smaller metabolic cages.

In Table 6, the nitrogen balances and variations in body-weight are presented at two different levels of nitrogen intake. It is interesting to note the higher fraction of the intake 'retained' by mice as compared with rats.

Over long periods of time, our animals have 'retained' large quantities of nitrogen. In some experiments, these were in excess of the amount the whole animal could have contained at the beginning of the experiment. Nevertheless, this nitrogen 'retention' was not represented by gain in weight.

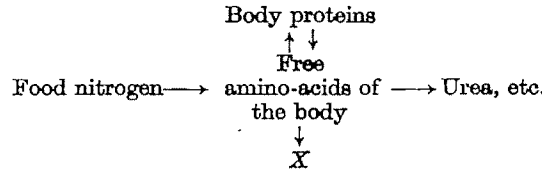
The 'retention' observed does not appear to be due to a technical artefact. This point is supported by the following considerations: The validity of the Kjeldahl method used was tested by analysing compounds the composition and purity of which were verified by independent carbon and hydrogen analysis. Twenty-five commonly occurring amino-acids and representative naturally occurring purines were analysed and gave results within 1 per cent of the theoretical value. Experiments were designed which maintained nitrogen equilibrium in dogs at suitably low nitrogen intakes, thus confirming the accuracy and completeness of our collections.

The length and magnitude of the 'retention' makes untenable the explanation that nitrogen could be stored at the expense of other constituents of the body. It should be added that, whenever tested[6,7], experimental evidence has not supported such an interpretation.

The hypothesis that some of the nitrogen fed in excess is eliminated through an unmeasured and hitherto unrecognized pathway would explain the discrepancies noted in a simple and rational way.

It does not seem likely that such a pathway could be represented by colonic flatus. Data available in man[3,9,10] show that such a pathway is possibly quantitatively insufficient as a route for loss of nitrogen. The small amounts of ammonia eliminated via respiration[14,15] would also fail to represent a quantitatively satisfactory explanation of our results.

The 'retention' occurs to a significant extent only when excess nitrogen is offered to the animal, as though such a pathway were active in providing a clearing mechanism for the nitrogen not warranted by metabolic need of the organism. This characteristic suggests the following schema:



That X is eliminated through respiration appears a likely possibility. If X exists and is represented by nitrogen gas, an amount which could explain the discrepancy between gain in body-weight and 'retention' would go undetected by the usual methods of analysis of nitrogen gas, being less than one-thousandth of the nitrogen involved in the respiration during 24 hr.

The non-participation of nitrogen in respiratory exchange has been postulated rather than proved. On the contrary, the few results available[12,15] suggest that nitrogen does participate in the respiratory exchange. The possibility that other gases in

Table 6. NITROGEN BALANCES AND VARIATIONS IN BODY-WEIGHT AT VARIOUS NITROGEN INTAKES IN MICE

No. of animals	Diet	Average weekly intake: Nitrogen (mgm.) Offered	Nitrogen (mgm.) Eaten	Calories Offered	Calories Eaten	Consecutive weeks observed	Av. total nitrogen 'retention' (mgm./mouse)	Av. body-weight (gm./mouse): Init.	Gain Expected*	Gain Found
5	*A*	1,210	1,170	157·5	141·0	6	492	44	+15	+1
	B	2,427	1,850	157·5	120	3	720	45	+22	0

* Nitrogen retention × 30.

addition to nitrogen and ammonia and involving nitrogen could be eliminated via respiration has not been excluded.

The presence of a metabolic route of food nitrogen different from those already known could offer an explanation for the so-called specific dynamic action of protein. It should be remembered that the specific dynamic action is shown when 'excess' protein is fed to an animal in weight-equilibrium, but is absent when the same protein, although possibly fed in 'excess', is stored in the growing organism. My schema is consistent with such findings, and could explain the production of the 'extra' heat with the production of X through a chain of metabolic steps which might well be exothermic. The fact that specific dynamic action does not occur after hepatectomy and that only a few amino-acids are capable of eliciting it under particular experimental conditions[16,17] is not inconsistent with my hypothesis.

Several anomalies of mammalian nitrogen metabolism could be explained in a simple and credible way by the loss in appreciable amounts of a nitrogen-containing metabolite, eliminated possibly through respiration. Adequate respirometers have been constructed, and an investigation involving the use of nitrogen-15 is under way in our laboratory, at the pre-clinical and clinical level, to confirm or disprove this hypothesis, with the ultimate aim of identification of the pathway and its metabolites.

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ENERGETIC ASPECTS OF THE MITOCHONDRIAL OXIDATION OF SUCCINATE

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THE reaction mechanism by which the enzymic oxidation of succinate is linked to the terminal electron transport system of intact mitochondria has been the subject of intense work during the past decade. Recent work in both the present laboratories, as well as in Chance's laboratory, has directed attention towards some new energetic aspects of this mechanism.

Prompted by an early observation of Chance and Hollunger[1], Klingenberg *et al.*[2,3], demonstrated that the addition of succinate to mitochondria, which were in a state of respiratory control ("State 4" in Chance's terminology), was followed by a considerable reduction of the intramitochondrial pyridine nucleotide. The extent of this reduction was higher than than obtained with pyridine nucleotide-linked substrates. It was postulated that this succinate-linked reduction of the mitochondrial pyridine nucleotide is an energy-requiring process, which, as recently reported by Chance and Hollunger[4], is inhibited by uncouplers of oxidative phosphorylation, and is not restored in this state by added adenosine triphosphate. It has also been shown that a similar high extent of reduction of the mitochondrial pyridine nucleotide may be obtained by another flavin-linked substrate, glycerol-1-phosphate[3,5], and that both the succinate- and the glycerol-1-phosphate-induced reduction may, in some instances, require the presence of added adenosine triphosphate[5]. In these instances also the reduction of a flavoprotein was found to be dependent on oxidative phosphorylation[6].

Recently it was reported by Azzone and Ernster[7], that the aerobic oxidation of succinate is greatly inhibited in rat liver mitochondria which had been depleted of endogenous high-energy phosphate by incubation, under appropriate conditions, with arsenate and/or agents which uncouple oxidative phosphorylation. In these mitochondria the rate of aerobic oxidation of succinate could be greatly stimulated by the addition of adenosine triphosphate, and this effect was not abolished by the simultaneous presence of uncouplers of phosphorylation. It was postulated that, under these conditions, the aerobic oxidation of succinate requires high-energy phosphate and that this energy can be supplied by added adenosine triphosphate through a reaction mechanism which is not inhibited by uncouplers of electron transport-coupled phosphorylation.

The objective of the present work was to elucidate the possible relation between the energy requirement of succinate oxidation and the energy-requiring reduction of pyridine nucleotide. In particular, it was of interest to investigate whether the adenosine triphosphate-induced stimulation of the aerobic

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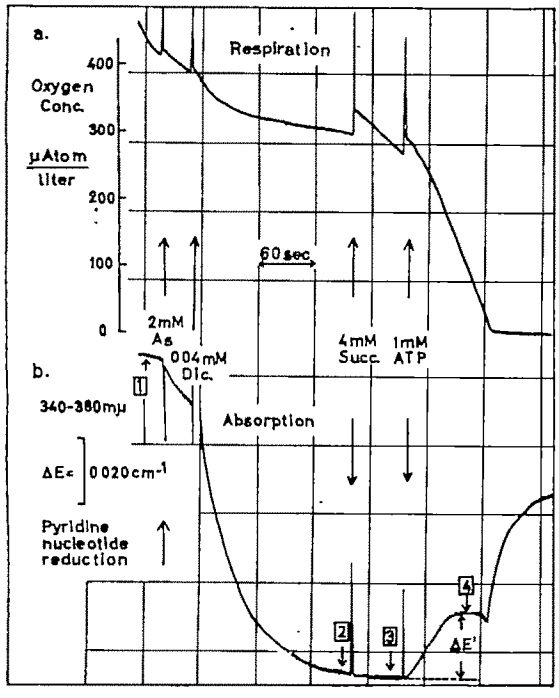

Fig. 1. Simultaneous recording of respiration (*a*) and pyridine nucleotide absorption (*b*). Rat liver mitochondria, 3·8 mgm. prot./ml. in 0·13 m*M* potassium chloride, 0·008 *M* Magnesium chlorate, 0·02 *M* triethanolamine hydrochloride, *p*H 7·5. *As*, arsenate; *Dic*, dicoumarol; *Succ*, succinate. Discontinuous absorption trace at the addition of dicoumarol because of compensation for the dicoumarol absorption. The numbers indicate the moments of extraction for pyridine nucleotide analysis, the results of which are given in Table 1

oxidation of succinate in mitochondria depleted of high-energy phosphate is accompanied by a reduction of the mitochondrial pyridine nucleotide, and whether this process, similarly to the adenosine triphosphate-induced respiratory stimulation, can take place in the presence of uncouplers. The results presented here clearly indicate that this is the case. Qualitative and quantitative estimates of the reduced pyridine nucleotides were also carried out, and, in addition, data were obtained on the oxido-reduction states of the mitochondrial flavin and cytochrome *b*. Some implications of these findings for the mechanism of the functional link of succinic dehydrogenase to the terminal electron transport system will be considered.

The experiments entailed a simultaneous measurement of the oxygen uptake and of the difference in spectral absorption at suitable wave-lengths, using a double-beam spectrophotometer equipped with a vibrating oxygen electrode[8]. Twice-washed rat liver mitochondria were prepared as previously described by Klingenberg *et al.*[2]. The incubation medium contained 0·13 *M* potassium chloride, 0·02 *M* triethanolamine buffer, *p*H 7·5, and 0·008 *M* magnesium chloride. The measurements were carried out at 25° C. in quartz cuvettes of 0·5 and 1 cm. light-path. Extractions and enzymic determinations of the reduced and oxidized pyridine nucleotides were performed essentially as described previously[2].

A typical experiment is shown in Fig. 1. In this experiment, the mitochondria were pre-incubated for 3 min. in the presence of arsenate and dicoumarol. The endogenous respiration was rather high at the onset of the pre-incubation, but declined to almost zero after about 2 min. Subsequent addition of succinate resulted in a relatively low respiration, which, however, could be greatly stimulated by the addition of adenosine triphosphate in accordance with previous findings[7]. As seen in the lower curve of Fig. 1, the 340–380 mµ absorption difference, indicative of the reduction state of the pyridine nucleotides, decreased rapidly during the initial period of the pre-incubation. This decrease levelled off concomitantly with the decline of the endogenous respiration. The addition of succinate induced no change in the steady state of the pyridine nucleotide, whereas the subsequent addition of adenosine triphosphate caused a reduction of the pyridine nucleotide. A new steady-state level was reached after about 1 min. It may be noticed that both the stimulation of the respiration and the increase of the 340–380 mµ absorption required a short lag-period, following the addition of adenosine triphosphate.

To ascertain if the spectrophotometric changes were relevant to the reduction of pyridine nucleotide, enzymic determinations were performed. For this purpose, a parallel experiment was carried out with a 10-ml. sample of the incubation mixture, from which successive aliquots were removed and extracted at the moments indicated in Fig. 1. The results of the di- and tri-phosphopyridine nucleotide determinations are given in Table 1 (*a*). The total levels of reduced pyridine nucleotide found in the various aliquots were in agreement with the spectrophotometric data. A decrease was found of the total reduced pyridine nucleotide during the pre-incubation, followed by no change on the addition of succinate, and by an increase on the addition of adenosine triphosphate.

It may also be seen in Table 1 that the adenosine triphosphate-induced reduction of the pyridine nucleotide was accounted for mainly by an increase of reduced triphosphopyridine nucleotide, and only to a small extent by an increase of reduced diphosphopyridine nucleotide. These results, which are in agreement with previous findings[2,3], indicate that in the mitochondria there occurs a transfer of hydrogen between reduced di- and tri-phosphopyridine nucleotide by way of a mechanism which favours the accumulation of the latter compound. The fact that the mitochondrial pyridine nucleotide transhydrogenase[9] cannot account for the presence of a higher level of reduced triphosphopyridine nucleotide suggests that other transhydrogenase mechanisms[10] may also be involved.

The total levels of both reduced pyridine nucleotides, attained upon the addition of adenosine

Table 1. PYRIDINE NUCLEOTIDE ANALYSIS ON EXTRACTS FROM LIVER MITOCHONDRIA

Successive additions	T†	DPNH µmol./gm. prot.	TPNH µmol./gm. prot.
(*a*) Arsenate-dicoumarol treatment			
—	10″ (1)*	0·78	3 60
2 m*M* arsenate			
0 04 m*M* dicoumarol	3′ 40″ (2)	0 07	0 47
4 m*M* succinate	5′ 40″ (3)	0·05	0 38
2 m*M* ATP	7′ 40″ (4)	0·15	0·83
(*b*) Dinitrophenol treatment			
—	10″	0·72	3·60
0 1 m*M* dinitrophenol	4′ 10″	0 05	0·46
4 m*M* succinate	6′ 10″	0 08	0·72
2 m*M* ATP	8′ 10″	0·15	1 37
1 m*M* KCN	18′	1 00	1·67

* Extraction indicated by the same numbers in Fig. 1*b*.
† Time of extractions after incubation.

triphosphate, were relatively low in these experiments (5–10 per cent for diphosphopyridine nucleotides and about 30 per cent for triphosphopyridine nucleotides) as compared with those previously observed[2,3] in mitochondria under respiratory control in the presence of succinate (75 and 95 per cent, respectively). However, the present levels are in fair agreement with those found[2,3] when an uncoupler of oxidative phosphorylation was added to this latter system, subsequent to the addition of succinate. These levels would therefore seem to represent the maxima obtainable in a state of uncontrolled respiration.

In Table 2, data are summarized which show the influence of various pre-incubating conditions on the phenomenon described above. Replacement of dicoumarol by dinitrophenol had no major effect on the respiratory-rate either before or after the addition of adenosine triphosphate. On the other hand, the extent of reduction of the mitochondrial pyridine nucleotide following the addition of adenosine triphosphate was lowered to about one-half.

Table 2. EFFECT OF ADENOSINE TRIPHOSPHATE ON SUCCINATE RESPIRATION AND PYRIDINE NUCLEOTIDE REDUCTION OF PRE-INCUBATED LIVER MITOCHONDRIA

Pre-incubation with	Oxygen uptake with 4 m*M* succinate before	after addition of 2 m*M* ATP	Absorbancy increase *E'* at 340–380 mμ (cf. Fig. 1*b*) on addition of 2 m*M* ATP
	μ atom O / min. gm. prot.		1 / cm. gm. prot.
2 m*M* arsenate + 0·04 m*M* dicoumarol	13	55	11
2 m*M* arsenate + 0 1 m*M* DNP	12	44	5 5
0 1 m*M* DNP	20	43	5
2 m*M* arsenate	40	no ATP added (succinate alone)	30

Pre-incubation with arsenate alone resulted in a low rate of respiration with succinate, which, however, gradually increased even without the addition of adenosine triphosphate. As suggested elsewhere[11], this effect may be attributed to a resynthesis of high-energy phosphate within the mitochondria during the course of succinate oxidation. The gradual increase of the respiratory-rate was paralleled by a reduction of the pyridine nucleotide, which reached a steady-state level of about twice that attained in the presence of adenosine triphosphate in the arsenate-dicoumarol-pretreated system.

When the mitochondria were pre-incubated with dinitrophenol (or dicoumarol) in the absence of arsenate, an inhibition of the subsequent respiration with succinate was also obtained, although the inhibition was weaker than in the simultaneous presence of arsenate. The rate of the inhibited respiration, however, was constant, exhibiting no tendency to increase without the addition of adenosine triphosphate as in the case of pre-treatment with arsenate alone. Adenosine triphosphate gave a stimulation of the respiration in this case also, and again, this effect was accompanied by a reduction of the pyridine nucleotide. The steady-state level reached in the presence of dinitrophenol alone was about the same as in the simultaneous presence of arsenate. Enzymic determinations on the reduced pyridine nucleotide levels in the dinitrophenol system are shown in Table 1 (*b*).

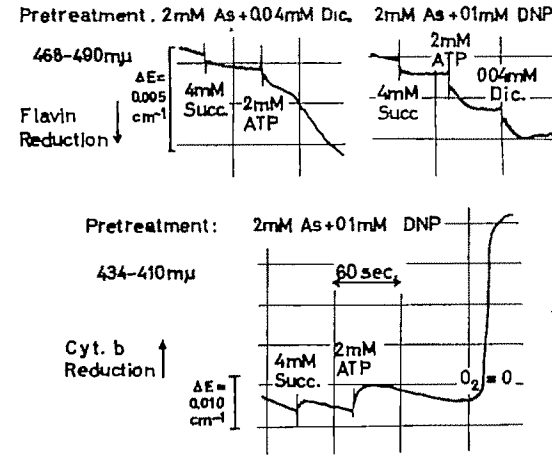

Fig. 2. Recording of flavin and cytochrome *b* absorption (cf. legend of Fig. 1). The mitochondria had been pre-treated, as indicated, for 3 min. until succinate addition

The difference in findings with dinitrophenol alone and arsenate alone as pre-incubating agents may be ascribed to the fact that although arsenate is very efficient in depleting mitochondria of high-energy phosphate it is a weak uncoupler of electron transport-coupled phosphorylation, whereas dinitrophenol is a potent uncoupler, but rather poor in depleting the mitochondria of high-energy phosphate. As shown elsewhere[11], dinitrophenol can efficiently deplete mitochondria of high-energy phosphate in the presence of adenosine-5′-phosphate.

Under all the conditions tested in Table 2, the rate of reduction of the pyridine nucleotide was approximately the same.

In other experiments, the changes in oxidation-reduction states of the mitochondrial flavin and cytochrome *b* were followed (Fig. 2). Increased levels of reduction of both these components were recorded following the stimulation of succinate oxidation by the addition of adenosine triphosphate in mitochondria that were depleted of high-energy phosphate.

A difference in the extent and rate of the adenosine triphosphate-induced reduction of the flavin was observed according to whether dinitrophenol or dicoumarol was used as a pre-incubating agent in combination with arsenate. In the case of dicoumarol, the change in the steady state of the flavin was diphasic and the amount of flavin reduced was about twice that obtained with dinitrophenol. As was observed above (Table 2), the reduced pyridine nucleotide-level was also about twice or higher in the dicoumarol system than that attained with the dinitrophenol system. These findings may be related to the observation previously reported that dicoumarol, besides its uncoupling effect, is a powerful inhibitor of a soluble, pyridine nucleotide-unspecific diaphorase which is also found in mitochondria[12]. In support of this concept, addition of both dinitrophenol and dicoumarol to the present system resulted in an adenosine triphosphate-induced reduction of flavin of the same rate and extent as that obtained in the presence of dicoumarol alone.

The possibility that oxaloacetate was responsible for the observed inhibition of succinate oxidation after the arsenate-dicoumarol incubation was previously[7] discarded on the evidence that cysteine sulphinic acid, which removes oxaloacetate by trans-

amination to aspartate, could not restore succinate oxidation. This question was re-investigated in the present work by measuring directly the oxaloacetate concentration after the arsenate–dicoumarol pre-incubation. In no case was it possible to find oxaloacetate in the incubation mixture in amounts exceeding the sensitivity of the method used; that is, 5×10^{-5} M. Furthermore, since it has been demonstrated that adenosine triphosphate can remove the oxaloacetic inhibition by formation of phosphoenol-pyruvate[13], this compound also was determined. The concentration of phosphoenol-pyruvate was ascertained to be less than 5×10^{-7} M and thus cannot account for the observed adenosine triphosphate effect.

The present findings are at some variance with those recently reported by Chance and Hollunger[4]. These authors found no increase in the reduction of pyridine nucleotides following the addition of adenosine triphosphate in the presence of even very low concentrations of uncouplers. In the present case, added adenosine triphosphate clearly was able to induce a reduction of the pyridine nucleotide in the presence of concentrations of dinitrophenol or dicoumarol, which fully uncouple oxidative phosphorylation. It would seem, however, that, although the experiments of Chance and Hollunger, and those in the present work, were made with mitochondria of very different initial functional states, the discrepancy in the findings may not be due to different reaction mechanisms, but rather to a possible difference in the suitability of the two sets of conditions for allowing this adenosine triphosphate effect to become manifest.

The results presented here indicate a striking parallelism between the effect of adenosine triphosphate on respiration and on pyridine nucleotide reduction, and therefore suggest that under the present conditions the energy requirement for the two processes is utilized through a common intermediate. It would also seem that the common high-energy intermediate, which is formed during the oxidation of succinate, and the energy of which may be utilized for pyridine nucleotide reduction, is situated in the initial part of the respiratory chain, thus being probably closely related to the primary high-energy intermediate involved in the first respiratory chain phosphorylation. Furthermore, since the need for energy to initiate succinate oxidation is thought to be a normal property of intact mitochondria, it follows from the above reasoning that the site of entrance of electrons from succinic dehydrogenase to the mitochondrial respiratory chain should be prior to the level of cytochrome b; otherwise, the aerobic oxidation of succinate could not result normally in a phosphate/oxygen ratio of 2.

From the fact that concentrations of dinitrophenol which uncouple oxidative phosphorylation do not abolish the stimulatory effects of adenosine triphosphate on succinate-oxidation and on reduction of pyridine nucleotide by succinate, it appears that energy of adenosine triphosphate is available to the respiratory chain in spite of the presence of uncouplers of oxidative phosphorylation. This observation seems scarcely compatible with those hypotheses of oxidative phosphorylation[14] in which a non-phosphorylated high-energy intermediate, susceptible to hydrolysis in the presence of dinitrophenol, is involved between adenosine triphosphate and the respiratory chain. On the other hand, these results are consistent with those hypotheses which postulate the formation of a high-energy phosphate compound involving a respiratory carrier such as flavin[16], or a quinone[16], as primary intermediate of electron transport coupled phosphorylation. As has been pointed out previously[15], in this type of hypothesis dinitrophenol is supposed to act by interfering with the activation of inorganic orthophosphate, thus inhibiting only the forward, but not the backward, reaction of respiratory chain phosphorylations.

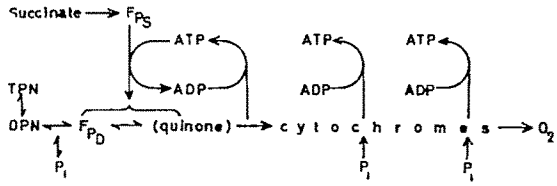

Fig. 3. Hypothetical scheme of the functional link of succinic dehydrogenase to the terminal electron transport system. Symbols: DPN, diphosphopyridine nucleotide; TPN, triphosphopyridine nucleotide; Fp_D, DPN diaphorase; Fp_S, succinic dehydrogenase; P_i, inorganic phosphate; ADP, adenosine diphosphate; ATP, adenosine triphosphate

Fig. 3 shows a tentative scheme covering these conclusions. It is suggested that the electrons from reduced succinic dehydrogenase enter the respiratory chain at the level of the diaphorase flavin, or alternatively, at the level of a quinone situated between the diaphorase flavin and cytochrome b. In order to react with these carriers the reduced succinic dehydrogenase requires the intervention of high-energy phosphate, with the reduced phosphorylated diaphorase or quinone as the reaction product. This product can react either with cytochrome b, resulting in the regeneration of adenosine triphosphate, or with diphosphopyridine nucleotide, with the liberation of orthophosphate.

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PREPARATION AND IMMUNOLOGICAL PROPERTIES OF AN ARTIFICIAL ANTIGEN WITH COLITOSE (3-DEOXY-L-FUCOSE) AS THE DETERMINANT GROUP

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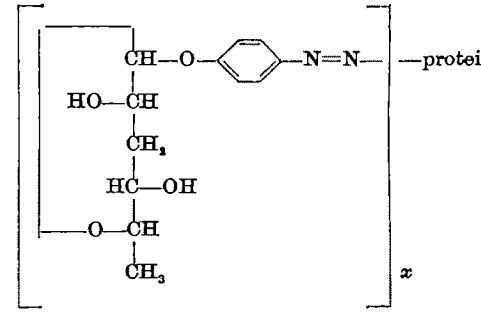
ANTIGENS are principally substances of high molecular weight of which only a small part, the determinant group(s), is responsible for specificity[1,2]. Most of our knowledge of natural antigens originates from immunochemical work on bacterial polysaccharides. Inhibition of the specific precipitation of bacterial polysaccharides with their respective antibodies by oligosaccharides of low molecular weight has demonstrated the important role of sugar constituents situated at the terminal non-reducing end of side-chains[3,4].

In the course of immunochemical work on *Salmonella*, *Escherichia* and other Enterobacteriaceae the terminal sugars of determinant groups of various *O* antigenic polysaccharides were recognized[5-8]. It was found that terminally linked colitose (3-deoxy-L-fucose)[9] functions as the determinant end-group of the *O* antigen of *E. coli O* 111 *B* 4 and of the cross-reacting *O* antigens of *Salmonella O* 35 (ref. 6) and of *Arizona O* 20 (refs. 10 and 11). It is further known that another group of cross-reacting enterobacterial organisms exists, namely, *E. coli O* 55 *B* 5, *Salmonella O* 50 and *Arizona O* 9, the *O* antigens of which also contain terminally linked colitose[10]. Using standard rabbit antisera, the *E. coli O* 111 (with *Salmonella O* 35, *Arizona O* 20) group on one hand, and the *E. coli O* 55 (with *Salmonella O* 50, *Arizona O* 9) group on the other, do not show any overlapping cross-reactivity. It was therefore concluded that colitose in the *O* antigens of both cross-reacting groups must be linked in a different manner, leading to different kinds of rabbit antibodies. It is, however, possible to obtain immune sera reacting with the *O* antigens of both groups after immunization of animal species other than the rabbit, such as horses, cows or goats. With horse immune sera it was shown that cross-reactions between *O* antigens of the *E. coli O* 111 and *E. coli O* 55 groups were in fact due to determinant groups both of which contained terminal colitose[6].

For the further elucidation of the role of colitose as the determinant end-group in bacterial polysaccharides artificial antigens containing colitose linked to a protein have been prepared. Antisera to these colitose-antigens were examined for possible cross-reactions with bacterial *O* antigens, containing terminal colitose, and with the corresponding micro-organisms.

Preparation of the colitose-antigens. Artificial antigens were prepared by coupling diazotized *p*-aminophenyl-α- and -β-colito-pyranosides to proteins according to the classical azo-method of K. Landsteiner (see refs. 1 and 2). Colitose[9] was acetylated and the resulting mixture of the α- and β-triacetates was heated with *p*-nitrophenol in the presence of mercuric chloride under reduced pressure[12,13]. A mixture was obtained in good yield of *p*-nitrophenyl-diacetyl-α- and β-colitopyranosides. On recrystallization from methanol the predominating and less soluble α-form was obtained in pure form (m.p. 180°; $[\alpha]_D^{20}$ − 213° (methanol)). The β-derivative, slightly contaminated by the α-form, was isolated from the mother liquor (m.p. 155°; $[\alpha]_D^{20}$ −0° (methanol)). After deacetylation the *p*-nitrophenyl-colitosides were converted into the corresponding *p*-aminophenyl-α- and β-colitosides by catalytic hydrogenation: *p*-aminophenyl-α-colitopyranoside: m.p. 180°, $[\alpha]_D^{20}$ − 166° (methanol); calc.: C, 60·2; H, 7·1; N, 5·8; found: C, 60·4; H, 7·1; N, 5·8. *p*-Aminophenyl-β-colitopyranoside: m.p. 75°, $[\alpha]_D^{20}$ + 99° (methanol). The β-isomer may still contain some α-form. For the preparation of the colito-phenylazoproteins the *p*-aminophenyl-colitosides were diazotized and added to alkaline solutions of purified bovine serum albumin or egg albumin. The red-coloured solutions of the azoproteins were dialysed, adjusted to the desired concentration and kept sterile with merthiolate (1 : 10,000). Antigen solutions contained about 1 mgm. of bound colitose and 16 mgm. of protein per ml. On the average, one molecule of serum albumin contained about 30 colito-phenylazo groups.



Colito-pyranosido-phenylazo-protein

The following artificial antigens were prepared:

α-colitose phenylazo-bovalbumin = α-*Co-Bo*
α-colitose phenylazo-ovalbumin = α-*Co-Ov*
β-colitose phenylazo-bovalbumin = β-*Co-Bo*
β-colitose phenylazo-ovalbumin = β-*Co-Ov*

Reaction of the artificial antigens and haptens with horse anti E. coli *sera.* Precipitation of *E. coli O*111 polysaccharide of a horse anti *E. coli O* 111 serum was inhibited by various preparations in the following order: α-aminophenyl-colito-pyranoside > β-amino-

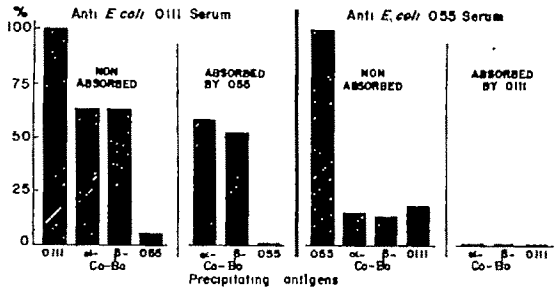


Fig. 1. Per cent precipitation of horse anti *E. coli. O* 111 and anti *E. coli O* 55 antibodies by artificial colitose antigens *O* 111 = Polysaccharide extracted from *E. coli O* 111; *O* 55 = polysaccharide extracted from *E. coli O* 55; *α*- and *β-Co-Bo* = *α*- and *β*-colitose phenylazo-bovalbumin

phenyl-colito-pyranoside > colitose. In the *E. coli O* 111 antigen the immunologically determinant colitose end-groups must therefore be linked as colito-pyranoside. It is not known at present whether or not the relatively strong inhibition of the β-isomer, as compared to colitose, is due to contamination with small amounts of the α-isomer.

The four colitose phenylazo-proteins gave strong precipitation with a horse anti *E. coli O* 111 serum and a weaker precipitation with a horse anti *E. coli O* 55 serum. Absorption of each of the antisera with the respective homologous polysaccharide markedly diminished the precipitating antibodies towards the artificial antigens. Moreover, after absorption of the antisera with the heterologous cross-reacting polysaccharide, precipitation of the anti *E. coli O* 111 serum with the artificial colitose antigens was only slightly diminished, whereas precipitation of the anti *E. coli O* 55 serum with the artificial antigens was completely abolished, as shown in Fig. 1. This suggests that in horse anti *O* 55 serum the small proportion of antibodies which reacts with the artificial colitose antigens is only contained in the antibodies cross-reacting with *E. coli O* 111 polysaccharide. In these experiments no difference in serological behaviour was found between the α- and β-colitosides.

Immunization of animals with artificial colitose-antigens. Rabbits were injected with each of the colitose-phenylazo-proteins. In nine out of thirteen sera precipitins against the artificial α- or β-colitose antigens were developed during immunization. Some of the precipitations were very strong. Inhibition by colitose and aminophenyl-colitosides indicated that these precipitations were due mostly, if not completely, to anti-colitose antibodies. Bacterial colitose-containing polysaccharides were not precipitated by anti-colitose rabbit sera. Two sera agglutinated *E. coli O* 111 suspensions as well as erythrocytes sensitized with the corresponding lipopolysaccharide[14,15]. However, the titres were relatively low, and no correlation was found with the levels of anti-colitose antibodies.

One goat (goat 1) was immunized with *α-Co-Bo* and a second goat (goat 2) with *β-Co-Bo*. The antisera obtained gave precipitin reactions with colitose-ovalbumin antigens (*α-Co-Ov* and *β-Co-Ov*), showing that specific anti-colitose antibodies had been formed. In addition, the sera were found to contain antibodies which specifically cross-reacted with *E. coli O* 111, that is, they precipitated *E. coli O* 111 polysaccharide; erythrocytes sensitized with *E. coli O* 111 lipopolysaccharide and suspensions of heated *E. coli O* 111 organisms were agglutinated, as shown in Table 1. On the other hand, the sera did not react with *E. coli O* 55 polysaccharide (no precipitation, no hæmagglutination), but one of the two sera agglutinated suspensions of *E. coli O* 55 organisms (goat 1). This antiserum behaved exactly like an anti *E. coli O* 111 horse or goat serum. *E. coli O* 111 polysaccharide removed all agglutinating antibodies from this serum. Furthermore, in hæmagglutination tests the two sera cross-reacted with all bacterial species serologically related to *E. coli O* 111 (*Salmonella O* 35, *Arizona O* 20), but not with species serologically related to *E. coli O* 55 (*Salmonella O* 50, *Arizona O* 9). The goat sera before immunization showed low titres of natural antibodies against practically all tested enterobacterial *O* antigens. After immunization with the artificial colitose-antigens only, titres against *E. coli O* 111 and serologically related strains were found to be markedly elevated (Table 1).

Twenty years ago W. F. Goebel[16,17] described the isolation of cellobiuronic acid as the determinant group of the capsular polysaccharide antigen of *Pneumococcus* type III and the synthesis of an artificial antigen by coupling diazotized *p*-aminobenzyl cellobiuronide to protein. The antisera so obtained strongly precipitated type III polysaccharide and agglutinated type III *Pneumococci*. Furthermore, they protected animals against otherwise fatal infections with virulent cultures of these Gram-

Table 1: Antimicrobial Antibody Titres of Goat Sera before and after Immunization with Artificial Antigens (*α*- and *β-Co-Bo*)

Antigen (Bacteria or lipopolysaccharides) used		Goat 1 (immunized with *α-Co-Bo*)				Goat 2 (immunized with *β-Co-Bo*)			
		Hæmagglutination*		Agglutination†		Hæmagglutination*		Agglutination†	
		before	after	before	after	before	after	before	after
(*a*) *E. coli*	*O* 111 *B*4	320	5,120	<100	800	80	2,560	40	800
(*b*) ,,	*O* 55 *B*5	80	80	<100	400	80	80	40	80
(*c*) ,,	*O* 26	20	20	320	400	40	40	160	100
(*c*) ,,	*O* 86	20	20	—	—	80	40	—	—
(*c*) ,,	*O* 8	80	40	—	—	80	40	—	—
(*a*) *S. adelaide*	*O* 35	—	—	20	400	—	—	20	320
(*a*) *S. monschaui*	*O* 35	40	2,560	—	—	40	1,280	—	—
(*c*) *S. cholerae suis*	*O* 6/7	<10	<10	<100	<100	160	40	—	—
(*b*) *S. greenside*	*O* 50	—	—	40	400	—	—	40	40
(*c*) *S. abortus equi*	*O* 4/12	10	10	20	<100	10	10	—	—
(*b*) Arizona	*O* 9*a*	—	—	40	200	—	—	20	40
(*a*) Arizona	*O* 20	—	—	—	—	—	—	20	320

* Hæmagglutination of erythrocytes sensitized with lipopolysaccharides (see ref. 14). † Agglutination of heated suspensions

All strains (*a*) contain colitose and cross-react. All strains (*b*) contain colitose and cross-react but not with strains (*a*). All strains (*c*) do not contain colitose and do not cross-react either between them or with strains (*a*) and (*b*).

positive organisms. The present article reports the first artificial antigen which stimulates antibodies against certain pathogenic Gram-negative bacteria.

In agreement with previous inhibition work[6], experiments described here show that a single monosaccharide unit—colitose—suffices to account to a high degree for the antigenic specificity of *E. coli O* 111 and serologically related bacteria (*Salmonella O* 35, *Arizona O* 20).

Rabbit antisera prepared against artificial colitose antigens were frequently found to be rich in specific anticolitose antibodies; they reacted only weakly, if at all, with the microbial colitose-containing polysaccharides. On the other hand, the two goat sera reacted strongly with the microbial polysaccharides although they showed lower titres of precipitating anticolitose antibodies, as compared with the rabbit sera. The quality of the antibodies obtained from the two species is obviously very different. This is a further example of the significance of the species in immunization with respect to the specificity of antibodies obtained by one and the same antigen.

Only one group of bacterial polysaccharides containing terminal colitose (*E. coli O* 111, *Salmonella O* 35, *Arizona O* 20) cross-reacted with goat antisera to the artificial colitose antigens, in perfect agreement with the finding that only anti *E. coli O* 111 antibodies precipitate colitose phenylazo-proteins. In the polysaccharide antigens of the *E. coli O* 111 group the structural arrangement of the terminally linked colitose appears to be similar to that of colitose in the artificial colitose antigens. On the other hand, on the basis of the findings reported here, the status of the likewise terminally bound colitose in the polysaccharides of the *E. coli O* 55 group (*E. coli O* 55, *Salmonella O* 50, Arizona *O* 9) has again been shown to be different[8,10].

It should be pointed out that, in contrast to the bacterial endotoxic *O* antigen complexes, the artificial colitose antigens are practically non-toxic.

Work on the biological properties of anticolitose goat sera is in progress. Anticolitose sera from other animal species will be examined. The preparation of other 3,6-dideoxy-hexose phenylazo-proteins and investigations of their immunological properties are also under way.

Experimental details will be given elsewhere.

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OCCURRENCE OF D-PHENYLALANINE, D-ALLOTHREONINE AND OTHER D-AMINO-ACIDS IN PEPTIDO-LIPIDS OF BACTERIAL ORIGIN

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WORK on the chemical constitution of antibiotics has shown that a large number of these substances contain amino-acids of the D-configuration[1,2]. The occurrence of D-amino-acids in functional structures of living cells has been reported much more rarely. However, D-alanine, D-glutamic acid, and D-aspartic acid have been shown recently to be common and major constituents of the bacterial cell wall[3-7], and D-alanine and D-glutamic acid have been found to be present in the 'spore peptide' of *Bacillus megaterium*[8]. Moreover, α,ε-diaminopimelic acid, a major constituent of many bacterial cell walls[9], possesses the *meso*-configuration for a large number of micro-organisms[10]. Certain nucleotides exemplified by those that accumulate in penicillin-treated *Staphylococcus aureus*[11], and which afterwards have been implicated as probable precursors in the biosynthesis of cell walls[12] also contain D-amino-acids. In all the above instances the D-amino-acids occur in products of microbiological origin. The occurrence of these compounds in higher plants and animals seems, from reports to date, to be a rarer event. Recently, however, D-serine has been found in lombricine isolated from the earthworm, *Lumbricus terrestris*[13].

We wish to describe here the general occurrence of several different D-amino acids in peptido-lipids and peptido-glyco-lipids from bacteria of the order Actinomycetales[14].

The general approach has been to separate individual amino-acids by column chromatography, and then to compare the analytical values obtained through application of the ninhydrin method with those obtained by optically specific microbiological assay methods. Major discrepancies between the two methods of analysis have proved very useful in pointing out the presence of 'unnatural' forms of certain of the amino-acids, the presence of which was then confirmed by other methods. The substances included in this work are described briefly below.

(1) 'Wax *D*' of *Mycobacterium tuberculosis* var. *hominis* (Brévannes). The purification and composition of this material has been previously described[15]. The amino-acid components were reported

Table 1. NITROGENOUS COMPONENTS OF THE PEPTIDO-LIPIDS AND PEPTIDO-GLYCO-LIPIDS OF *Mycobacterium* AND *Nocardia* SPECIES

Component	Method (see footnotes)	'Wax D' of *M tuberculosis*	Mycoside *C* of *M. avium*		Mycoside *C* of *M. marianum*	Peptido-lipid of *N. asteroides*	
			Jav 5	*Jav* 4		I	II
		Total μmoles					
Alanine, total	(*a*)	176	13·1	5 05	8 8	31 5	36 5
Alanine, total	(*b*)	155	13 5	4 3	8 3	29·6	32 0
Alanine, D	(*c*)	51	13·5	5 25	9 6	20 9	19 9
'Threonine', total	(*a*)		11 0	4 75	8·9	32 7	34 2
Threonine, L	(*d*)		< 0 5	< 0 4	< 0·3	34 8	35 0
Allothreonine, D	(*c*)		11 5	5·4	8·7		
Phenylalanine, total	(*a*)		7 8	4 4			
Phenylalanine, L	(*d*)		1 6	0 7	0 07		
Phenylalanine, D	(*c*)		5 4	3 0	1 65		
Valine, L	(*d*)					27·3 (*i*)	25 0 (*i*)
Valine, D	(*c*)					< 1·3	< 0 7
Proline, total	(*a*)					17 25	17·25
Proline, L	(*d*)					16 2	16 8
Leucine-*iso*leucine, total	(*a*)					19 9 (*j*)	19·8 (*j*)
Leucine-*iso*leucine, D	(*c*)					13·3 (*j*)	13 4 (*j*)
Leucine, L	(*d*)					< 1	< 1
*Iso*leucine, L	(*d*)					1 0	0 9
Glutamic acid, total	(*a*)	105					
Glutamic acid, total	(*e*)	109					
Glutamic acid, L	(*f*)	24					
Diaminopimelic acid	(*a*)	84					
Glucosamine	(*a*)	58					
Ammonia	(*g*)	332	3 5 (*h*)	1·5	1 9	7·2	7 7

(*a*) Colorimetric ninhydrin method (ref. 21).
(*b*) Microbiological assay with *Leuconostoc citrovorum* (ref. 22).
(*c*) D-Amino-acid oxidase assay. An active enzyme preparation was obtained by extraction of acetone-dried sheep kidney powder with 0 017 *M* pH 8 3 pyrophosphate buffer (ref. 23) followed by high-speed centrifugation. To the test sample in 1·3 ml. volume in water were added 1 ml. of 0·1 *M* pH 8 3 pyrophosphate buffer and 0 2 ml. enzyme and the mixture incubated at 37° with shaking for 1 hr. One ml. of 0·1 per cent 2,4-dinitrophenylhydrazine in 2 *N* hydrochloric acid was then added, the mixture allowed to stand at room temperature for 15 min., 5 ml. of 2·5 *N* sodium hydroxide added, and the optical density at 520 mμ. read after 10 min. (ref. 24). The appropriate D-amino-acid was used as the standard. Control experiments showed no oxidation of the L-amino-acids.
(*d*) Microbiological assay with *Leuconostoc mesenteroides* (ref. 25).
(*e*) Microbiological assay as described in ref. 25, but using *Lactobacillus pentosus* 124-2 as test organism. Turbidities were read after 48–72 hr. of incubation.
(*f*) Microbiological assay (ref. 25) but using *Streptococcus faecalis R* as test organism.
(*g*) Direct Nesslerization of the ammonia fraction from the 'Dowex-50' columns with modified Nessler's reagent (ref. 26).
(*h*) Glycine (6 μmoles) and the following amino-acids of undetermined configurations were also detected; serine-threonine, 41 μmoles; valine, 8 μmoles; leucine-*iso*leucine, trace.
(*i*) The valine fraction also contained α-aminobutyric acid (*c.* 3 μmoles). Since this fraction was inert on treatment with D-amino-acid oxidase, it probably contains only L-α-aminobutyric acid.
(*j*) The possible presence of D- and/or L-allo*iso*leucine has not as yet been excluded.

to be *meso*-diaminopimelic acid, alanine, of which at least one-third was L, and glutamic acid, of which at least 85 per cent was D.

(2) Mycoside *C* of *Mycobacterium avium*. The mycosides, a new class of type-specific glycolipids of Mycobacteria, have recently been described[16]. The results reported here include two mycoside *C* fractions *Jav* 5 and *Jav* 4. *Jav* 5 was eluted from a silicic acid column by chloroform–methanol (95 : 5) and had the following properties: m.p. 210°, $[\alpha]_D = -34°$ ($c = 2·0$ per cent in chloroform). The analysis was: C, 62·16; H, 8·76; N, 4·35; OCH_3, 5·52; acetyl, 5·50 per cent. ($C_{80}H_{137}N_5O_{24}$ requires: C, 61·84, H, 8·89, N, 4·51, 3 OCH_3, 5·86, 2 acetyl, 5·54). *Jav* 5 appears to be a pentapeptide linked to a hydroxy acid of approximate composition $C_{32}H_{64}O_3$, the whole being linked to 3 molecules of partially O-methylated 6-deoxyhexoses containing two O-acetyl groups[17]. *Jav* 4 was isolated from the same extract as *Jav* 5 by elution from silicic acid with chloroform–methanol (94 : 6) and had the following properties; m.p. > 200°, $[\alpha]_D = -44°$ ($c = 1·9$ per cent in chloroform). The per cent analysis was: C, 58·68; H, 8·57; N, 3·82; OCH_3, 6·62; acetyl, 6·90 ($C_{78}H_{131}N_5O_{23}$ requires: C, 59·07; H, 8·35; N, 4·48; 3 OCH_3, 5·87; 2 acetyl, 5·43). The probable structure of *Jav* 4 is a pentapeptide linked to a hydroxy acid of approximate composition $C_{34}H_{68}O_3$, the whole being linked to 4 molecules of partially O-methylated 6-deoxyhexoses containing two O-acetyl groups[17].

(3) Mycoside *C* of *Mycobacterium marianum*. This substance (m.p. 198–200°, $[\alpha]_D = -31°$ in chloroform, C, 64·65; H, 8·52; N, 4·70; OCH_3 5·02; acetyl, 6·53 per cent) was isolated by Michel and Chaput[18] (Laboratory of Biochemistry, Faculté Catholique, Lyon) from a strain isolated by Sister Marie-Suzanne and Penso[19] from a leproma and now classified as a non-photochromogenic or avian strain.

(4) Peptido-lipid of *Nocardia asteroides*. Results are given for two separate preparations of the peptido-lipid of this organism[20].

Each sample was hydrolysed in 6 *N* hydrochloric acid at 105° for 24 hr. After evaporation to dryness *in vacuo*, the hydrolysate was dissolved in a small amount of water and placed on a 'Dowex-50 (H^+)' column (9 × 850 mm., 200–400 mesh). The column was developed successively with 1, 2·5, and 4 *N* hydrochloric acid[4], and the effluent collected in 5-ml. fractions. Aliquots of each fraction were analysed by the ninhydrin method of Yemm and Cocking[21]. The ninhydrin-positive fractions were concentrated *in vacuo* to dryness and the residues dissolved in 5 ml. of water and analysed. The results are given in Table 1.

Table 2. PAPER CHROMATOGRAPHY OF THE 'THREONINE' FRACTIONS OF THE MYCOSIDES OF *M. avium* AND *M. marianum*

Compound	R_F* (allothreonine)
DL-Allothreonine	1 00
Jav 4 'threonine'	0 99
Jav 5 'threonine'	0 99
M. marianum 'threonine'	0 97
DL-Threonine	1 39
DL-Serine	0·62

* Solvent system: upper phase of *n*-butanol : water acetone : concentrated ammonia (200 : 150 : 25 25) (ref. 27). Due to variability in absolute R_F values, values are given relative to allothreonine. R_F (allothreonine) = 0 11–0·13

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The 'threonine' fractions from the 'Dowex-50' chromatography of the hydrolysates of the mycosides of *M. avium* and *M. marianum* were chromatographed on paper and showed only a single ninhydrin-reacting spot corresponding in position to allothreonine (Table 2) and no serine or threonine. Since D-allothreonine is attacked by D-amino-acid oxidase[13], the configuration of the allothreonine was determined by this method (Table 1). That the substance was eluted from the column in the correct position for allothreonine was demonstrated by the overlapping emergence of threonine and allothreonine, the former slightly preceding the latter, when a mixture of these compounds was chromatographed on a 'Dowex-50' column and then eluted with 1 *N* hydrochloric acid.

The results demonstrate the widespread occurrence of D-amino-acids in the peptido-lipids and peptido-glyco-lipids of members of the order Actinomycetales. The alanine of 'Wax *D*' of *M. tuberculosis* var. *hominis* was found to be 1/3 D and the glutamic acid 78 per cent D, values essentially in agreement with those previously reported[15]. It is probable that the glutamic acid of this substance is completely of the D-configuration and that a certain amount of L-glutamic acid may have arisen from racemization during hydrolysis[4]. The mycosides of *M. avium* and *M. marianum* are unusual in that all the amino-acid components (alanine, allothreonine, and phenylalanine) possess the D-configuration. An additional unusual feature in these substances is the occurrence of D-allothreonine, a compound not hitherto reported in a natural product. D-Allothreonine would result from racemization of the α-carbon atom of L-threonine, and this may be the pathway by which it is formed by the micro-organism. The peptido-lipids of *N. asteroides* differ considerably in composition from the mycosides. They contain threonine, valine and proline, all of the usual L-configuration, and alanine, which appears to be 2/3 D. The composition with regard to leucine and *iso*leucine has not been completely clarified. It is clear that there are only negligible amounts of L-leucine and of L-*iso*leucine present. The discrepancy between total leucine plus *iso*leucine as determined by ninhydrin and D-leucine plus D-*iso*leucine as determined by D-amino-acid oxidase would suggest the presence of L-allo*iso*leucine. These results also do not exclude the possibility of the presence of D-allo*iso*-leucine. Experiments to clarify this point are in progress.

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NEW PATHWAYS IN THE OXIDATIVE METABOLISM OF AROMATIC COMPOUNDS BY MICRO-ORGANISMS

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THERE exists a restricted number of pathways open for the breakdown of naturally occurring aromatic amino-acids in mammalian metabolism; inherited blocks in these have greatly influenced the development of our concepts of biochemical genetics[1].

Micro-organisms, however, are the main agents which release organic carbon locked up in benzenoid structures by the plant world. Although they display a notorious versatility in this respect, only two methods of cleavage of the aromatic nucleus by microbial enzymes have been clearly demonstrated, until very recently. These are: (1) Oxidative fission of the bond between carbon atoms bearing the hydroxyl groups of an *o*-dihydroxyphenol (for example, Fig. 1*a* and *b*): catechol → *cis-cis*-muconic acid by pyrocatechase[2,3]; protocatechuic acid →

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cis-cis-β-carboxymuconic acid through the action of protocatechuic acid oxidase[4,5]. β-Oxoadipic acid is eventually produced in both these cases[6,7], which is then enzymically split to acetyl-coenzyme *A* and succinate, to be metabolized by reactions of the tricarboxylic acid cycle[8,9]. This ring cleavage mechanism appears to play little or no part in mammalian metabolism. (2) Rupture of the bond between the carbon atom bearing a hydroxyl and an adjacent carbon atom carrying a carbon side-chain or carboxyl (for example, Fig. 2): homogentisic acid → maleyl-acetoacetate by homogentisicase[10,11]; gentisic acid → maleyl-pyruvate by gentisicase[12-14]. This method is common to micro-organisms and mammals.

It appeared until recently that the main problems of interest in the catabolism of aromatic compounds by the lower organisms were those concerned with unexplored reaction sequences leading to the already known modes of ring-fission. Work at Leeds and Bangor has now made it clear that this view is much too limited; the established mechanisms of disruption of the aromatic ring, and subsequent reactions leading from the benzene nucleus to the citric acid-cycle, are by no means ubiquitous in their occurrence. In many soil bacteria, pathways of dissimilation of aromatic compounds exist which are radically different from those previously described.

Furthermore, the clear separation, as in Fig. 1*a* and *b*, of known channels cannot now be justified for all species of microbes, for example, enzyme systems from *Neurospora crassa*[5], some *Pseudomonads*[4], a *Vibrio* (0/1)[15], and *Nocardia*[16], all split protocatechuic acid to *cis-cis*-β-carboxymuconic acid from which they afterwards produce β-oxoadipic acid, but the intermediary steps employed may differ somewhat. Moreover, the preliminary steps by which various aromatic compounds are converted to the compound which undergoes fission (that is, catechol, or protocatechuic acid, etc.) also prove to be more diverse than hitherto suspected, since an anaerobic decarboxylase has been discovered in some organisms[17,18], whereby a carboxyl group attached to the benzene nucleus is replaced by hydrogen.

Throughout this work, summarized here, both departments have benefited by a free exchange of information and biochemicals.

New Modes of Aromatic Ring-fission by Bacteria

(1) *Cleavage of protocatechuic acid by a new enzyme —'protocatechuic acid 4 : 5-oxygenase'*: Dagley and Patel[19] disrupted cells of a *Pseudomonas* grown with *p*-cresol as carbon source, the cell-free extract oxidized each mole of protocatechuate with the uptake of 1 mole of oxygen, but no carbon dioxide was liberated. Similar extracts of *Vibrio* 0/1[15] also oxidized protocatechuate; 1 mole of oxygen was utilized, 1 mole of carbon dioxide was evolved, and β-oxoadipate was produced. In the case of the *Pseudomonas* system the product was a white, crystalline, dibasic acid, m.p. 235°, shown by Trippett, Dagley and Stopher[20] to be 2 : 4-lutidinic acid. The formation of the nucleus of pyridine as a consequence of oxidizing that of benzene was surprising; the realization that it had occurred was delayed by the coincidence that the percentage of carbon and hydrogen in lutidinic acid monohydrate is practically

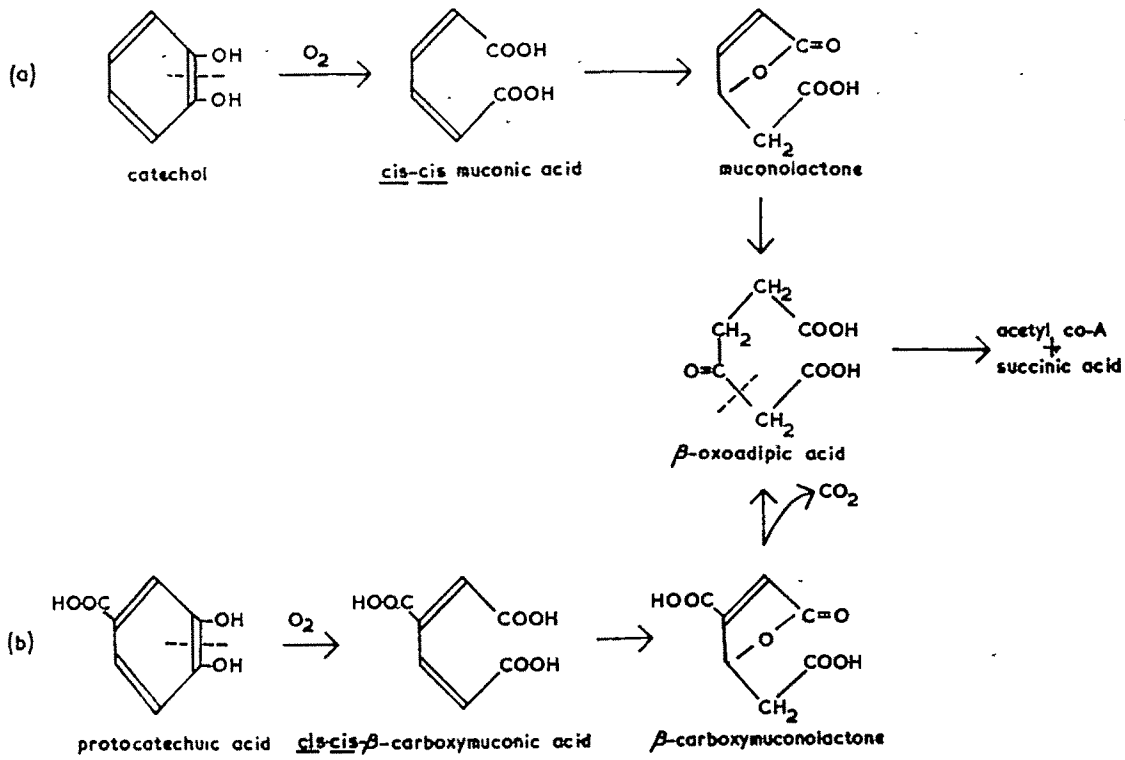

Fig. 1. Oxidative fission of *o*-dihydroxyphenols by some micro-organisms. *a*, Pathway of dissimilation of catechol by some *Pseudomonads*; *b*, pathway of dissimilation of protocatechuate by *Neurospora crassa*

the same as that for a compound formed from 1 mole of protocatechuic acid and 1 mole of oxygen. Stopher *et al.*[20], using dialysed enzyme extracts of this *Pseudomonas*, showed that the initial product formed from protocatechuate was an acid possessing reactive carbonyl groups, and with an absorption spectrum shown in Fig. 3*a*. Ribbons and Evans[42] followed this reaction in a respirometer, and as soon as it reached completion, extracted the keto-acid into ethyl acetate. It was re-extracted into dilute aqueous sodium hydroxide or carbonate, giving a characteristic yellow colour to the solution (reminiscent of keto-enol tautomerism), which persisted. When dilute ammonia, however, was used, the yellow colour initially produced vanished within a few minutes, and a new compound was formed having spectrographic and chromatographic properties identical with 2 : 4-lutidinic acid. It is clear, therefore, that in the original experiments of Dagley and Patel[19], this compound was formed by a non-enzymic reaction between the initial product of ring-fission and the ammonium ion, present accidentally in the cell-free extract, since ammonium sulphate had been used for its fractionation. These facts support the formula, α-hydroxy-γ-carboxymuconic semialdehyde (6-formyl-4-carboxy-2-oxohex-4-enoic acid) we assign to the intermediate. It gives an acidic *bis*-2 : 4-dinitrophenylhydrazone, m.p. 170–2° (decomp.) and is somewhat unstable on recrystallization (Found: C, 39·8, 43·5; H, 3·4, 3·8; N, 19·2, 20·6; $C_{18}H_{14}N_8O_{12}$ requires C, 41·8; H, 2·6; N, 20·6 per cent).

When a non-dialysed cell-free preparation of this *Pseudomonas* is used to oxidize protocatechuate, α-hydroxy-γ-carboxymuconic semialdehyde is further metabolized to give a compound containing an additional carboxyl group, but the carbonyl groups have now disappeared. This second acid has a characteristic absorption maximum at 284 mμ and forms a *p*-bromophenacyl derivative (tri-ester) m.p. 101–2°; the fact that it appears without any further gaseous exchange supports the view that an internal oxidation-reduction is involved, to give 2-hydroxy-4-carboxy-2 : 3-dihydromuconic acid (5-hydroxy-3-carboxyhex-2-enedioic acid). Concentrated, dialysed enzyme extracts degrade protocatechuate further, with the production of pyruvate as one end-product. In the presence of sodium arsenite (5×10^{-3} *M*) and/or pyridine-3-sulphonic acid (2×10^{-2} *M*), whole cells oxidize protocatechuate with substantial accumulation of pyruvate and oxaloacetate. The suggested sequence of reactions of the new pathway are depicted in Fig. 4. The fission proposed for 2-hydroxy-4-carboxy-2 : 3-dihydromuconic acid has not been demonstrated for cell-free systems; this investigation is in progress.

The two different ring-cleavage mechanisms of protocatechuic acid may be followed stoicheiometrically in an automatic titrator, as shown in Fig. 5*a* and *b* with the following results:

Dialysed, cell-free preparations from organisms employing the 3 : 4-split produce from protocatechuate two equivalents of acid, with the formation of *cis-cis*-β-carboxymuconate; undialysed extracts produce approximately 1·3 equivalents with stoicheiometric formation of β-oxoadipate (one carboxyl group having been lost through decarboxylation).

Dialysed, cell-free preparations from microbes performing the 4 : 5-split acting on protocatechuate, give rise to one equivalent of acid with the formation of α-hydroxy-γ-carboxymuconic semialdehyde ($\lambda_{max.}$ 293 mμ (acid); 410 mμ (alkali)); undialysed extracts metabolize this keto-acid further, with the appearance of a second acid equivalent, corresponding to 2-hydroxy-4-carboxy-2 : 3-dihydromuconate ($\lambda_{max.}$ 284 mμ).

(2) *Cleavage of catechol by a new enzyme—'catechol 2 : 3-oxygenase'*: The degradation of catechol by two strains of Gram-negative bacteria has been investigated by Dagley and Stopher[21]. One was supplied by Dr. Eileen Pankhurst, London Research Station of the Gas Council, and readily grows with *m*-cresol as sole carbon source; the other was isolated from garden soil, and utilizes *o*-cresol. Cell-free extracts from either organism oxidized 1 mole of catechol with the uptake of 1 mole of oxygen, but no carbon dioxide was evolved. During the reaction a transient yellow colour was produced, shown to be due to an

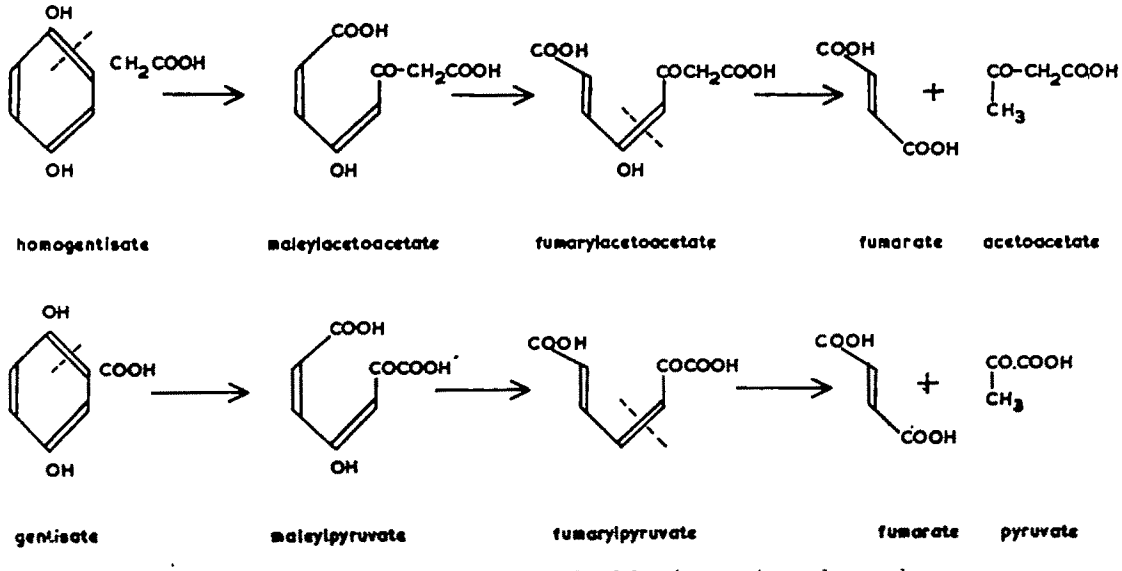

Fig. 2. Oxidative fission of *p*-dihydroxyphenols by micro-organisms and mammals

acidic intermediate; it gave an immediate bright orange colour with *o*-dianisidine (aldehyde test), and formed a *bis*-2 : 4-dinitrophenylhydrazone derivative. The keto-acid absorbed strongly at 373 mμ in neutral or alkaline solution; in acid this absorption and the yellow colour were abolished, and another peak appeared at 317 mμ (Fig. 3*b*). Clearly, this intermediate has similar properties to α-hydroxy-γ-carboxymuconic semialdehyde, although it differs in being much less reactive towards ammonia, since α-picolinic acid is formed only after standing with ammonium hydroxide for two days at room temperature[20]. Fortunately, it proved possible to isolate the intermediate itself. Stopher observed that when cell-free extracts of the *o*-cresol-utilizing *Pseudomonad* were maintained at 53° for 10 min., the enzymes that degraded the intermediate were destroyed, but not those involved in its production from catechol. By use of heat-treated extracts, a small quantity of an orange-coloured solid was isolated, which on analysis gave: C, 50·9; H, 4·3. α-Hydroxymuconic semialdehyde (6-formyl-2-oxohex-4-enoic acid), $C_7H_6O_4$ requires C, 50·8; H, 4·2 per cent. When reduced with platinum in ethanol, reactions for carbonyl groups were no longer given, and 3 moles of hydrogen were taken up per mole of substance, as required for reduction of two double bonds and one aldehyde group.

Untreated extracts gave pyruvate as one end-product of catechol oxidation, and the reaction could be followed in a spectrophotometer by measurements of absorption at 275 mμ ($\lambda_{max.}$ for catechol) and at 430 mμ where the intermediate absorbs (though not maximally) but catechol does not. During the course of this experiment the intermediate was rapidly formed and then degraded; *cis-cis*-muconic acid, present in a control vessel, was not attacked by the extract (Fig. 6). A heat-treated extract which decomposed catechol also attacked 4-methylcatechol to form an intermediate with an absorption spectrum similar to that from catechol ($\lambda_{max.}$ = 378 mμ) but differing in some details. Various other phenolic compounds were not attacked.

For certain strains, notably the *Pseudomonas* of Dagley and Patel[19], ferrous ions can readily be shown to be a requirement for the enzymes catalysing the new mode of ring-fission but in other cases, the iron, if it should prove to be essential, is very strongly bound to the protein and cannot be removed by dialysis.

The product of ring-fission of catechol (α-hydroxymuconic semialdehyde) has already been encountered in work with mammalian systems. Wiss[22], and Mehler[23], have shown that an enzyme from liver oxidizes 3-hydroxyanthranilic acid to a derivative of muconic semialdehyde (Fig. 7). On standing in acid, carbon dioxide and ammonia are lost to form a compound, the spectrum of which agrees with that shown in Fig. 3*b*, and is similarly affected by changes in *p*H (ref. 23). Dr. Mehler kindly supplied us with a small amount of this compound; although not pure, material present which absorbed strongly at 375 mμ was rapidly decomposed by our cell-free extracts.

One product of the action of crude bacterial extracts on α-hydroxymuconic semialdehyde has been identified as pyruvate (Fig. 7), but details of the degradation are not yet known. By analogy with the reactions of Fig. 4 it might be suggested that the semialdehyde is first converted into 2-hydroxy-2 : 3-dihydromuconate, although in this case extracts have not been obtained which accumulate this compound. It is conceivable that 2-hydroxy-2 : 3-dihydromuconate would then undergo a hydrolytic split between carbon atoms 3 and 4 to produce malonic semialdehyde and lactate; a coupled oxidation-reduction would then produce pyruvate and β-hydroxypropionate.

Proctor and Scher[18] have recently investigated the metabolism of benzoate by a *Rhodopseudomonas* strain, and found that the pathway of degradation by this organism is different from those described to date, but consistent with the following sequence: benzoate → protocatechuate → catechol → an unidentified α-oxo acid which appears to be similar to α-hydroxymuconic semialdehyde. Extracts of this organism degraded catechol to an α-oxo acid only when hydrogen peroxide was added; oxygen would not be substituted. This system appears to differ therefore

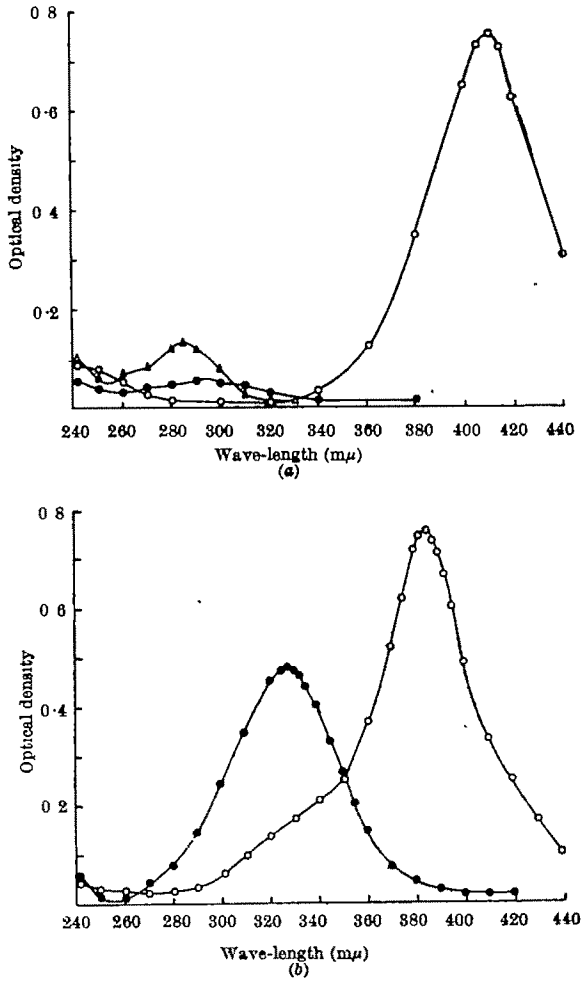

Fig. 3. Absorption spectra of the new ring fission products. *a*, Initial ring fission product (α-hydroxy-γ-carboxymuconic semialdehyde) of protocatechuate oxidation by protocatechuic acid 4 : 5-oxygenase. In acid (—●—), in alkali (—○—); molar extinction coefficient at λ_{max} = 410 mμ is 29,000. Also of the further metabolite, 2-hydroxy-4-carboxy-2 . 3-dihydromuconate (—△—). molar extinction coefficient at $\lambda_{max.}$ = 284 mμ is 5,000. Molar extinction coefficients are calculated on the basis of protocatechuate oxidized

b, Initial ring fission product (α-hydroxymuconic semialdehyde) of catechol oxidation by catechol 2 : 3-oxygenase. In acid (—●—), in alkali (—○—); molar extinction coefficient at $\lambda_{max.}$ = 378 mμ (*p*H 7 3) is 29,700, calculated for a solution of the purified compound containing 2 7 μgm./ml.

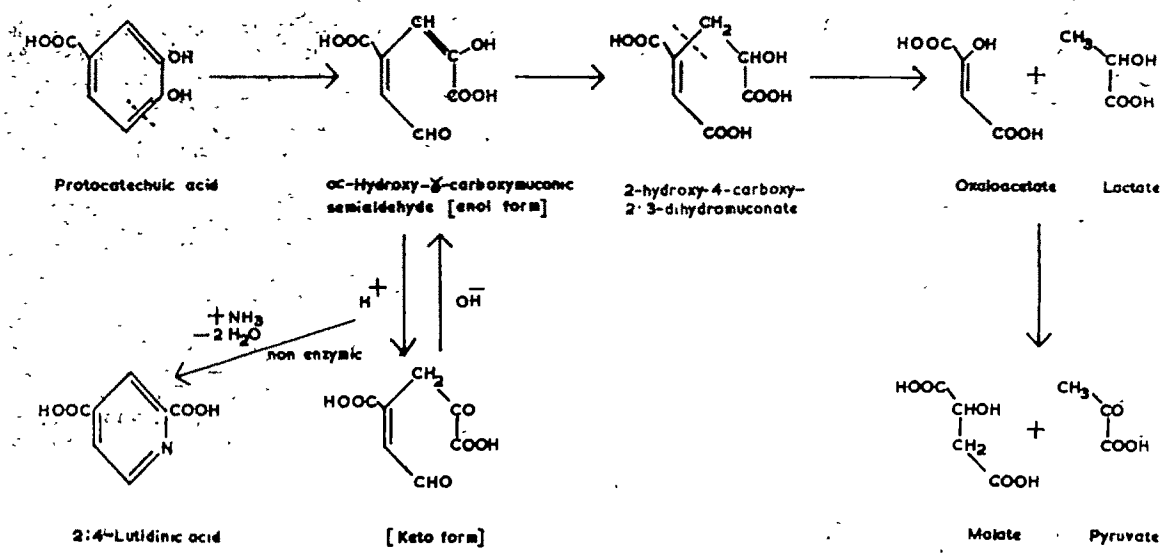

Fig. 4. Suggested new pathway of protocatechuate oxidation by micro-organisms which possess the protocatechuic acid 4 : 5-oxygenase system

from both pyrocatechase and catechol 2 : 3-oxygenase, and may well be yet another ring-fission enzyme. Their observations, published in abstract form, are complicated, since whole cells in the presence of oxygen or hydrogen peroxide produced a β-oxo acid (identity not disclosed) from catechol.

(3) *Variations in the subsequent pathway of cis-cis-β-carboxymuconic acid:* Several microbial species metabolize protocatechuate through *cis-cis*-β-carboxymuconate to the common intermediate β-oxoadipate; it now transpires that the intervening steps are not identical in all cases. Gross, Gafford and Tatum[5], using 2 : 6-$^{14}C_2$-labelled protocatechuic acid, showed that the carbonyl-C of β-oxoadipate produced by a *Neurospora crassa* enzyme system originated solely from C-6 of protocatechuate, whereas using a *Pseudomonas fluorescens* system (strain *A*, 3·12, Stanier) it was randomly derived from C-1 and C-6 of this substrate. This *Pseudomonas* route diverges from the *Neurospora* pathway (shown in Fig. 1*b*) after the *cis-cis*-β-carboxymuconate stage, since β-carboxymuconolactone was not attacked; *cis-cis*-muconate and muconolactone were not degraded by either of these enzyme systems. The tracer results for this *Pseudomonas* pathway imply the formation of a symmetrical precursor to β-oxoadipate, which

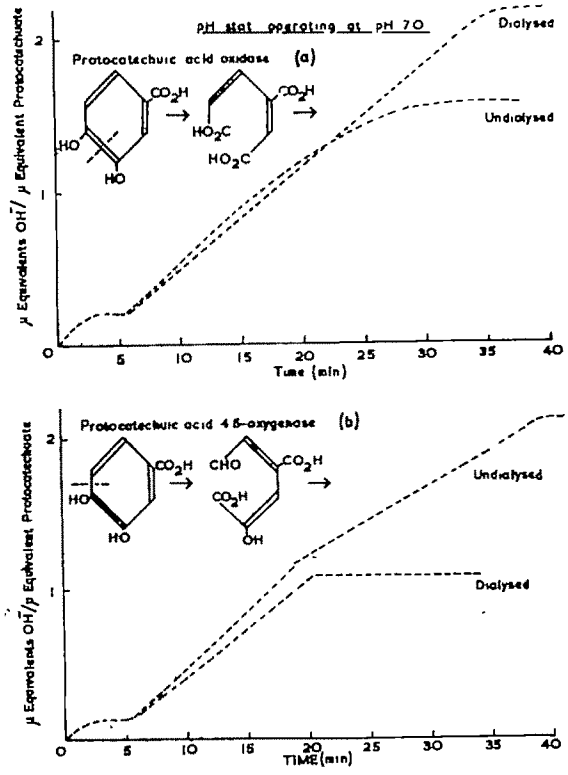

Fig. 5. A comparison of acid production during ring fission and further metabolism of protocatechuate by: *a*, protocatechuic acid oxidase; and *b*, protocatechuic acid 4 : 5-oxygenase

The reaction cuvette contained enzyme solution (sonic extracts in distilled water, 1 ml.) as indicated, and distilled water (4 ml.), brought to *p*H 7. Temperature, 30°. Reactions were initiated by addition of protocatechuate (10 μmoles in 1 ml. water, previously neutralized to *p*H 7). The micro-burette contained 0·1 *N* sodium hydroxide, and automatic additions during reaction were recorded graphically (Radiometer, Ltd., Copenhagen)

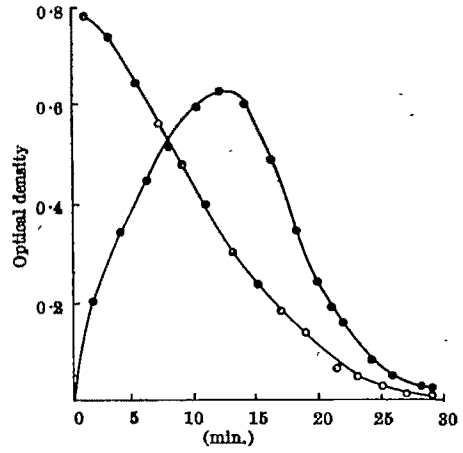

Fig. 6. Spectrophotometric assay of catechol oxidation by the catechol 2 : 3-oxygenase system. Optical density due to catechol at 275 mμ (—○—); optical density due to α-hydroxymuconic semialdehyde at 430 mμ (—●—)

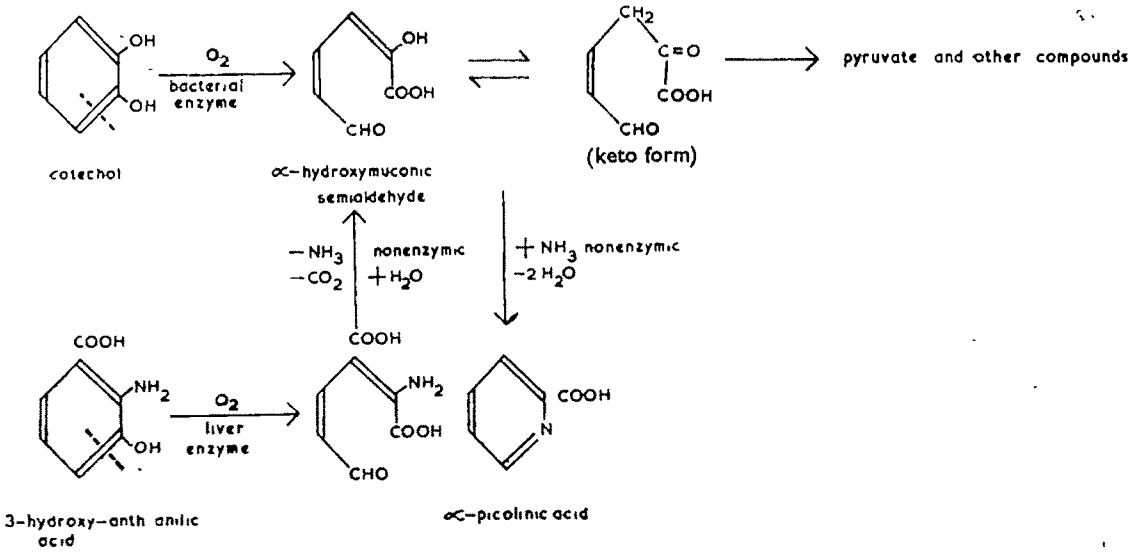

Fig. 7. Suggested new pathway of catechol oxidation by micro-organisms possessing the catechol 2 : 3-oxygenase system. The formation of α-hydroxymuconic semialdehyde from catechol, and its relation to the ring fission product of 3-hydroxyanthranilate by the liver enzyme, is indicated

Elsden and Peel[24] suggested might be the dilactone of *cis-cis*-muconic acid (butanolido-βγ-γ′β′-butanolide). Cain, Ribbons and Evans[25] found that this dilactone gave rise to β-oxoadipate with extracts from another *Pseudomonas* strain and *Vibrio* 0/1 induced to protocatechuate. At slightly acid, neutral and alkaline *p*H, however, the dilactone itself underwent a non-enzymic rearrangement to muconolactone. Moreover, muconolactone also produced β-oxoadipate with these enzyme systems. The spontaneous hydrolysis of the dilactone to muconolactone followed by enzymic attack on this product is responsible for apparent attack on the dilactone itself; this dilactone cannot therefore be an intermediate in these particular systems, but ββ′-dihydroxyadipate and carboxydilactone are further possibilities to be explored. Cain[15] has shown that muconolactone, which he rigidly identified, accumulated when heat-treated extracts of *Vibrio* 0/1 grown on *p*-hydroxybenzoate oxidized protocatechuate with consumption of 1 mole of oxygen and the evolution of 1 mole of carbon dioxide per mole of substrate. From these results it is probable that muconolactone is an intermediate in the conversion of *cis-cis*-β-carboxymuconate to β-oxoadipate by *Vibrio* 0/1 and by some, but not all, *Pseudomonas* strains (Fig. 8).

Yet another route from *cis-cis*-β-carboxymuconate to β-oxoadipate is taken by *Nocardia erythropolis* according to the work of Cain and Cartwright[16]. A lactone-like intermediate is produced having $\lambda_{max.}$ at 215–218 mμ; it differs from any known lactone of these series, and awaits identification.

(4) *Diversity of pathways in the oxidative metabolism of aromatic compounds prior to ring fission.* Hayaishi and Stanier[26] showed that there were two distinct pathways of tryptophan metabolism among the *Pseudomonads*. Most organisms oxidize this amino-acid through kynurenine, anthranilate and catechol; some strains diverge from this sequence at the kynurenine stage, producing kynurenic acid, the subsequent fate of which has been partially clarified[27].

Microbial dissimilation of phenylacetate shows an analogous dichotomy, as demonstrated by Kunita; one strain of *Pseudomonas fluorescens* produces homoprotocatechuate[28] from this substrate, while another appears to take the homogentisate route[29].

The pathways employed for the utilization of the benzoates among microbial species and strains prior to ring-fission, discovered to date, are illustrated with references in Fig. 9; a more remarkable diversity than was at one time supposed is clearly evident.

The enzymic transformations involved in these reactions are hydroxylations or perhydroxylations (followed by dehydrogenation), and decarboxylations or oxidative decarboxylations. The particular route taken by a micro-organism capable of utilizing an aromatic compound will presumably depend on its genetic potential, coupled with the influence of

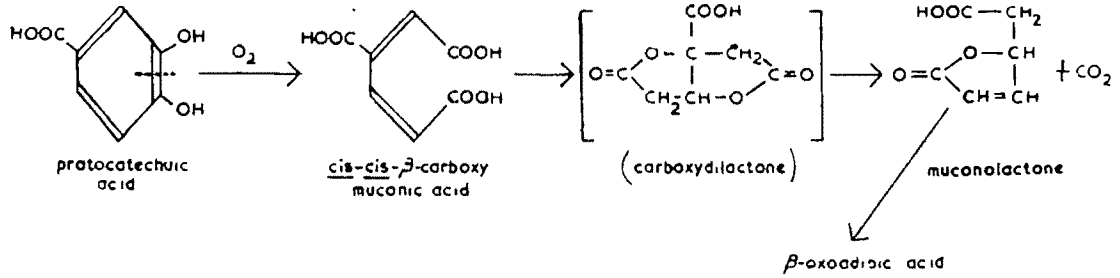

Fig. 8. Pathway of dissimilation of protocatechuate by *Vibrio* 0/1. The carboxydilactone step is hypothetical

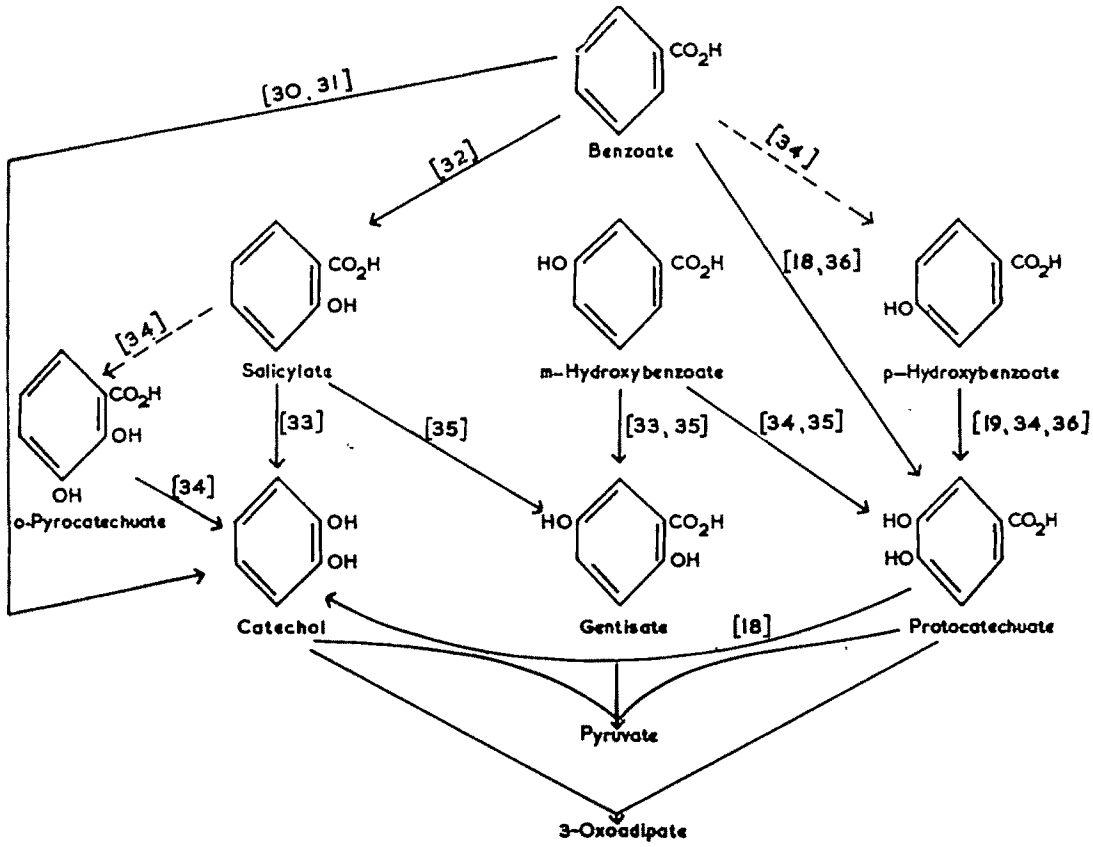

Fig. 9. Diversity in metabolism of the benzoates by micro-organisms

environment, for the syntheses of the relevant enzymes.

Micro-organisms which degrade polycyclic aromatic compounds appear to employ a stepwise, end-ring attack (for example, naphthalene, anthracene, phenanthrene and their derivatives)[38–40]. The discovery of this new method of ring cleavage now makes it probable that there exist several alternative routes for the metabolism of condensed ring systems. Similarly, the metabolism of herbicides of aromatic nature by soil microbes[40,41] may well show diversity due to species and/or strains.

Although we have no statistics as to the relative prevalence of the various modes of ring fission, bacteria which employ all of them abound in the soil.

We wish to thank the Department of Scientific and Industrial Research and the Agricultural Research Council for their financial support.

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LETTERS TO THE EDITORS

GEOPHYSICS

Formation of the Sporadic *E* Layer in the Temperate Zones

In a recent communication Heisler and Whitehead[1] noted that the fraction of time the critical frequency of the sporadic E layer (f_0E_s) exceeded 5 Mc./s. depended on the horizontal component of the Earth's magnetic field, increasing as the horizontal component increased. This relationship is consistent with sporadic E formation arising from a vertical gradient of horizontal movement of the neutral air. In a region where the gyro-frequency of the ions, ω_{Hi}, is less than their collision frequency, ν_i, it is possible to show that, if there is no vertical electric current and the net horizontal current is zero (a horizontal current at one height being cancelled by a reverse current at some other height), the vertical velocity of ions and electrons is given approximately by :

$$V_z \sim \frac{-\omega_{Hi} \cos \theta}{\nu_i} \cdot \Delta U_y$$

where θ is the dip angle and ΔU_y is the departure of the horizontal wind velocity at right angles to the Earth's magnetic field from the mean value in the region. A thin layer of ionization will form where V_z is zero but where the vertical gradient of V_z is large. The probability of such formation depends on $\omega_{Hi} \cos \theta$, which is proportional to the horizontal component of the Earth's magnetic field.

Thus the global distribution of E_s in the temperate zones may be explained.

A more detailed analysis shows that at the height at which an E_s layer is already formed, ΔU_y, and hence V_z, remain nearly zero, independent of the horizontal winds. Thus the E_s layer continues to form at the same height. This explains the persistence of the E_s layer even when the horizontal winds leading to its original formation might be expected to have changed.

The detailed analysis will be presented elsewhere.

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Electrical Engineering Department,
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Telluric Current Micropulsations on Arctic Drifting Station Charlie

Telluric current recording equipment was operated on Arctic Drifting Station Charlie during the epoch October 15–December 31, 1959. The station was located on a 4-mile by 7-mile ice floe of quite uniform thickness, the thickness averaging perhaps 10 ft. The electrodes consisted of 8-ft. by 2-in. lead strips prepared from electric cable sheathing. Electrode pairs were cut from continuous lengths of sheathing to assure identity of material in the two electrodes. No difficulty was experienced with contact potentials. The d.c. voltage never exceeded a few millivolts and was very steady. The electrodes were suspended in the sea just below the ice at a spacing of 1·082 km. The relatively long spacing was necessary because of the low mV./km. values experienced over the highly conducting sea water.

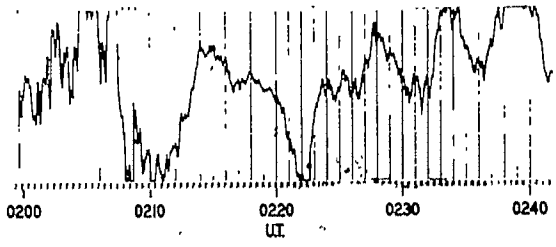

Fig. 1. Telluric current, Arctic Drifting Station Charlie, December 11, 1959

On December 11, 1959, micropulsations of less than 1-sec. period were recorded for an interval of more than 2 hr. On this date the floe was located at 75° 57′ N. and 171° 01′ W., which corresponds to geomagnetic co-ordinates of 70° 55′ N. and 222° 33′ E. During the afternoon of this day (0200–0240 U.T.) a very sensitive recorder, 2 mV. full scale on the 1·082 km. spaced electrodes, was operated to search for micropulsations. Even though this was a very quiet period, based on normal recording, it was necessary to return the pen to scale several times by inserting a voltage in the electrode lines. This trace is presented as Fig. 1. A slight widening of the trace is evident, but the effect is so small as to be inconclusive as an indication of the occurrence of micropulsations.

On returning to the laboratory in the evening a quiet auroral arc was observed. The arc extended to the horizons and passed through the zenith. The normal sensitivity telluric current recorders were essentially quiet, the normal condition during such an auroral display. The high-sensitivity recorder was reconnected to the electrodes and the trace of Fig. 2 recorded. It is impossible even on the original trace to discern the individual fluctuations. However, the upward motions of the pen were counted by visual observation for six 1-min. intervals, extended over an hour of the activity. These counts gave 70, 70, 70, 67, 68, and 70 cycles per minute. It was also noted that the rate of fluctuation tended to be very uniform throughout the activity. The amplitude of the pulsations ranged from 0·05 to 0·10 mV./km. The circumstances of the experiment assure beyond any reasonable doubt that these were natural micropulsations and not variations introduced by the instrumentation.

No previous record of telluric current micropulsations of this short period has come to my attention.

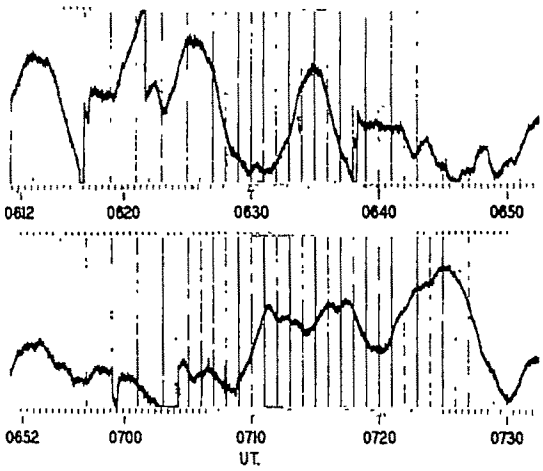

Fig. 2. Telluric current micropulsations, Arctic Drifting Station Charlie, December 11, 1959

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PHYSICS

Shock Excitation of Solid Aromatic Hydrocarbons

SHOCK excitation of a wide range of powdered inorganic solids (mainly metallic oxides) by helium-driven shock-waves in argon[1] has not only provided a powerful means of producing relatively clean spectra of astrophysically important diatomic molecules[2], but also has given some insight into the physical processes which take place when the powder particles undergo severe thermal transients. From the general observation that molecular spectra alone are excited (in the hot stagnant region behind the reflected shock wave) at low temperatures (~2,000° K.), mixed molecular and atomic spectra are excited at intermediate temperatures (~5,000° K.) and entirely atomic spectra are excited at high temperatures (~10,000° K.), and from other experimental considerations (refs. 1*a* and 1*c*), it is thought that a predominantly atomic vapour is evaporated from the solid inorganic surfaces, which, if the temperature is low enough, partially or completely recombines to form diatomic species. It is therefore a logical extension of this work to examine the variation with environmental temperature of the spectra from shock excitation of powdered organic materials, and in this communication experiments with benzene, naphthalene, and anthracene are discussed.

Greene[3] has examined the spectra from shock excitation of the aliphatic vapours: (*a*) XCN (X = Br, Cl); (*b*) CX_3Y (X = H, F; Y = Br, I) and reports the presence of CN violet bands and C_2 Swan bands in the case of (*a*), and a carbon particle continuum, C_2 Swan bands, and a CH band in the case of (*b*). Fairbairn and Gaydon[4] have reported spectra from the shock excitation of a much wider variety of aliphatic vapours, and find that the carbon particle continuum and the C_2 Swan bands predominate while OH and CN sometimes appear. They find no trace of CH even for molecules containing C and H. Johnson and Campbell[5] report CH and C_2 bands in absorption through shock-heated benzene vapour.

In our experiments a few grams of each powdered solid to be studied were placed at the end window of a small shock-tube (except in the case of benzene, which was frozen on to the inner wall of the shock tube near the window by means of an external dry ice jacket). A series of spectra were photographed on a Hilger *f*/4 spectrograph over as large a range of calculated stagnant-region temperatures as possible. These temperatures are undoubtedly inaccurate as they take no account of the contamination of the argon with organic vapours. However, Parkinson and Nicholls (refs. 1*d*, 6) have shown that (in shock-excitation of inorganic solids) the rotational temperature of the CN molecule is only about 10–15 per cent lower than the calculated gas kinetic temperature, and in good agreement with the temperature inferred from the measured shock-speed. The shock tube was cleaned and recharged with organic material between each exposure.

In each case the main contributions to the spectra were the (0;0,1,2) (1;0,1,2,3) (2:0,1,2,3,4) (3;1,2,3,4,5) (4;2,3,5,6) (5;6) C_2 Swan bands, the (0;0,1) (1;1,2)

Table 1. SPECTRA FROM SHOCK EXCITATION OF SOLID BENZENE, NAPHTHALENE AND ANTHRACENE

Temperature range used	Benzene 4,900–8,440° K.			Naphthalene 3,890–13,000° K.			Anthracene 3,630–12,020° K.		
	Temp. of appearance	Temp. of maximum intensity	Comments	Temp. of appearance	Temp. of maximum intensity	Comments	Temp. of appearance	Temp. of maximum intensity	Comments
Atomic impurities (Na, Ca)	4,900°	6,990°	Present at lowest temp. Not present at 8,440°	3,890°	6,870°	Not present at 13,000°	—	—	—
C-particle continuum	—	—	Benzene not in powder form	3,890°	4,800°	Reaches low value at 6,900°, remains until 13,000°	3,630°	5,950°	Reaches low value at 6,350° and remains constant to 12,020°
C_2 Swan bands	4,900°	6,990°	Weak at 8,440°	4,800°	10,250° ?	Constant to 13,000°	5,950°	6,350°	Weak at 12,020°
CN violet bands	4,900° (weak)	6,990°	Not present at 8,440°	6,080°	?	Gradual increase to 13,000°	4,970°	5,950°	Absent above 8,600°
OH λ4315 Å. band	6,990°	?	Present at 8,440°	6,870°	?	Gradual increase to 13,000°	5,950°	6,350°	Absent above 8,600°

(2;2,3) (3;3,4) (4,5) (5,6) CN violet bands (nitrogen was an impurity in the argon), the (0,0) CH band (λ4315 Å.), and (except in the case of benzene) a carbon particle continuum the intensity and spectral range of which were extremely sensitive to temperature. The circumstances in which the various spectra appear are summarized in Table 1. The lack of carbon-particle continuum in the case of benzene is probably due to the fact that it is not powdered but a solid coating on the wall of the tube. In the case of the other two compounds, the powdered configuration and consequent large surface area gave greater chance for pyrolysis in the hot gas. Abundant solid carbon particles were present in the shock tube after each experiment.

There is a striking contrast between these entirely molecular spectra (except for a few atomic impurity lines due to sodium and calcium) over the entire temperature-range, and the smooth transition with increasing temperature from molecular to atomic spectra observed in the case of the inorganic compounds. It is therefore doubtful whether the same mechanism is operative in both cases. It seems more probable (in view of the much lower volatilization temperatures of the organic compounds) that the shock treatment causes evaporation of a molecular vapour which is pyrolysed to carbon at lower temperatures (possibly by Porter's acetylene mechanism[7] confirmed by Greene, Taylor and Patterson[8] for a number of simple hydrocarbon vapours). At higher temperatures reactions between the carbon vapour and other gases (nitrogen and hydrogen), present in the tube following pyrolysis, qualitatively explain the CH and CN spectra. Spectra of atomic carbon are not observed in the spectral range of our instrument because of the inaccessibility to thermal excitation (at the temperatures used) of the upper states of allowed transitions in C.

This work has been supported in part by contracts with the Department of Defence Production of Canada and the U.S. Air Force Cambridge Research Center, and in part by research grants from the Defence Research Board of Canada, the National Research Council of Canada and the Ontario Research Foundation. One of us (M. D. W.) gratefully acknowledges the award of scholarships by the Ontario Research Foundation.

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The Critical Phenomena between Solids and Fluids

IN the phase diagrams of simple pure substances, the unknown fundamental problem is only the upper limits of melting points. Is there any critical phenomena between solids and fluids? (Generally at their melting points solids change to gases without going through the liquid stage in the high-temperature and high-pressure range.)

Experimental research on this problem was begun by the late Sir Francis Simon and his school thirty years ago. Up to the present, investigations have been carried out up to 7,500 atm. for helium[1] and 10,000 atm. for nitrogen and argon[2], but there is no evidence of the existence of critical points. Therefore Prof. P. W. Bridgman[3] and Prof. C. Domb[4] and the others have been inclined to doubt the existence of this point. Profs. L. Landau and E. Lifschitz[5] have also stated definitely there is no intermediate state between crystal and liquidus, for these states have distinct characteristics of internal symmetry.

As this problem is of the utmost importance for understanding the structure of liquids too, I wish to discuss the problem in connexion with my structural model of liquids[6].

Recently, Prof. J. D. Bernal[7] reached the important conclusion that "there is an absolute impossibility of forming a homogeneous assembly of points of volume intermediate between those of long-range order and closest packed disorder". Therefore, by the geometrical model with its static characteristics, the liquidus (disordered) state cannot truly change to the solid (ordered) state continuously. Meanwhile[6] I have presented a simple structural model of liquids with dynamical characteristics, which is consistent with Bernal's model. From this model, the structure of liquids near their melting points is approximated by a quasi-face-centred cubic lattice in which there are many vacant sites occupying about 10 per cent of the structure, but these empty spaces are distributed through all the interstices, causing the disappearance of the long-range order of lattice. Therefore, if the concentration of vacant sites is increased up to several per cent in crystals at sufficiently high temperatures and pressures, the regular lattices of the crystals will be gradually distorted under these conditions, resulting in irregular liquid structures.

The free-energy change ΔG in going from the regular perfect crystals to this intermediate state at constant temperature and pressure is:

$$\Delta G = \Delta E + p.\Delta V - T.\Delta S \qquad (1)$$

where ΔE, ΔV and ΔS are the changes of internal energy, volume and entropy respectively. Generally, the first and second terms of the right-hand side of equation (1) are positive, and the third is negative; and generally $\Delta G > 0$, corresponding only to the low concentration of vacant sites in crystals at melting points under ordinary pressures. But, in highly compressed condensed systems, if the equilibrium positions of the bottoms of molecular potential wells are higher than zero, which corresponds to the potential energy of free gas molecules (see Fig. 1), ΔE will become negative, and in the higher temperature range $-T.\Delta S$ will also take large negative values, with the result that $\Delta G < 0$. Therefore in these highly compressed and high-temperature conditions the vacant sites will be produced spontaneously in crystals

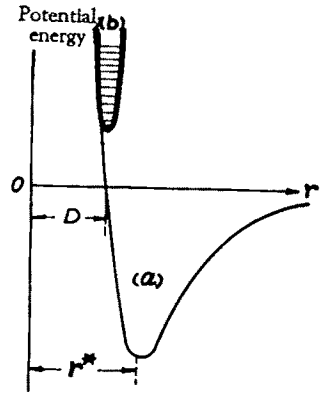

FIG. 1. Intermolecular potential curve (*a*) and a potential well of a molecule in the condensed phase (*b*)

In general, the following formulæ representing the intermolecular potentials φ is applicable to monatomic van der Waals' and metallic liquids, including spherico-symmetrical molecular liquids[6]:

$$\varphi = -ar^{-m} + br^{-n}, \qquad m < n$$

and

$$\frac{D}{r^*} = \left(\frac{m}{n}\right)^{1/(n-m)}$$

where r^* is the distance apart of molecules at the minimum potential and D is the distance at zero energy-level (see Fig. 1).

Table 1. ESTIMATED CRITICAL POINTS BETWEEN SOLIDS AND LIQUIDS

	P_c (atm.)	T_c (° K.)	V_c (c.c./mol.)	P_cV_c/RT_c	m	n
He	11–14 × 10³	65–75	6·5–6·0	14	6	12
N_2	22·8 × 10³*	302*	20	18·5	6	12
CCl_4	17·4 × 10³*	631*	60	20·2	6	12
K	2–3 × 10⁴	700–1,000	15–12	45	2	4
Fe	3–4 × 10⁴	3,000–4,000	3·9–3·5	40	4	7

* Values estimated by Ebert in ref. 8.

In 1954 the late Prof. L. Ebert[8] estimated the critical temperatures T_c and pressures P_c of nitrogen, carbon tetrachloride and other gases by ingenious extrapolations from Bridgman's experimental data (see Table 1). From his values I have estimated the critical molar volumes V_c of nitrogen and carbon tetrachloride using Bridgman's data[9] (see Table 1), and found that these values are a little smaller than the volume calculated from D and thus support my views. In an infinitesimal change of the intermediate state of critical regions, $\delta G = 0$ and (1) becomes:

$$T_c\,(\partial S/\partial V)_{P_cT_c} = P_c + (\partial E/\partial V)_{P_cT_c} \qquad (2)$$

and we can explain approximately and verify this equation for nitrogen by using the data of Table 1 and my model.

Therefore, if φ is known, V_c can be calculated approximately. Next, by the extrapolation of experimental compressibilities and fusion curves, we can estimate P_c and T_c in an effort to make the above values consistent. This procedure is made easier by using the hypothesis that the non-dimensional quantity P_cV_c/RT_c will not vary as widely in several substances. This hypothesis is supported by the fact that at the critical points between gases and liquids, it is 0·29 for the spherico-symmetrical van der Waals' gases, which have values of $n = 12$ and $m = 6$, and $0{\cdot}46 \sim 0{\cdot}77$ for mercury[10], which has lower values of n and m than the above (see Table 2).

My estimated critical values are given in Table 1. For helium I used the value of φ from Johnston and Grilly[11], the fusion curve of Holland, Huggill and Jones[1] and the molar volume of Dugdale and Simon[12]; for potassium, φ ($m = 2$, $n = 4$) was from Birch[13] and Gilvarry[14] and the data of Bridgman[3]; for iron φ ($m = 4$, $n = 7$) was from Furth[15], the density estimated by Birch[16] and Valle[17], with experimental compressibility from Walsh, Rice, McQueen and Yarger[18], and the fusion equation from Strong[19].

Table 2. EXPERIMENTAL CRITICAL POINTS BETWEEN GASES AND LIQUIDS

	P_c (atm.)	T_c (° K.)	V_c (c.c./mol.)	P_cV_c/RT_c	m	n
He	2·26	5·3	57·8	0·30	6	12
N_2	33·5	126	90·2	0·29	6	12
Hg	1,640[10]	1,730[10]	67–40[10]	0·46–0·77	6 ?[11]	8 ?[11]

My values for helium are about twice as large as those of the previous experimental region. The values for potassium and iron only have a meaning concerning the order of magnitudes owing to the low reliabilities of φ and other data, and owing to their body-centred cubic structure, which is not the close-packed structure. But it is interesting that the values for iron are near those for the Earth's core. Moreover, on the surface of the Earth's core, putting $P = 1{\cdot}4 \times 10^6$ atm., $V = 5{\cdot}74$ c.c./mol. for iron and $T = 2{,}600°$ K., which is the melting point of iron calculated from Strong's equation[19], we obtain a non-dimensional quantity $PV/RT = 37{\cdot}7$, very near that of the estimated critical point of iron. Hence it seems likely that there is an internal relation between the critical phenomena and the fluid characteristics of the Earth's core.

In any event, it will be valuable to examine, by modern techniques, the critical limits of the melting points of nitrogen or helium at pressures about twice as high or more as those used in previous experiments.

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Velocity of Ultrasonic Waves in Aqueous Solutions of Zinc Halides

ZINC and cadmium belong to sub-group II of the Periodic System. Their compounds exhibit properties characteristic of the second group. Deviations from the normal thermodynamic behaviour have been reported in the case of halides of these metals[1].

Investigation by ultrasonic radiation[2,3] of aqueous solutions of cadmium halides showed interesting deviations from the normal behaviour of electrolytic solutions. Hence, it is expected that zinc halides would also exhibit similar anomalies.

Ultrasonic velocity as a function of concentration has been studied using a variable-path, single-crystal interferometer, working at 780 kc./s. Velocity measurements were made at $32 \pm 0{\cdot}5°$ C., and are accurate to $\pm$ 0·15 per cent.

Experimental results showing the variation of velocity with molar concentration are presented in Fig. 1. All the halides show exceptional behaviour. In the case of zinc chloride, the velocity increases with concentration up to $0{\cdot}25\,M$, after which it decreases continuously, reaching a value of 1,503 m./s. at $1{\cdot}5\,M$. Thereafter the velocity remains constant in the concentration-range studied (up to $2{\cdot}5\,M$). Zinc bromide also exhibits a similar tendency, but to a lesser degree; up to $0{\cdot}5\,M$ the velocity remains practically constant and thereafter it decreases. Zinc iodide shows a continuous decrease with increasing concentration.

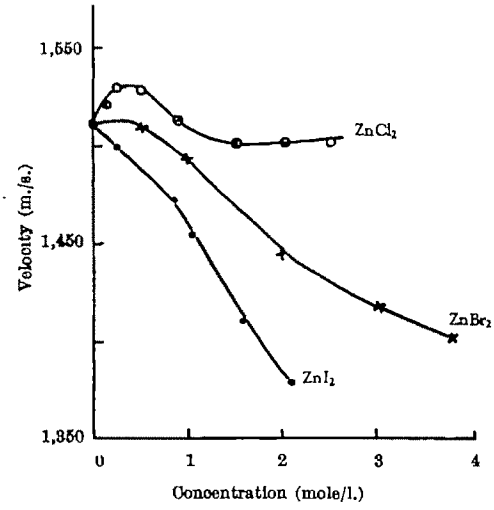

Fig. 1

Balachandran[2] has studied the ultrasonic behaviour of zinc iodide in the concentration-range 0–$0{\cdot}5\,M$. His results also indicate decrease of velocity of sound with increasing concentration.

Adiabatic compressibility decreases with increasing concentration in all three cases. At any molar concentration, the decrease in compressibility of water is a maximum in the case of iodide and a minimum in the case of chloride. It is to be noted that this order is the reverse of that found among cadmium halides[3].

Full details of this investigation will be published shortly. I thank Dr. J. Bhimasenachar for his encouragement and helpful discussions.

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The Unit of Neutron Flux

HAVING lectured for several years on the physics of nuclear reactors, we have often felt the need for a unit of neutron flux. It is comparatively easy to write "ns per cm.^{2} per sec.", but much more clumsy to speak aloud the expression "neutrons per square centimetre per second" while lecturing.

We have adopted the name 'chad' as the unit of neutron flux in our lectures, in honour of Sir James Chadwick, and we would like to suggest that this name becomes the accepted unit, defined as follows:

1 chad $\equiv$ 1 neutron per cm.^{2} per sec.

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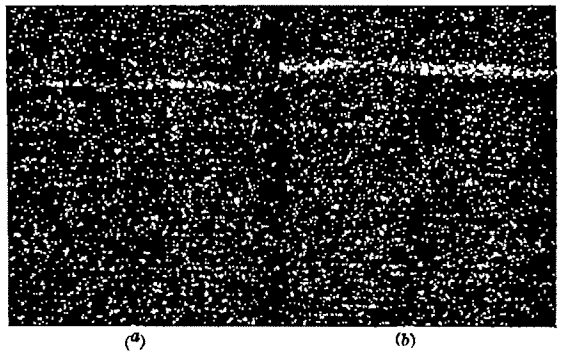
Electron Microscope Out-of-focus Image of the Edge of a Crystal Lattice

IN 1957, Cowley and Moodie[1] pointed out, theoretically and by optical analogue experiments, that so-called Fourier images can be observed in out-of-focus images of a periodic object. According to them, Fourier images are interference fringe systems arising from the transmitted primary and several diffracted waves, and are a series of images in particular planes both in front of and behind the object and having the same geometrical form as the periodic object. In electron microscope images, passing through the focus, of copper–phthalocyanine, Komoda[2] observed that the periodic structure in the image appeared again after it had become diffuse. He concluded that the periodic structures appearing at a different focus are the Fourier images of the crystal lattice predicted by Cowley and Moodie. In the out-of-focus image of copper–phthalocyanine crystal taken by Komoda, we have detected a few extra lines outside an edge of the crystal (see Fig. 1). Such lines are not explicable by the theory of Cowley and Moodie. By using a light optical analogue, it has been shown that these lines are due to effects arising from the termination effect of the Fourier images and Fresnel diffraction of electron waves at the edge of the crystal.

Fig. 2 is a schematic diagram which demonstrates the Fourier images on the exit side of a grating for



(a) (b)

Fig. 1. Fringes of copper–phthalocyanine crystal for in-focus (a) and out-of-focus (b) image. By courtesy of Komoda. (× 433,000)

the case of $n = 0, \pm 1$ waves, where n is the order of reflexion. The spacing of the fringes is equal to that of the grating, and the intensity alternates as the distance from the grating becomes larger, with increase in order of the Fourier images, $N = 0, \pm 1/2, \pm 1, \pm 3/2, \ldots$ (negative sign indicates a virtual image). From Fig. 2 it can be seen that the number of fringes increases as the Fourier image of higher order is focused; for example, in the Fourier image of $N = 1/2$ one more fringe appears than in the image of $N=0$. In the out-of-focus image of a crystal edge, Fresnel diffraction takes place at the edge both for beams which pass inside and outside of the crystal. Then the character of the fringes is slightly changed from that expected from Fig. 2. These effects can easily be demonstrated optically by using a plane grating and light.

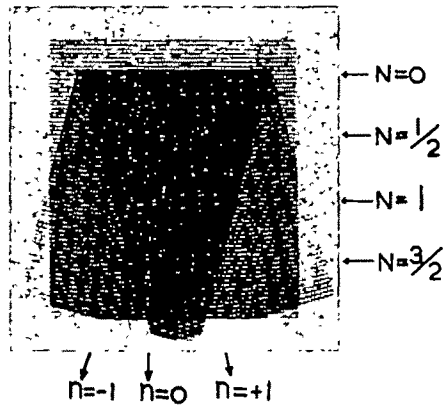
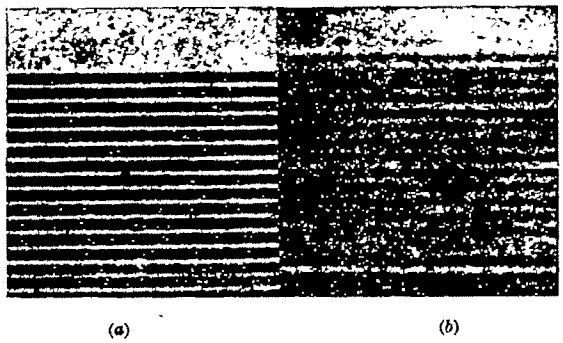


Fig. 2. Mode of interference of the electron waves passing through the lattice

In our demonstration, a plane grating of 66-μ spacing with an edge was irradiated by an almost parallel light beam of wave-length 4900 Å. This corresponds to a thin crystal of 6·6 Å. lattice spacing with an edge, which is irradiated by a 60-keV. electron beam. Figs. 3*a* and *b* are images of the plane grating obtained by focusing on the Fourier images $N = 0$ and $N = 1/2$ respectively. One more line is clearly formed outside the grating, and two more faint lines are also detectable. From this experiment, we can expect in the out-of-focus image of the crystal lattice many more extra lines would be formed outside the crystal than are predicted by the Fourier image theory. In Fig. 1, three additional lines are detectable and the amount of de-focus, which is estimated from the Fresnel fringe at the edge of the contaminating substance, is about 0·5μ, which corresponds to $N \doteqdot 1/2$. The number of extra lines outside the crystal agrees with that in the optical model.



(*a*) (*b*)

Fig. 3 (*a*) and (*b*) are the fringes in the Fourier images of $N = 0$ and $N = 1/2$ respectively. In (*b*) one strong and two faint fringes can be observed outside the grating

In a real crystal the intensity of beams reflected by the lattice planes is expected to vary according to the thickness and the inner potential of the crystal and to the amount of deviation from the Bragg angle, and a full analysis using the dynamical theory, taking these quantities into account, will be published shortly.

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METALLURGY

Potential-Time Curves obtained during the Stress Cracking of Metals

WE have investigated some of the electrochemistry of two 12 per cent chromium martensitic steels while undergoing cracking in acid media. Since it is known that these steels can be made to crack through hydrogen embrittlement as well as by stress corrosion, we were curious as to the cause of cracking in 1 per cent hydrochloric acid with 1 per cent dissolved selenium dioxide. Following the procedure of Brown[1], increasingly larger polarizing currents, both anodic and cathodic, were applied to stressed beam specimens to determine which reaction hastened the time to failure. From these results we concluded that the cracking in this medium was by hydrogen embrittlement. Further proof was obtained by substituting sulphuric acid for hydrochloric acid (to eliminate the possible stress corroding influence of the chloride ion) without any change in the pattern of results. Simultaneously with our tests on the effect of applied currents on time to fracture, potential-time curves were automatically recorded. The rather unusual changes in potential we observed are primarily the reason for this communication.

Potential-time curves have been plotted by several investigators studying the stress corrosion cracking of metals[2-4]. We are not aware of similar curves for hydrogen cracking. As a means of reference we have summarized the characteristics of potential-time curves obtained when austenitic stainless steels undergo stress corrosion cracking in magnesium chloride and mild steels stress-crack in boiling nitrate solutions. Certain of these features are also duplicated by aluminium and magnesium alloys in chloride environments.

(1) There is a gradual rise in potential in the noble direction immediately after the specimen is exposed to the cracking medium. The shape of this portion of the curve is independent of applied load.

(2) After a limiting potential is reached, breaks may occur in the potential-time curves when the

specimen is under load. These breaks are evidenced by very rapid drops in potential to a more active value and fairly rapid return to the 'normal' value.

(3) When the specimen finally fractures by stress corrosion, there is a very rapid drop to a more active potential.

(4) Application of cathodic current delays or possibly prevents failure. Anodic polarization may hasten time to failure.

The following outline describes the almost completely opposite effects found with the 12 per cent chromium steels: *A*, carbon, 0·129 per cent; manganese, 0·55 per cent; silicon, 0·40 per cent; phosphorus, 0·012 per cent; sulphur, 0·012 per cent; chromium, 12·15 per cent; nickel, 0·38 per cent; molybdenum, 0·02 per cent; copper, 0·11 per cent; *B*, carbon, 0·050 per cent; manganese, 0·63 per cent; silicon, 0·26 per cent; phosphorus, 0·012 per cent; sulphur, 0·017 per cent; chromium, 11·73 per cent; nickel, 1·76 per cent; molybdenum, 0·01 per cent; copper, 0·06 per cent; stressed to approximately 80 per cent of their yield strengths in a room temperature solution of 1 per cent selenium dioxide in 1 per cent hydrochloric acid (or 5 per cent sulphuric acid):

(1) There is a gradual drop in potential to a value of approximately −0·450 V. more active than the saturated calomel electrode during the first 30 min. of exposure. The initial change in potential with time is independent of applied load on the specimen.

(2) After the lowest potential has been reached there may be a gradual increase in potential of approximately 25 mV. or very little change at all. Short breaks in the potential-time curve may occur. These are seen as very rapid rises in potential to a more noble value and then return to 'normal'. The same result is obtained if the surface of the specimen is scratched.

(3) When the specimen fails, there is a sudden rise to a more noble potential.

(4) Cathodic polarization hastens time to failure. Anodic polarization prevents failure but causes pitting and etching attack.

We have a tentative explanation to offer for the observed potential changes. The reason that we qualify our explanation as 'tentative' is that we have additional work in progress to test our theory.

During the initial change in potential to a more active value, dissolution of metal proceeds fairly rapidly. The cathodic process is predominantly the reduction of selenous acid to selenium metal, which appears to be catalysed by the metal surface and deposits there. After the surface is covered by selenium, the potential remains steady or gradually becomes more noble, depending on the adhesion and porosity of the selenium layer. During this interval, if one scratches the surface and breaks the selenium layer exposing bare metal, a repetition of the deposition process occurs at this spot. This is reflected in a sudden rise in the potential and subsequent gradual return. We assume that hydrogen charging becomes the predominant cathodic process after the surface of the specimen is covered by selenium. As one increases the cathodic polarization, the time to failure after the selenium deposition process occurs is greatly decreased. The actual failure of the specimen is mechanical, that is, by hydrogen embrittlement. The reason for the sudden rise in potential is the sudden exposure of bare metal to the corrosive environment.

Another interesting environment is 5 per cent acetic acid with 0·1 per cent ammonium sulphide. The two 12 per cent chromium steels also crack in this environment by hydrogen embrittlement, but there is a major difference in the electrochemical behaviour. The steels still show a gradual potential drop in the more active direction, initially, reaching a value of about −0·520 V. more active than the saturated calomel electrode when cracking occurs. This time, however, there is no apparent change in potential when the specimen fractures or the surface is scratched. We believe the explanation here is that there is no competing cathodic process with hydrogen reduction and no insulating film on the metal surface; the mechanical breaking of the metal, therefore, will not cause a potential change.

These results confirm our opinion that the potential-time curve can be an effective tool in investigations into the cause of cracking of metals even when hydrogen embrittlement is suspected.

We wish to thank the Carpenter Steel Co. for the privilege of publishing this work and Dr. D. van Rooyen for his helpful information on stress corrosion cracking.

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Random Slip Model of Fatigue and Coffin's Law

Coffin[1] has shown that for a number of metals and alloys the relation between n the number of cycles to fracture and ε the plastic strain in each cycle is of the simple form:

$$n^{1/2}\,\varepsilon = \text{constant} \qquad (1)$$

This equation can be interpreted in a simple way on the model I have proposed[2]. According to this model the surface of the metal is roughened by a more or less random distribution of slip steps. Thus hills and valleys are formed on the surface, and subsequent slip tends to be concentrated in the valleys, roughly in proportion to their depths. The depth of each valley increases or decreases during fatigue in a step-wise manner analogous to a random walk. If $f(z, t)$ is the fraction of valleys (of width w) with depth between z and $z + dz$ after t cycles of fatigue, then $f(z, t)$ obeys a diffusion equation:

$$\frac{df}{dt} = D\,\frac{d^2f}{dz^2} \qquad (2)$$

The diffusion coefficient D is given by the expression $kbw\varepsilon$, where b is the slip vector and k is a geometrical factor of the order of unity.

The enhanced concentration of slip in the deeper valleys is taken into account by letting D be a function

of z. As a rough approximation we suppose that D increases linearly with z and put :

$$D = kbw\varepsilon\ (1 + \beta z/w)$$

where β is a constant of the order of unity.

The solutions of equation (1) with D a linear function of z have been given by Kepinski[3]. For large z they behave like $F \exp - z/\alpha t$, where α is the rate of increase of D with z, and F is a slowly varying function of z and t. In our case $\alpha = kb\beta\varepsilon$. For small values of t the exponential factor is very small, and no valleys attain any considerable depth. If Z is some large depth then a few valleys attain the depth Z after a number of cycles of the order $Z/15\alpha$. Thus if we take Z to be the depth at which a valley becomes an incipient crack the life-time of the specimen will be given by :

$$n = Z/15\alpha = Z/15\ kb\beta\varepsilon \qquad (3)$$

We now have to consider how this will change when ε is varied. We may anticipate that the value of Z will depend on the stress-level at which the specimen is fatigued, and thus on the value of ε. On the simple assumption that the plastic strain in each valley is linearly dependent on the depth z, we are led to suggest that the critical depth Z is given by an equation of the form :

$$\varepsilon Z/w = \varepsilon_c$$

where ε_c is a critical value of the plastic strain in a notch which leads to fracture. Combining this value of Z with equation (3) we obtain :

$$n\varepsilon^2 = w\varepsilon_c/15\ kb\beta \qquad (4)$$

which is equivalent to Coffin's equation.

From this derivation it might appear that this relation is a consequence of the simple linear dependence of D and ε on z. However, the calculation can be carried through for more general forms of dependence of D and ε and a relation of the form (4) is still obtained.

We may derive a value for ε_c from a comparison of equations (4) and (1). The experimental value of the constant in (1) is near unity, and we may insert the values of b and w which were used in the previous note[3], $w = 10^{-4}$ cm., $b = 5 \times 10^{-7}$ cm. The value of ε_c so obtained is $15\ b/w$ or $7{\cdot}5 \times 10^{-3}$. This is of course an extremely rough estimate ; but it appears to be a likely order of magnitude for a local plastic strain sufficient to propagate a crack.

One remarkable feature of Coffin's equation is that it is still valid for $n = \frac{1}{4}$, that is, the real strain in fracture by uni-directional strain obeys the same relation. This suggests that the formation of small notches by slip may be relevant in simple ductile fracture as well as in fatigue.

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RADIATION CHEMISTRY

Formation of Activated Hydrogen Peroxide by Irradiation of Water with α-Rays

WHEN water is exposed to ionizing radiations the radicals H and OH are produced and these can combine either with each other to give the molecular products H_2 and H_2O_2, or with solutes[1]. In regions of high energy loss (such as α-particle tracks) the local concentration of radicals is sufficiently high for combination between them to occur sooner than reaction with the solute. Consequently, while the chemical effects of X-rays on aqueous solutions are brought about chiefly by radical reactions, those of α-rays are chiefly by molecular reactions. However, in α-irradiations there are δ-rays associated with the α-particle tracks and these always introduce a small fraction of relatively sparsely ionizing radiation which prevents any absolute distinction being made between the effects of X- and α-irradiations.

While studying the effect of ionizing radiations on solutions of proteins, we noticed that polonium α-rays gave rise to changes which were qualitatively different from those brought about by X-rays[2], but which could not be obtained by treatment with hydrogen peroxide even when this was added to a final concentration of $0{\cdot}6\ M$, a thousand times greater than that produced by the α-rays in the water. To elucidate this phenomenon we have compared the effects of X- and α-radiations on solutions of certain amino-acids. With tryptophan in particular, there is clear evidence that an oxidizing agent of reactivity greater than that of normal hydrogen peroxide is formed by the α-rays.

The α-ray source was 100 mc. of polonium-210, deposited on a gold-foil disk, and mounted so that it could be screwed down over an open vessel containing the solution. The whole arrangement was within a container filled with nitrogen. Nitrogen was bubbled through the solution for 30 min. before irradiation and blown over it during irradiation, while the solution was being stirred with a glass-covered rotating magnet. The source of X-rays was a Westinghouse deep-therapy set, run at 220 kV. with no filter. Dose-rates were measured with ferrous sulphate solutions held in the same position as the experimental solutions. The α-radiation was delivered at the rate of 20,000–45,000 rads/hr. ($G = 5{\cdot}6$) and the X-radiation at 6,640 rads/min. ($G = 15{\cdot}6$). The tryptophan, from a commercial sample of high purity, was used at a concentration of $2 \times 10^{-4}\ M$ in water redistilled in an all-glass apparatus.

Changes in the ultra-violet absorption spectra (differences in extinction coefficient between the irradiated and unirradiated solutions) produced by X- and α-rays are shown in Fig. 1. The loss of absorption at 280 mμ is in both cases connected with loss of the tryptophan chromophore (the indole ring), but the products of the two radiations are evidently different. Hydrogen peroxide at a final concentration of $8 \times 10^{-3}\ M$ for 3 days produced no detectable changes. We have confirmed the spectral changes produced by treating tryptophan with ozone[3], and find that these closely match the changes produced by α-irradiation. However, the conditions of our experiments preclude the formation of ozone, and even if the irradiations had been carried out in an atmosphere of pure oxygen the yield of ozone would need to be unreasonably large ($G > 50$) if it were to

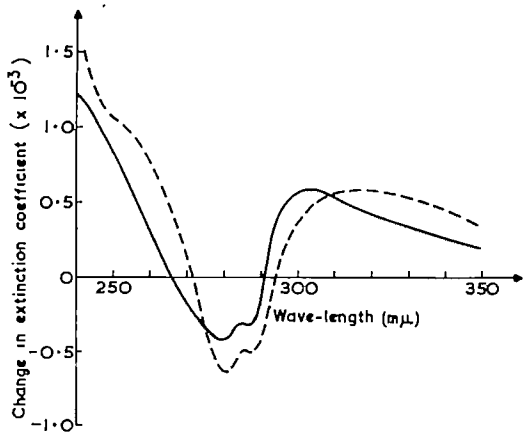

Fig. 1. Differential absorption spectra (difference between extinctions of irradiated and unirradiated samples) for 2×10^{-4} M tryptophan following X-irradiation (66,400 rads) and α-irradiation (59,000 rads). Both irradiations were under nitrogen ---, α-irradiation; ——, X-irradiated

produce the observed effects. Treatment of the tryptophan with chemically produced OH radicals (from hydrogen peroxide and ferrous sulphate) caused changes in the absorption spectrum which, as expected, closely matched those caused by X-irradiation.

A direct measurement of the indole ring concentration, by the method of Spies and Chambers[4], showed (Fig. 2a) that the concentration fell more rapidly on α-irradiation (with an initial yield per 100 eV. of $G^{\alpha}_{\text{-indole}} = 1 \cdot 8$) than on X-irradiation ($G^{X}_{\text{-indole}} = 0 \cdot 92$). However, estimation with Nessler's reagent of the amount of ammonia released (by deamination of the tryptophan) showed (Fig. 2b) that in this respect the radiations were equally efficient ($G^{\alpha, X}_{NH_3} = 1 \cdot 8$). Addition to the solution of 0·1 per cent ribonuclease, a protein containing no tryptophan, protected tryptophan against the radiations; but, whereas in the α-irradiated solution the effective dose to the tryptophan moiety was reduced to about 70 per cent of the dose given to the whole solution, in the X-irradiated solution, the effective dose to the tryptophan was reduced to 35 per cent. These experiments indicate that the molecular product formed in water by α-rays is more reactive and more selective than the radicals produced by the X-rays. Ribonuclease can act as an efficient scavenger for OH radicals, which react readily with all the amino-acids constituting the protein, but it does not compete so effectively for the α-radiation products.

The results show that α-irradiation of water yields a highly oxidizing product which reacts with particular readiness with the indole ring of tryptophan, as

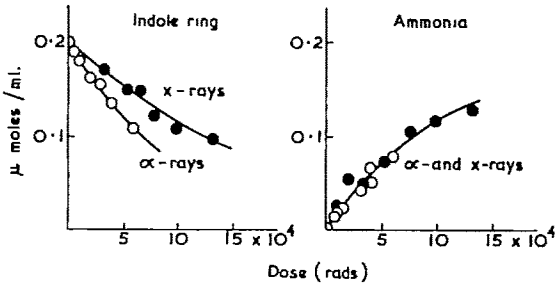

Fig. 2. Analysis of irradiated solutions of 2×10^{-4} M tryptophan after various doses of X- and α-radiation
○, α-irradiated; ●, X-irradiated. a, indole ring concentration; b, ammonia concentration

does ozone[3]. However, direct experiment shows that hydrogen peroxide has insufficient reactivity, and the experimental conditions rule out ozone as the product in question. Furthermore, the yields are too high for the product to be the radical HO_2 ($G^{\alpha}_{HO_2} = 0 \cdot 15$, ref. 1). We suggest that the product is hydrogen peroxide formed, by the combination of two OH radicals, either in an excited state, or, less probably, in a reactive isomeric form. Since it reacts with a substrate at a concentration of 10^{-4} M the life-time of this intermediate must be at least 10^{-5} sec. This eliminates the possibility that a singlet state is involved. But although we have not been able to find any work establishing a triplet state of hydrogen peroxide, the existence of this state is probable on general grounds.

The formation by α-rays of activated hydrogen peroxide as an intermediate of relatively long life-time would create a situation in which α-rays could be more effective than X-rays. A molecule, such as a protein containing tryptophan, would be particularly susceptible to attack in a complex mixture, such as exists in a cell, where the OH radicals formed by X-rays would be used up to a greater extent in reaction with the other substances present. The formation of an activated form of hydrogen peroxide could in this way be one of the causes making the biological efficiency of densely ionizing radiations (for example, α-rays) greater than that of sparsely ionizing radiations (for example, X-rays) though other factors are certain to be involved[5].

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Simultaneous Determination of Scandium and Dysprosium by Neutron Activation followed by γ-Ray Spectrometry

A NEUTRON activation analysis method has been devised for the non-destructive, simultaneous determination of scandium and dysprosium.

It is known that when natural scandium and dysprosium are irradiated with neutrons, scandium-46*m* (19·5 sec.) and dysprosium-165*m* (1·25 min.) are formed, respectively. The method of analysis by the use of these nuclides has never been described in the literature examined.

In the present work, the sample (3–80 mgm.) is placed in the nuclear reactor *JRR*-1 for 30 sec. to be irradiated with neutrons at a flux of 4×10^{10} neutrons/cm.²/sec. (when operated at 5-kW. level), cooled for 10 sec., counted for 30 sec., again cooled for 30 sec. and counted for 30 sec. The counting apparatus used is a 256-channel pulse height analyser to which a 2-in. thick, well-type sodium iodide crystal is attached. In the first counting 128 channels in the analyser are used, and in the second counting the rest used. In the resultant γ-spectrum the height of photopeak due to 0·142-MeV. γ-ray of scandium-46*m*

and that due to 0·108-MeV. γ-ray of dysprosium-165*m* are measured, respectively.

The relations between photopeak height and the amount of scandium or dysprosium have been obtained by use of standards.

Table 1. EXAMPLES OF THE COEFFICIENT OF VARIATION AND THE CORRESPONDING SIZE OF PHOTOPEAK

Sample	Coefficient of variation of single analyses (per cent)	Average photopeak height (counts per channel)	Average area of photopeak (counts)
Scandium, 3·07 μgm.	3·8[a]	$1·88 \times 10^3$	$4·3 \times 10^4$
Dysprosium, 1·62 μgm.	2·1[a]	$4·56 \times 10^3$	$7·4 \times 10^3$
	9·5[b]	$2·60 \times 10^3$	$4·7 \times 10^3$

a, Obtained from the first counting; *b*, obtained from the second counting.

The examples of the coefficient of variation of single analyses have been obtained by use of five scandium samples, each of which includes 3·07 μgm. of scandium, and of four dysprosium samples, each of which includes 1·62 μgm. of dysprosium. The coefficients estimated are shown in Table 1 with the related data.

Results of analyses are shown in Tables 2 and 3.

Table 2. RESULTS OF ANALYSES FOR SYNTHETIC SAMPLES

Sample	Scandium added (μgm.)	Dysprosium added (μgm.)	Scandium found[a] (μgm.)	Dysprosium found (μgm.)	
				(*a*)	(*b*)
A	0·98	1·62	0·98	1·62	1·77
B	0·98	1·62	0·97	1·59	1·53
C	0·98	1·62	0·92	1·53	1·34

a, Obtained from the first counting; *b*, obtained from the second counting.

Table 3. RESULTS OF ANALYSES

Sample	Amount of sample (mgm.)	Scandium found (p.p.m.)	Dysprosium found (p.p.m.)
A (Soil)	49·6	19	<3
B (Monazite sand)	3·26	$< 5 \times 10^1$	$6·7 \times 10^3$
C (Orthite, Korea)	3·55	<10	$8·1 \times 10^1$
D (Columbite, Japan)	47·5	26	<8
E (Yttrium oxide)	84·5	<0·4	<2

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CHEMISTRY

Nature of Fluids in the Hypercritical Region

IN the opinion of Andrews[1] the question of the appropriate nomenclature to be applied to a fluid at temperatures and pressures above the critical point "does not admit . . . of a positive answer. . . . Carbonic acid at 35·5°, and under 108 atmospheres pressure, stands nearly midway between the gas and the liquid; and we have no valid grounds for assigning it to the one form of matter any more than to the other". The absence of any sharp visible transition when a substance is taken from the gas state below the critical temperature to the liquid state, also below the critical temperature, by a route which does not enter the two-phase region of the p,v diagram (that is, cross the two-phase line on the T,p diagram), gave rise to the concept of the 'continuity of gaseous and liquid states'; and this has, perhaps, discouraged inquiry into the structural changes which must occur on passing from a dilute gas to liquid. Suggestions concerning the distinction between gaseous and liquid states of hypercritical fluids were made by Thiessen[2] in 1897, and later by Eucken[3] and by Plank[4]. In recent years, interest in this subject has revived, and several suggestions have been made[5–8] that the hypercritical region of the T,p diagram should be divided into areas corresponding to 'gas-like' and 'liquid-like' states of matter by what Bernal[6] proposes should be called the 'hypercritical line'. The present communication discusses the criteria which have been suggested for making this subdivision.

Smith[5] has directed attention to the fact that whereas, below the critical temperature, the coefficient of thermal expansion of a substance at constant pressure when plotted against temperature goes to infinity at the boiling point, above the critical temperature it has a maximum. Since real gases are usually characterized by $\partial^2 v/\partial T^2 < 0$ and liquids by $\partial^2 v/\partial T^2 > 0$, this maximum may be regarded as separating gas-like and liquid-like states of the hypercritical fluid. It is found empirically that this maximum occurs at roughly $v_{max.} \approx v_c$, although $v_{max.}$ tends to fall with increasing pressure[7]. In a recent lecture[6], Bernal suggests that since a sharp maximum is observed when C_p is plotted against temperature at constant pressure[8,9], and since such maxima in general reveal the existence of higher-order phase transitions, the locus of this maximum in T, p co-ordinates should be called the hypercritical line separating 'incoherent' from 'coherent' states. Bernal suggests, on geometrical grounds, that this transition should occur at a volume slightly greater than three times the close-packed volume of the molecules. Kaganer[7] has discussed various ways of dividing up the hypercritical region, and has shown by analysis of the available data that the two methods described above lead to different boundary lines, although they are both smooth prolongations of the saturated vapour pressure curve. He appears to favour the locus of $(\partial C_p/\partial T)_p = 0$ as the most appropriate boundary between liquid and gaseous states, on the grounds that it is the "most natural continuation" of the vapour pressure curve. A similar view is expressed by Jones and Walker[8].

The close connexion between the criteria suggested by Smith and by Bernal is revealed by the thermodynamic equation $(\partial^2 v/\partial T^2)_p = -(1/T)(\partial C_p/\partial p)_T$, which shows that the locus of maxima in $(\partial v/\partial T)_p$ as a function of T will follow the same path on the T, p diagram as the locus of maxima in C_p as a function of p. This relationship is best illustrated by a three-dimensional model (Fig. 1) in which C_p for argon is shown as a function of T and p. Smith's criterion corresponds to choosing the locus of maxima of the plane sections of the model at constant T (line i), whereas Bernal's is the locus of maxima of plane sections at constant p (line ii). If, however, we choose to employ C_p as the thermodynamic function in terms of which we wish to distinguish the two forms of hypercritical fluid, then the line of the ridge

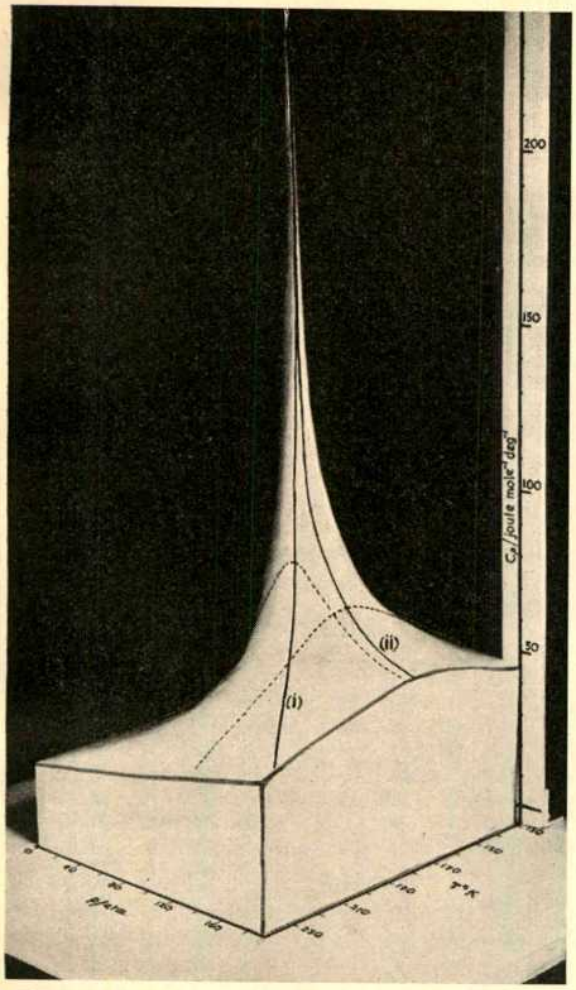

Fig. 1. C_p for argon as a function of temperature and pressure above the critical point. Data are from refs. 8 and 9.
Line (i): locus of $(\partial C_p/\partial p)_T = 0$
Line (ii): locus of $(\partial C_p/\partial T)_p = 0$

or watershed in the three-dimensional model has a strong claim to be used to define the hypercritical line in the T,p plane. It turns out, however, that although the watershed lies between (i) and (ii), there is no general mathematical criterion which identifies its position uniquely; and, even when the watershed can be defined, its locus on the T,p plane depends on the relative scales employed for T and p. (We are indebted to Dr. T. H. K. Barron for investigating the mathematical definition of the watershed and for pointing out that its locus cannot be defined generally.)

It seems, therefore, that a unique definition of the hypercritical line should not be attempted, but that the physical characteristics of the transition are better described by talking of a 'hypercritical transition region' commencing as a smooth extrapolation of the saturated vapour pressure curve at the critical point, but fanning out at higher temperatures and pressures, and having as its most intense regions the area between the lines defined by $(\partial^2 v/\partial T^2)_p = 0$ (or $(\partial C_p/\partial p)_T = 0$) and $(\partial C_p/\partial T)_p = 0$. The transition is very intense near the critical point so that, for some distance above it, the two lines are barely distinguishable.

It is perhaps also worth noting that, whereas Bernal has invoked a geometrical model to predict that the transition region should correspond to volumes approximately three times the close-packed volume, an essentially similar conclusion follows directly from the van der Waals' equation, for which $(\partial^2 v/\partial T^2)_p = 0$ when $v_{max.} = 3b = v_c$. It is not clear to us why this result should follow from the van der Waals' model, and it is probably a fortuitous mathematical result; nevertheless, it seems empirically to provide a reasonable approximation to the position of the hypercritical transition region.

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Effect of Corona Discharges on Polyethylene

It is known that organic insulation materials deteriorate when subjected to corona discharges. Although many workers have studied the breakdown of insulation materials under the influence of corona, particularly for the purpose of obtaining standardized testing procedures, few have been concerned with the fundamental physical and chemical processes involved.

In the present work n-eicosane was used as a model compound for polyethylene. The paraffin was subjected to corona discharges in air, oxygen and carbon dioxide. The experiments were carried out in a cell consisting of two superimposed glass plates spaced 3–5 mm., the outer surfaces of which were made conducting. The paraffin was cast as a thin layer on one of the inner surfaces. The voltage source was a 20-kV. r.m.s. 50 c./sec. transformer.

After exposure to corona discharges for 25–50 hr., the paraffin, which was now partly oxidized, was treated with lithium aluminium hydride in tetrahydrofuran, after which the resulting alcohols were separated by gas chromatography on an 'Apiezon' grease column at 210° C. The chromatogram is shown in Fig. 1.

As will be seen from Fig. 1, only the n-mono-alcohols are present. It will further be seen that the

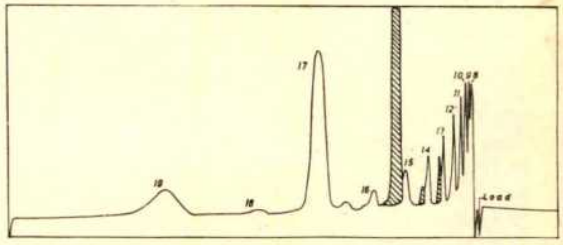

Fig. 1. Gas chromatogram of n-mono-alcohols with carbon numbers 8–19 derived from oxidation products of n-eicosane. The shaded peaks are n-eicosane and its impurities

amount of n-heptadecanol ($C_{17}H_{35}OH$) is without comparison the largest. It must therefore be concluded that the discharges cause a scission of a C—C bond, and that the bond between the third and fourth carbon atom is most likely to be attacked.

From mass spectrometer work[1] it is known that this is exactly what happens in the mass spectrometer, where the molecule is ionized after which a charged fragment splits off. The similarity of the fragmentation pattern strongly suggests that the same mechanism is operative also under the influence of corona discharges.

When an alternating voltage is applied to the cell, a discharge will pass when the potential between the two surfaces exceeds the breakdown voltage of the air-gap. In air the breakdown gradient at 1 atm. is 30 kV./cm. and the calculated mean energy of electrons 3·2 eV., whereas the ionization potential for most n-paraffins is 10–11 eV. (R. F. Grossman and W. A. Beasley[2] have suggested a mechanism for the breakdown of polyethylene by corona discharges, based on the assumption of the presence of 28 keV. electrons, which in my opinion is incorrect.)

Assuming a Maxwellian distribution of the energy of the electrons around the mean of 3·2 eV. it can be calculated that 4·2 per cent of them possess energies of 11 eV. or more. As only a minute fraction of the energy input to the cell is involved in chemical transformations of the paraffin, the number of electrons possessing this energy is sufficient to explain an ionization mechanism for the fracture of the molecules.

By varying the experimental conditions, further evidence was furnished in favour of this mechanism, as the extent of bond scission was found to be proportional to the number of electrons that collide with the paraffin surface.

Polyethylene film was then exposed to corona discharges in the same cell. After 25–50 hr. treatment the film was treated with lithium aluminium hydride in tetrahydrofuran. The soluble material was now expected to be diols and was difficult to separate by gas chromatography. Successful separation was accomplished after converting the diols into their trimethylsilyl ethers by treatment with trimethylchlorosilane in pyridine.

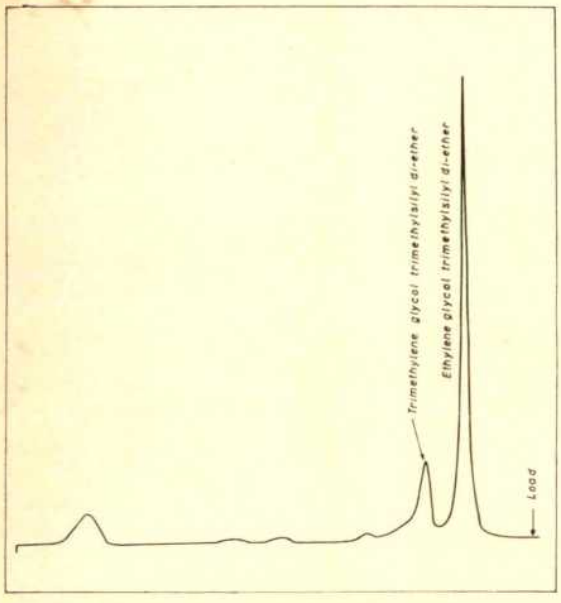

Fig. 2. Gas chromatogram of trimethylsilyl ethers of diols, derived from oxidation products of polyethylene. Peaks belonging to solvent and pyridine are omitted for sake of clarity

The chromatogram is shown in Fig. 2.

The presence of large amounts of ethylene glycol was not unexpected as crystals of oxalic acid were found on the surface of the film in most experiments. Oxalic acid was also found and characterized by other investigators[2,3].

The suggested ionization mechanism applied to polyethylene leads to the following reaction scheme.

When polyethylene is subjected to corona discharges in an oxygen-containing atmosphere, molecules are ionized and a positive ion splits off the molecule end, leaving a free radical which combines with oxygen to an alkoxy radical. This radical is again ionized, splitting off preferably a two-carbon ion, and this process is repeated along the chain. The radical ion which is split off the chain is further oxidized to the diol, the diacid and to carbon dioxide and water, which were also detected as reaction products. Instead of starting at the molecule end only, it can also be assumed that chain end radicals are formed by random scission of the polyethylene chain, after which the process continues as described.

Further work is being carried out and will be reported in more detail elsewhere.

This work was made possible by a grant from N.T.N.F., Royal Norwegian Council for Scientific and Industrial Research. I am also indebted to the University of Glasgow, where this work was carried out, and to Dr. N. Grassie and Dr. G. Eglinton of that University for helpful suggestions.

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An Ultra-sensitive Ionization Detector for Permanent Gas Analysis

THE development of a high-sensitivity detector responsive to all elements or compounds in the chromatographic analysis of gaseous mixtures is of importance in the determination of substances present in micro amounts.

A radioactive ionization-type detector similar to the argon detector described by Lovelock[1] was used with helium carrier gas. The metastable helium atoms (19·8 eV.) formed are capable of ionizing, with the exception of neon, all elements and compounds. This means that the technique may be used in the chromatographic analysis of permanent gases where the ionization potentials range from 12 to 16 eV.

Using a molecular sieve 5A column of 4 mm. diameter and 30 cm. long, it is possible to determine less than 0·001 μl. of hydrogen, argon, oxygen, nitrogen, methane and carbon monoxide in less than 2 min. Up to 1 μl. of gas can be determined before the detector is saturated. The column is operated at room temperature, except when oxygen–argon mixtures are analysed, when cooling to $-80°$ C. is re-

quired. The limit of detection is approximately 10^{-12} mole of component per ml. of carrier gas.

It is essential to purify the helium carrier gas from all substances other than neon, otherwise too high a background current occurs and the system becomes saturated. It is difficult at this stage to state the permissible impurity level. The ratio of ionization currents for 1 v.p.m. added impurity (nitrogen, oxygen, methane, argon) against the 'pure' helium is 1·05. This is better than the value obtained by Jesse and Sadauskis[2] of 1·003.

The helium purification system used is a combination of physical and chemical methods, comprising molecular sieve at 20° and −196° C., titanium at 1,000° C. and 'Hopcalite' at 400° C.

A detailed report on the application of this technique to the analysis of permanent gases is to be published.

The electronic equipment for this work was loaned by W. G. Pye, Ltd.

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Proton Magnetic Resonance of the Water Phase of Gelatin Gels

RESULTS have recently been reported concerning the proton magnetic resonance line-width of the water phase of starch gels[1]. I have examined the solvent line-width of gelatin gels at 16·7 Mc./sec. in a field of 3,910 gauss with the spectrometer now in use at this laboratory. The samples were contained in soda glass tubes of 1·2 mm. inside diameter. Sample spinning at about 1,200 r.p.m. was employed. The instrumental resolution was 0·12 p.p.m. The measurements were carried out at +20° C. The gels were made by solution at 85–90° C. of commercial gelatin in distilled water. The most concentrated gel (0·2 gm. gelatin per ml. water) was also examined with various concentrations of sodium chloride.

The line-width as a function of gelatin concentration is given in Fig. 1 (upper curve). The line-width increases rapidly up to about 6 c./s. at 0·05 gm./ml. At higher concentrations of gelatin the increase in line-width was small. On addition of sodium chloride, the line-width decreased considerably, but did not reach the value for water. As suggested in the article on starch gels[1], this upper limit of line-width of the aqueous phase may be due to the molecular mobility of macro-molecules. Approximate measurements of T_2 by the wiggle regrowth method[2] indicated that T_2 decreased from about 1·5 sec. for distilled water (in equilibrium with air oxygen) to about 0·05 sec. for the most concentrated gel. Approximate measurements were also made on T_1 by the progressive saturation method[3]. T_1 decreased from about 2 sec. in distilled water to about 0·15 sec. in the most concentrated gel (0·2 gm./ml.).

Work on different types of biological gels is being continued, and the proton resonance of organic macro-molecules is being investigated on gels in heavy water (D_2O).

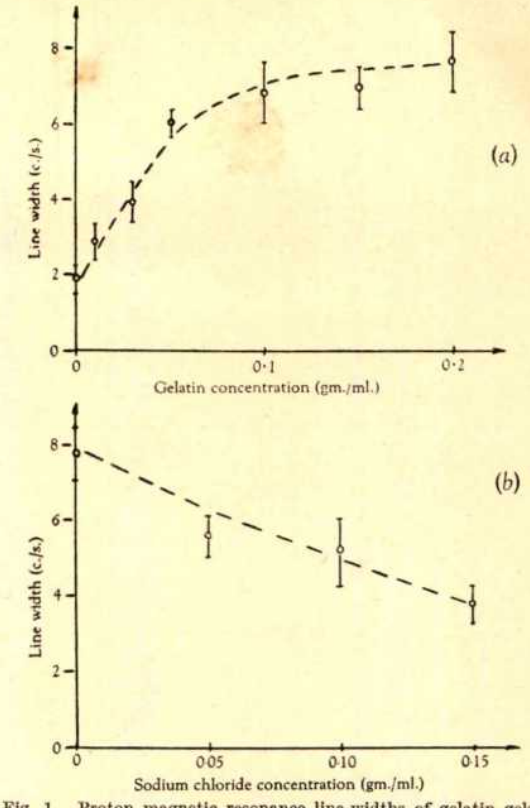

Fig. 1. Proton magnetic resonance line-widths of gelatin gels. (*a*) Line-width as a function of gelatin concentration in distilled water. (*b*) Line-width of a gelatin gel containing 0·2 gm. gelatin/ml. water as a function of concentration of sodium chloride in the gel

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BIOCHEMISTRY

Analysis of Human Leucocyte Deoxyribonucleohistone by Immunoelectrophoresis on Cellulose Acetate

THE internal composition of the nucleus is still unrevealed to a large extent despite many recent advances. The work described here constitutes a new approach to the problem made possible by a combination of histochemistry and immunoelectrophoresis on cellulose acetate membranes. Kohn[1] first introduced cellulose acetate as a supporting membrane for zone electrophoresis, and Consden and Kohn[2] showed that this material was elegantly suited to the entire process of immunoelectrophoresis. In this laboratory the techniques were found to be easily reproducible[3] and are now being used to study the human leukæmic leucocyte, with particular reference to the nucleus.

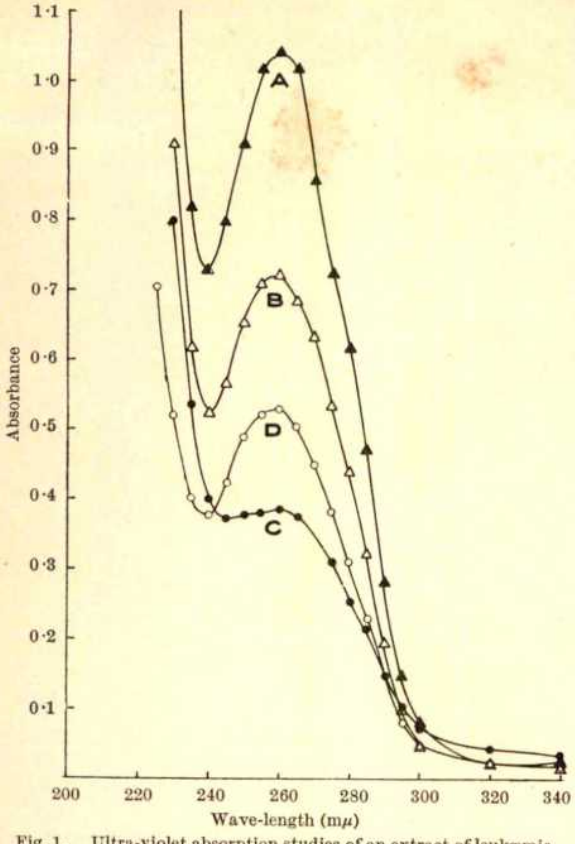

Fig. 1. Ultra-violet absorption studies of an extract of leukæmic leucocytes. Curve *A* is the spectrum of the whole, fresh extract; curve *B* is the spectrum of the material remaining in the sac after overnight dialysis against copious amounts of 0·1 *M* glycine; curve *C* is the spectrum of that portion of the extract which remains soluble after dialysis against 0·15 *M* sodium chloride; curve *D* is the spectrum of the material which is insoluble in 0·15 *M* sodium chloride after it has been re-dissolved in 0·1 *M* glycine. All samples were studied at a dilution of 1 : 40

In a typical experiment, leucocytes which have been obtained by venepuncture from patients with leukæmia are separated from the erythrocytes after accelerating the sedimentation of the latter by the addition of 'Dextran'. Serum proteins are removed by washing the leucocytes three times with 0·1 *M* sodium chloride–0·1 *M* sodium citrate alternating with periods of centrifugation for 1 min. at about 1,500 r.p.m. Two more washes with 0·05 *M* sodium citrate help leach soluble components from the cytoplasm of the now presumably non-viable cells and promote the ultimate dissolution of the nucleus[4]. Treatment with 0·1 *M* glycine then lyses the cells and puts the entire nucleus into solution as shown by phase microscopy. (This method of extracting deoxyribonucleoprotein was suggested by Dr. Daniel Mazia; further discussion of its applications will appear elsewhere.) After extraction has continued overnight, the preparation is freed of sediment by centrifugation at 20,000 r.p.m. for 30 min. All steps are performed at 4° C. and all solutions contain 0·001 *M* ethylenediamine tetraacetate as a further precaution against the action of the enzyme deoxyribonuclease.

The extracts are virtually colourless, slightly opalescent, and not viscous despite the presence of 0·5–1·5 mgm. per ml. of deoxyribonucleic acid as measured by the Dische diphenylamine reaction. About five to eight times as much protein is present on a weight basis as measured by the Biuret reaction calibrated with crystalline bovine albumin. Typical ultra-violet absorption studies of an extract of leucocytes from a patient (Dal.) with acute lymphocytic leukæmia are shown in Fig. 1. Curve *A* shows that the fresh extract has a peak absorption at 260 mμ and a shoulder at 280 mμ; curve *B* shows that the majority of the extract is non-dialysable; curve *C* shows that most of the ultra-violet absorbing material is insoluble in physiological saline; and curve *D* shows that this insoluble material can be redissolved in 0·1 *M* glycine to give an absorption spectrum characteristic of a nucleoprotein. It is apparent that the extracts are extremely rich in a high molecular weight deoxyribonucleic acid and associated proteins.

Electrophoresis was performed on cellulose acetate membranes supported in a micro-electrophoretic apparatus[3]. Separations were carried out for 90 min. at a constant voltage of 150 V., which gave an average current of 1·5 m.amp., using a barbital buffer *p*H 8·6 with an ionic strength of 0·075. At the conclusion of the electrophoretic separation the strips were dried and stained for histone by the method of Alfert and Geschwind[5] and for deoxyribonucleic acid by the Feulgen technique.

Fig. 2 shows the electrophoretic separation of an extract of cells from a patient (Peg.) with chronic granulocytic leukæmia. Strip *A* has been stained for histone and shows two prominent bands migrating toward the anode, one more rapidly than the other. Strip *B* has been stained for deoxyribonucleic acid and shows only a single band migrating also toward the anode. Strip *C* was divided length-wise into two parts after the electrophoretic separation and then stained, *C*1 for histone and *C*2 for deoxyribonucleic acid. It is clear that all the deoxyribonucleic acid is associated with the faster-moving histone band. Examination of the original strips shows several bands of protein migrating toward the

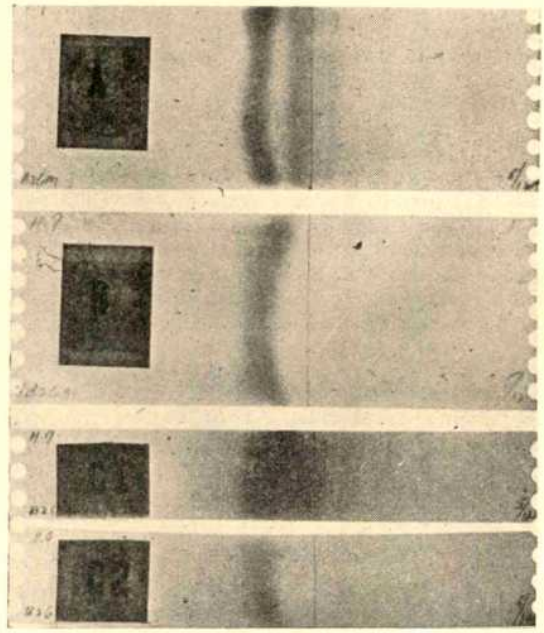

Fig. 2. Replicate electrophoretograms of an extract of leukæmic leucocytes. Strip *A* has been stained for histone, strip *B* has been stained for deoxyribonucleic acid, strip *C* has been divided length-wise after electrophoretic separation and *C*1 stained for histone, *C*2 for deoxyribonucleic acid. (The anode is at the left)

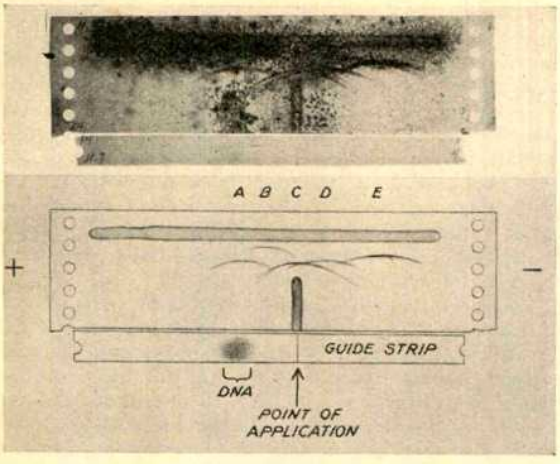

Fig. 3. Immunoelectrophoretic analysis of an extract of leukæmic leucocytes using homologous antiserum. The narrow guide strip along the bottom has been stained for deoxyribonucleic acid, but the Feulgen-positive material reproduced poorly in the photograph. A line drawing of the experiment has been added for extra clarity

cathode which stain very faintly with the histone stain, but the significance of these remains to be determined.

Antisera were prepared by emulsifying cell extracts with equal parts of Freund's complete adjuvant and injecting the mixture subcutaneously into a rabbit at weekly intervals for four weeks. Serum was collected after the sixth week and used for immunoelectrophoretic work on the composition of the extracts. The technique was that described by Consden and Kohn[2] with the following modification. Immediately after the electrophoretic separation a narrow guide-strip was cut from one edge of the membrane so that, by appropriate staining, it might serve to identify the location and nature of the substances present on the larger strip. Antiserum was then applied to the opposite edge of the latter and immuno-diffusion allowed to occur at room temperature for two days, following which the precipitin lines were stained with nigrosine.

In Fig. 3 is depicted a typical immunoelectrophoretic and histochemical analysis of an extract of leucocytes from patient Peg. using an antiserum to the extract prepared as described above. The precipitin line under the letter *A* was clearly seen to be associated with that portion of the electrophoretic separation which gave a positive stain for deoxyribonucleic acid by the Feulgen reaction, thus indicating the location of the deoxyribonucleic acid–histone complex described in the electrophoretic work mentioned above. Line *B* and possibly line *C* may well represent precipitin reactions due to the presence of slower moving histones, but definitive evidence is not yet available. The number of precipitin lines indicates the presence of at least five antigenically distinct components in the extract, none of which reacts with potent serum from a rabbit sensitized to human serum.

It remains to be determined which portion of the deoxyribonucleic acid–histone complex is responsible for the antigenicity demonstrated. Other experiments under way include efforts to determine the total number of basic proteins present, to identify the chemical nature of all the antigenically distinct components, to demonstrate possible organ and species differences, and to compare the patterns of leukæmic cells with those of normal cells.

This work was supported by grants from the Public Health Service (*C*-5060), the Martha and Spencer Love Foundation, and Mrs. Sherley W. Morgan. I am indebted to Dr. Daniel Mazia for frequent consultation on this project, to Mary Morrison for valuable technical assistance, and to Dr. David A. Wood, director of the Cancer Research Institute, for his continued interest and support.

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Reduction of Nitroso Group in Heterocyclics

IN search of a better and convenient method for the reduction of the 5-nitroso group of substituted pyrimidines, an intermediate for the synthesis of substituted pteridines, required for the synthesis of antagonist of folic acid, as a possible tumour-inhibiting agent (cf. aminopterin and amethopterin), nickel–aluminium alloy in alkaline solution is found to be a very suitable and convenient reagent. Besides the use of nickel–aluminium alloy as catalyst for hydrogenation of various unsaturated compounds, it has been used most successfully in alkaline medium for the reduction of carbonyl groups to the corresponding hydrocarbons or carbinols[1], for the exchange of halogens by hydrogens[2], for the reduction of isolated, conjugated or cyclic double bonds[3], for the hydrogenolysis of alkoxy or methylene dioxy groups in aromatic compounds[4], various sulphur compounds[5] and furan derivatives[6].

It has been reported earlier that the reduction of the 5-nitroso group of the various substituted pyrimidines can be carried out with sodium hydrosulphite, and the corresponding amino derivatives were isolated as their bisulphite salt[7–9]. Attempts were made to prepare 2 : 4 : 5-triamino-6-hydroxy pyrimidine from the corresponding 5-nitroso derivative by the reduction of the latter with sodium hydrosulphite, both in neutral and alkaline medium ; but the yield was found to be unsatisfactory, possibly due to the quality of the hydrosulphite used for this purpose. The present method using nickel–aluminium alloy in alkaline medium, as the reducing agent, was found to be very satisfactory.

2 : 4-Diamino-6-hydroxy pyrimidine was converted into the corresponding 5-nitroso derivative with sodium nitrite in cold hydrochloric acid, which was isolated as an orange-coloured precipitate. Reduction was carried out in warm (50–55° C.), dilute sodium hydroxide solution by adding powdered nickel–aluminium alloy (50 per cent) in portions with vigorous stirring until the red colour of the nitroso compound was completely bleached. The mixture was immediately cooled and filtered from the unreacted alloy when the smell of ammonia was noticed. The cooled filtrate was acidified with sulphuric acid and kept in the cold overnight, when the sulphate of the 2 : 4 : 5-triamino-6-hydroxy pyrimidine was crystallized out in fairly good yield. The base was isolated from the corresponding sulphate with sodium bicarbonate and

crystallizing the precipitated base from water, the compound was identified by its analysis as well as the ultra-violet absorption spectrum.

Using the same procedure, 2 : 4 : 6-trihydroxy pyrimidine, 2 : 4-dihydroxy-6-amino pyrimidine and 2-amino-4 : 6-dihydroxy pyrimidine were converted into their 5-nitroso derivatives, which in turn were smoothly reduced to the corresponding amino derivatives in very good yield. It was, however, observed that 2 : 4-dihydroxy-6-methyl pyrimidine and 2-hydroxy-4 : 6-dimethyl pyrimidine could not be converted into their 5-nitroso derivatives under similar conditions. A steric effect possibly is the reason for this failure.

The details of the work will be published elsewhere in due course.

We thank Dr. Subodh Mitra, director of this Centre, for his advice and constant encouragement during the progress of the work.

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Selective Inactivation of the Plasminogen Contaminant in Thrombin

THE contamination of preparations of thrombin and fibrinogen with plasminogen, the precursor of the fibrinolytic enzyme, has always presented great difficulties in the measurement of fibrinolytic activity.

When clots prepared from such 'contaminated' substances are used for the assay of fibrinolytic material having activator activity, the resulting lysis will be due to (*a*) activity of the added plasmin itself, and (*b*) activation of the contaminant plasminogen in the clot.

While plasminogen contamination of fibrinogen can be reduced to a minimum by applying Laki's procedure[1] three times, no satisfactory procedure has been available to free thrombin preparations from plasminogen. Milstone's method[2] and an alcohol-fractionation adopted by us (unpublished) result in yields of less than 1 per cent and are therefore impractical. The procedure described here involving incubation of thrombin with the reducing agent, 2-mercaptoethylamine, and its subsequent removal by dialysis results in loss of potential fibrinolytic activity with no impairment of clotting ability.

The contents of 1 vial of bovine 'Thrombin Topical' (Parke, Davis and Co.) containing 10,000 N.I.H. units are dissolved in 10 ml. of 0·5 *M* 2-mercaptoethylamine hydrochloride (Calif. Found. for Biochem. Res.) previously adjusted to *p*H 7·4. After 10-min. incubation at room temperature, the solution is dialysed at 4° C. against 10 litres of $1 \cdot 5 \times 10^{-4}$ *M* imidazole buffer, *p*H 7·0. After 5 hr. the dialysate is changed and the dialysis continued for 16 hr. Since the two dialyses amount to a million-fold dilution of the original 2-mercaptoethylamine concentration, any amount remaining in the solution is, for all practical purposes, negligible. At the end of dialysis the bag contents (now at *p*H 6·3 and slightly turbid) are clarified by adjustment of the *p*H to 7·4. The preparation is poured into siliconized tubes and kept frozen. Even brief exposure of the thrombin to *p*H values below 5 or above 9, while in the presence of the reducing agent or after its removal, results in rapid loss of clotting activity.

Testing for clotting activity and for plasminogen contamination was done under the conditions of the fibrinolytic assay as used in our laboratory[3]. Clotting activity was determined by mixing 0·3 ml. of 0·6 per cent human fibrinogen, 0·1 ml. thrombin and 0·2 ml. of a 0·05-*M* imidazole buffer at *p*H 7·2 at 45° C. Tests for changes in clotting activity due to the procedure were carried out by determining the clotting time of the above mixture using thrombin treated, and untreated, with 2-mercaptoethylamine, at several dilutions (Table 1). All dilutions of thrombin were made in imidazole buffer. Treatment with 2-mercaptoethylamine resulted in no impairment of clotting activity. Testing for the plasminogen contamination of thrombin samples was carried out by determination of the lysis-times of clots containing increasing amounts of streptokinase (Lederle-Varidase). Three-tenths of a ml. of 0·6 per cent human fibrinogen was mixed with 0·1 ml. containing 1 N.I.H. unit of thrombin (15 sec. clotting time) and 0·2 ml. of a streptokinase dilution ; the clots were incubated at 45° C. and observed for lysis. It is essential to employ a series of streptokinase concentrations since full activation of plasminogen by streptokinase occurs only at an optimal ratio of the two substances : too high concentrations of streptokinase depress plasminogen activation[4,5]. Streptokinase does not directly activate bovine plasminogen present in the thrombin ; however, by interacting with traces of human plasminogen[6] or 'proactivator'[7] in the human fibrinogen, streptokinase will form 'activator' which now will convert bovine plasminogen to plasmin. Table 2 shows lysis-times of clots made as described above with (*a*) untreated bovine thrombin, and (*b*) thrombin treated with 0·5 *M* 2-mercaptoethylamine, both thrombins in the 1 : 70 dilution which gave a 15-sec. clotting time. The results indicate a very high degree of inactivation of the plasminogen present as a contaminant in the thrombin preparation. Samples of human plasmin assayed on clots formed with thrombin purified with alcohol or treated with 2-mercaptoethylamine gave identical results indicating that treatment with the latter did not interfere with the lysis of clots by plasmin.

Occasional reactivation of the plasminogen, presumably by re-oxidation of the disulphide bonds on

Table 1. COMPARISON OF THE CLOTTING TIMES OF THROMBIN* BEFORE AND AFTER TREATMENT WITH 0·5 *M* 2-MERCAPTOETHYLAMINE

Dilution of thrombin	Thrombin untreated	Thrombin treated with 2-mercaptoethylamine
1 : 10	3 sec.	5 sec.
1 : 20	5 ,,	6 ,,
1 : 50	11 ,,	10 ,,
1 : 70	14 ,,	14 ,,
1 : 100	26 ,,	25 ,,

* 'Topical Thrombin' (Parke, Davis and Co.) 10,000 N.I.H. units dissolved in 10 ml. of 0·05 *M* imidazole buffer, *p*H 7·2, used as starting solution. Further dilutions made with the same buffer.

Table 2 COMPARISON OF THE LYSIS TIMES OF CLOTS MADE WITH HUMAN FIBRINOGEN AND 1 N.I.H. UNIT OF THROMBIN BEFORE AND AFTER TREATMENT WITH 0·5 *M* 2-MERCAPTOETHYLAMINE

Streptokinase units per clot	Thrombin untreated	Thrombin treated with 2-mercaptoethylamine
None	no lysis	no lysis*
0·1	45 min.	no lysis*
1	29 ,,	15 hr.
10	31 ,,	15 ,,
50	65 ,,	no lysis*
100	72 ,,	no lysis*

* Clots observed for 3 days.

storage, was prevented by treatment of the preparation with 0·1 *M* iodoacetamide after the dialysis has reduced the concentration of mercaptoethylamine to approximately 0·01 *M* as estimated by the nitroprusside test. The excess iodoacetamide was then dialysed out. This procedure, while it sometimes slightly decreases clotting activity, was found to give increased stability.

Inhibition of plasmin by sulphydryl compounds has been reported[8,9]. In experiments to be described elsewhere we have found that 2-mercaptoethylamine inactivates not only plasmin but also plasminogen. The inactivating effect of 2-mercaptoethylamine on plasminogen is probably due to its reducing property, rather than to the formation of an unactivable complex, since the effect persists after removal of the reducing agent. The most likely explanation of this effect is the splitting of one or more disulphide bonds essential for the activity of the plasminogen molecule. Structural distortion following reduction of disulphide bonds has been observed for several other proteins[10]. Since some of the disulphide bonds of thrombin also were probably reduced, as suggested by the increased *p*H sensitivity of these preparations, we conclude that the readily reducible disulphide bonds are not critical for the maintenance of the functional structure of the thrombin molecule.

Both treated and untreated thrombin tested at a high concentration (10,000 N.I.H. units per ml.), in the absence of streptokinase, lysed the purified clot in 5 hr. Mercaptoethylamine treatment, therefore, did not interfere with the fibrinolytic activity of thrombin itself[11,12].

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Blood Trehalose and Fat-Body Glycogen in the Silkworm, *Bombyx mori*

SINCE the report by Wyatt and Kalf[1] that trehalose is the principal carbohydrate in silkworm blood, attention has been paid to the biosynthetic process of this disaccharide in insects. Treherne[2] showed that trehalose labelled with carbon-14 is synthesized from labelled glucose, fructose and mannose in the locust, *Schistocerca*, and Candy and Kilby[3] demonstrated with this insect that the fat-body participates in the biosynthesis of trehalose, where adenosine triphosphate and uridine diphosphate glucose are required as cofactors for the enzymatic reactions involved. However, there are no publications dealing extensively with the correlation between *in vivo* formation of trehalose and various carbohydrates ingested by insects. As for the biosynthesis of glycogen, such a correlation has been elucidated, to some extent, with the fat body and other tissues of insects[4].

I have recently determined total blood carbohydrates and fat-body glycogen in the silkworm, *Bombyx mori*. The phenol–sulphuric acid method[5] was employed for the assay of total carbohydrates and glycogen, which was precipitated in alcohol in the presence of added sodium sulphate after digesting lyophilized fat-body in alkaline solution[6]. The same method was used for assaying trehalose, which was extracted from the trehalose spot developed on the filter paper by means of the solvent: *n*-butanol 4, acetic acid 1, and water 1. Trehalase obtained from silkworm midgut was also successfully used for trehalose determination.

When starved, fat-body glycogen decreased rather quickly, to a 60 per cent level of the original in 6 hr., and to a 15 per cent level in 12 hr. This level was maintained during prolonged starvation until the larva started feeding again. The original glycogen-level of the fat-body was resumed in several hours by feeding. Rather a different figure was obtained with total carbohydrates of the blood, the level of which did not decrease during early starvation period, but began to descend around the time when the amount of fat-body glycogen had reached the minimum level. The decrease was gradual so far as 49 hr. starvation. Food intake at the end of starvation resulted in a rapid increase in blood carbohydrates. The adminis-

Table 1

	Carboyhdrates	Increase in fat-body glycogen	Increase in blood trehalose
Pentose	Arabinose	−	−
	Xylose	±	±
	Ribose	−	−
	Rhamnose	−	−
Hexose	Glucose	+++	+
	Fructose	+++	+
	Mannose	±	±
	Galactose	±	±
	Sorbose	−	−
Disaccharide	Sucrose	+++	+
	Maltose	+++	+
	Cellobiose	+++	+
	Melibiose	+	+
	Trehalose	+	+
	Lactose	+	+
Trisaccharide	Melezitose	++	+
	Raffinose	++	+
Polysaccharide	Dextrin	±	−
	Starch	+	±
	Glycogen	−	−
	Inulin	−	−
Glycoside	Methyl-α-glucoside	−	−
	Methyl-α-mannoside	−	−
Sugar alcohol	Sorbitol	+++	+
	Mannitol	−	±
	Inositol	−	−
	Dulcitol	−	−
	Erythritol	−	−

tration of some carbohydrates to the starved larvæ also resulted in an increase in blood trehalose. Thus, the increase in both trehalose and glycogen after carbohydrate administration (20 mgm. per larva) in the form of a solution was determined by the use of larvæ which had been starved for 49 hr. The rates of increase were different with different carbohydrates, as shown in Table 1.

The most efficient sugars for the increase in fat-body glycogen were glucose, fructose, sucrose, maltose, cellobiose and sorbitol. Melezitose and raffinose were effective, but not so efficient as glucose. Melibiose, trehalose, lactose and starch were intermediate. Xylose, mannose, galactose, and dextrin occasionally resulted in some increase. No effect was obtained with sorbose, arabinose, ribose, rhamnose, methyl-α-glucoside, methyl-α-mannoside, mannitol, inositol, dulcitol, erythritol, glycogen or inulin.

Glucose was the most efficient also for increase in blood trehalose, and the list of carbohydrates falling into this group includes fructose, sucrose, maltose, cellobiose, melibiose, trehalose, lactose, melezitose, raffinose and sorbitol. Xylose, mannose, galactose, mannitol and starch seemed to be slightly effective, but not consistently. Sorbose administration resulted in an accumulation of sorbose in the blood, instead of an increase in trehalose. A similar result was obtained with arabinose, ribose, rhamnose, methyl-α-glucoside and methyl-α-mannoside. Inositol, dulcitol, erythritol, dextrin, glycogen and inulin were not efficient.

It is apparent from those results that the carbohydrates causing an increase in blood trehalose are generally also effective for that in fat-body glycogen. There is a good agreement in the kinds of carbohydrates between nutritive values[7] and efficiency of the increase in either trehalose or glycogen. Thus, the method determining the rate of increase in either compound by the use of starved larvæ is considered to be useful for the evaluation of nutritive values of carbohydrates.

Further details of this work will be published elsewhere.

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Reduced Folic Acid Analogues as Antimetabolites

HYDROGENATION of the folic acid analogues aminopterin (4-aminopteroylglutamic acid) and amethopterin (N^{10}-methyl-4-aminopteroylglutamic acid) is reported to result in diminished antibacterial activity[1,2] against *Streptococcus faecalis R* (A.T.C.C. 8043) and *Pediococcus cerevisiae* (A.T.C.C. 8081). In view of the lability of tetrahydrofolic acid it seemed desirable to repeat these experiments taking precautions to avoid destruction of the reduced analogues; hence they were added to the assay medium in a potassium ascorbate solution after autoclaving[3]. The ascorbate did not greatly affect the growth of either organism. The media employed were similar to those described[4,5].

Table 1. ANTIBACTERIAL ACTION OF FOLIC ACID ANALOGUES

Analogue	Amount of inhibitor producing a 50 per cent decrease in turbidity (mμgm./ml.)[a]	
	S. faecalis R[b]	*P. cerevisiae*[c]
Aminopterin[d]	0·35	> 100
Tetrahydroaminopterin	0·09	2·5
N^{10}-Formylaminopterin[e]	0·40	> 100
N^{10}-Formyltetrahydroaminopterin	0·03	2·0
Amethopterin[f]	0·13	50
Tetrahydroamethopterin	0·02	20

[a] Ascorbate concentration in all tubes, 0·6 mgm./ml.
[b] Contained 0·5 mμgm. folic acid/ml.
[c] Contained 0·4 mμgm. of the calcium salt of *dl*-N^5-formyltetrahydrofolic acid/ml.
[d] Commercial preparation hydrogenated without further purification.
[e] Commercial preparation partially purified by adsorption on 'Dowex-1'-chloride and elution with hydrochloric acid prior to formylation and hydrogenation.
[f] Lederle 85 per cent pure obtained from Dr. V. Oliverio, National Cancer Institute.

The hydrogenated analogues were synthesized by the procedure described for the preparation of tetrahydrofolic acid[6], and each product yielded four atoms of hydrogen per mole on iodine titration. They were dissolved in 1 *M* potassium phosphate, *p*H 7·8, in serum bottles filled with hydrogen. All dilutions were carried out with a sterile ascorbate solution (6 mgm./ml., *p*H 6·0).

As shown in Table 1, the reduced compounds are considerably more inhibitory in every instance than the corresponding unreduced analogue. The inhibitory action of aminopterin and N^{10}-formylaminopterin for *P. cerevisiae* is increased more than 50-fold by hydrogenation. Since reduced folic acid is required for the growth of this organism, the reduced analogues are most likely inhibiting at the tetrahydro level, rather than the reduction of folic acid to tetrahydrofolic acid where the unreduced antifolic compounds are known to act[7,8]. This suggestion is supported by the fact that with *S. faecalis R* it is more difficult to reverse, with folic acid, the inhibition caused by the reduced analogues than that caused by the unreduced analogues (Table 2). However, the inhibition caused by the reduced compounds is readily reversed by N^5-formyltetrahydrofolic acid ('Leucovorin') in both organisms excepting the case of the tetrahydroamethopterin inhibition of *S. faecalis R*. It therefore appears as if the enzyme sites involved do not in general bind the tetrahydro analogues tightly.

In the only cell-free enzyme system so far tested, the tetrahydrofolic acid-dependent methionine syn-

Table 2. REVERSAL OF THE ANTIBACTERIAL ACTION OF FOLIC ACID ANALOGUES

Analogue	Amount of reversing agent required to restore half-maximum turbidity (mμgm./ml.)[d]		
	S. faecalis R[a] Folic acid	*S. faecalis R*[a] 'Leucovorin'[c]	*P. cerevisiae*[b] 'Leucovorin'[c]
Aminopterin	5·8	2·0	—
Tetrahydroaminopterin	35·0	1·0	80
N^{10}-Formylaminopterin	1·5	0·8	—
N^{10}-Formyltetrahydroaminopterin	> 80·0	1·6	80
Amethopterin	50·0	4·4	—
Tetrahydroamethopterin	> 80·0	15·0	20

[a] Contained 1·0 mμgm. analogue/ml.
[b] Contained 0·1 μgm. analogue/ml.
[c] Calcium salt of *dl*-N^5-formyltetrahydrofolic acid.
[d] Ascorbate, as in Table 1.

thesis in *Escherichia coli* extracts[9] was inhibited 50 per cent by $2 \cdot 5 \times 10^{-4}$ *M* tetrahydroaminopterin or N^{10}-formyltetrahydroaminopterin, one-third the concentration of the tetrahydrofolic acid present. The unreduced analogues in each case were not inhibitory under the same conditions. In contrast, tetrahydroamethopterin was no more inhibitory than amethopterin. Both compounds yielded only 20 per cent inhibition when equimolar with tetrahydrofolic acid ($7 \cdot 5 \times 10^{-4}$ *M*).

These findings suggest that the hydrogenated analogues may be effective therapeutic agents and that they may also be useful in enzyme studies.

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Biotin in the Synthesis of Fatty Acid and Cholesterol by Mammalian Liver

Wakil, Titchener and Gibson[1] have shown that the formation of malonate from acetate and carbon dioxide is an early step in the synthesis of fatty acids in cell-free preparations of pigeon liver. They have also shown that biotin is necessary for this reaction, since it is inhibited by avidin, a specific inhibitor of biotin. By observing the effect of avidin, we have been able to show that, in cell-free preparations of rat liver, biotin is also required for the synthesis from acetate of fatty acids, but is not required for synthesis of cholesterol. It is thus possible to inhibit one biosynthetic pathway without influencing the other.

Homogenates of rat liver were prepared in ice-cold buffer by Bucher and McGarrahan's method[2], and were centrifuged for 20 min. at 2,000*g* to remove nuclei and cell debris, and then for 25 min. at 10,000*g* to remove mitochondria. The supernatant from the second centrifugation, containing the lighter subcellular particles, was transferred to flasks for incubation at 37° C. with air as the gas phase. Each flask received 2·5 ml. of supernatant, 20 μmoles of carbon-14-acetate as precursor of fatty acids and cholesterol, and the additions shown in Table 1. After incubation for 2 hr., the contents of the flasks were hydrolysed with sodium hydroxide. Fatty acids as soaps and cholesterol as digitonide were then isolated from the hydrolysate and assayed for radioactivity by methods previously described[3]. Table 1 shows the results of a typical experiment. The specific activity of the fatty acids from the flasks containing avidin without biotin was less than 10 per cent of that in the controls. Addition of biotin restored the synthesis of fatty acids almost to the control-level. Avidin had no significant effect on the specific activity of the cholesterol isolated at the end of the incubation.

Table 1. Each flask received 2·5 ml. of liver supernatant fraction and 1·0 ml. of buffer (magnesium chloride, 0·005 *M*; nicotinamide, 0·03 *M*; potassium phosphate, 0·1 *M*, *p*H 7·4) containing reduced coenzyme I, 1·0 μmole; coenzyme II, 0·5 μmole; glutathione, 30 μmoles; adenosine triphosphate, 17·5 μmoles; glucose-6-phosphate, 10 μmoles; potassium bicarbonate, 35 μmoles; potassium malonate, 25 μmoles; coenzyme A, 0·1 μmole; sodium 1-carbon-14-acetate, 20 μmoles/5 μc.

Additions	Specific activity (counts/min. at infinite thickness)	
	Fatty acids	Cholesterol
None	24,600	1,860
Biotin, 10 μgm.	32,500	1,860
Avidin (equivalent to 2 μgm. biotin)	1,910	1,690
Avidin + biotin	23,300	1,735

The avidin used in these experiments was kindly supplied by Miss H. Hellig, who prepared it by Woolley and Longsworth's method[4].

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PHYSIOLOGY

Effect of Season on the Follicle Stimulating Hormone and Luteinizing Hormone Potency of Sheep Anterior Pituitary Glands

IT has been shown in the ewe that the 'total gonadotrophin' hormone content of the pituitary remains about the same during the breeding and during the non-breeding season (Warwick[1]). Kammlade *et al.*[2] noticed a rather higher total gonadotrophin hormone-level in the pituitary of the ewe during the non-breeding than during the breeding season. Lamond *et al.*[3] found no seasonal variation.

We[4] have carried out work on the change in levels of follicle stimulating hormone and luteinizing hormone (interstitial-cell stimulating hormone) activity of the pituitary glands of sheep collected at precise stages of the œstrous cycle. In this communication a comparison is made between some of these values and values obtained during the non-breeding season.

The anterior lobes of pituitary glands collected from Welsh mountain ewes kept under controlled conditions have been studied. The seasonal distribution for the collection of these glands in given in Table 1.

Table 1

Reproductive state	Time of year when samples were collected
36 hr.*	7.11.56 – 12.12.56
10 day*	20.11.56 – 14.12.56
Anœstrus	25.7.57 – 28.7.57

* From onset of œstrus.

All glands were excised, the posterior lobe removed, and the anterior lobe trimmed, weighed and frozen over solid carbon dioxide within 15 min. of death. Electrical stunning was not used on any of these animals. The individual glands were then freeze-dried, ground to a fine powder and stored in a desiccator over calcium chloride. The number of glands for each group was 9. For the follicle stimulating hormone determination, aliquots of the samples to be assayed were pooled, homogenized in ice-cold saline and assayed using a slight modification of the Steelman and Pohley[5] augmentation technique. A 2 × 2 × 1 slope-ratio design with five rats per dose was employed and the assays were analysed by the method of Finney[6,7]. The follicle stimulating hormone potencies of the pituitaries assayed are expressed in terms of a purified ovine follicle stimulating hormone standard[8]. Estimates of the luteinizing hormone potency of the glands were carried out using the method of Parlow[9]. For these assays pituitary homogenates were extracted with ice-cold saline. A 2 × 2 or 2 × 1 design with five rats per dose was employed and the assays were analysed by the method of Gaddum[10]. The luteinizing hormone potency of the pituitaries assayed is expressed in terms of a purified ovine luteinizing hormone standard[11]. The results obtained are given in Table 2. It should be noted that in some cases the fiducial limits are rather wide.

Table 2

Stage of cycle (from onset of œstrus)	Potency (% of standard preparation)	Fiducial limits (95%)	Type of assay
Follicle-stimulating hormone values			
36 hr.	0·071	0·042–0·102	2 × 2 + 1
10 day	0·143	0·111–0·183	2 × 2 + 1
Anœstrus	0·180	0·145–0·228	2 × 2 + 1
Luteinizing hormone values			
36 hr.	0·472	0·301–0·776	2 × 1
10 day	1·535	0·748–9·040	2 × 1
Anœstrus	1·051	0·471–6·682	2 × 2

From the above values it would appear that the follicle stimulating hormone and luteinizing hormone potency of the pituitary gland during the anœstrous state is of a similar order to that found during the breeding season. The value for follicle stimulating hormone is as high as the maximal value found during the pre-ovulatory phase of the cycle while the value for luteinizing hormone is similar to the mean value for the cycle.

During the non-breeding season the ovary is far from inactive in the ewe. The ovaries from the non-breeding ewes in the present work have as many large (4 mm. diam. or greater) follicles as, and a greater number of small (2–3 diam.) follicles than, the ovaries of ewes during the œstrous cycle. The size of the largest follicle in the ovaries of the ewes during the non-breeding season is similar to that for ewes during the breeding season excluding a 20 hr. pre-ovulatory period. No recent corpora lutea were present in the ovaries of the ewes during the non-breeding season, indicating a lack of ovulation during this time. If the maintenance of the large follicles found in ovaries of ewes during the non-breeding season is under gonadotrophin control then a constant or cyclic release of gonadotrophin from the pituitary should occur at this time. There must also be a constant production to maintain the levels of follicle stimulating hormone and luteinizing hormone which we have found in the pituitary. Kammlade *et al.*[2] suggested that the lack of ovulation during the breeding season was due to a deficiency of luteinizing hormone in the pituitary. The values reported here for the potency of luteinizing hormone of the pituitaries would indicate that the pituitary of the non-breeding ewe is not devoid of the hormone. The lack of ovulation observed during the non-breeding season may be due to a lack of a sudden substantial release of luteinizing hormone and follicle stimulating hormone from the pituitary such as we[4] have found to occur during the ovulatory phase of the œstrous cycle, rather than to a lack of these hormones in the gland.

A full account of this investigation is being published elsewhere.

We are indebted to Messrs. Armour Laboratories for the samples of purified follicle stimulating hormone and luteinizing hormone, to Messrs. Parke, Davis for chorionic gonadotrophin and to Messrs. Boots for pregnant mares' serum gonadotrophin.

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Uptake of Small Resin Particles (1–5μ Diameter) by the Alimentary Canal of the Calf

THE intact skin and mucous membranes of the healthy body appear to present an impenetrable barrier to the entrance of particulate material, but yet bacteria are able to enter. How they do so is unknown. The tonsil is thought to be a vulnerable site: *Mycobacterium tuberculosis* has been shown to enter here[1], and even carmine granules dusted on to the tonsils before surgical removal penetrated very rapidly into the connective tissues[2]. The wall of the small intestine is also permeable to bacteria; coliform organisms[3], *M. tuberculosis*[1] and *Salmonellae*[4] have been shown to pass through the apparently intact mucous membrane and spread to the mesenteric lymph nodes, the blood, liver and spleen. More recently, at this Station, we have found that *Mycobacterium johnei* is also capable of rapid and extensive invasion of the body after the administration of an oral dose of culture to calves (Payne, J. M., and Rankin, J. D., unpublished work).

It was decided to see if inert particles would be taken up in the same way as bacteria. Previous experiments of this kind, using inert particles such as carmine[5], graphite[6] and polymethyl methacrylate spheres[7], to imitate bacteria have had limited or no

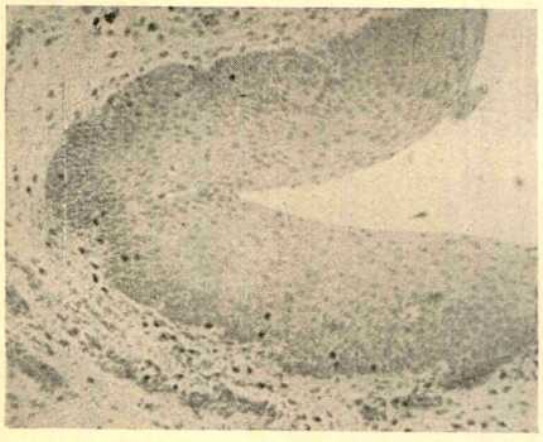

Fig. 1. Radioactive particles in the wall of the pharynx. Hæmatoxylin stain. (× 80)

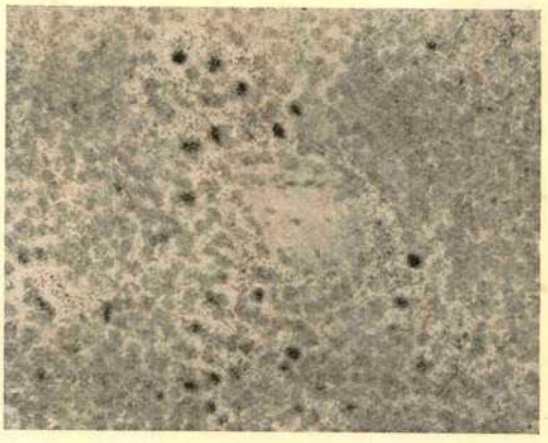

Fig. 2. Radioactive particles in cells lining a sinus in a lymph node. Hæmatoxylin stain. (× 360)

success, for even when fed in large amounts they only passed through to a limited extent or not at all. In view of the difficulty of estimating small quantities of these substances, we decided to use radioactive particles, which had the advantages of being easily detected and counted in body tissues.

Radioactive resin particles were prepared by one of us (B. J. M.). A stock suspension of these was made by grinding resin beads in a vibratory ball mill, followed by gravity sedimentation, centrifugation to eliminate large particles and finally filtration, with repeated washing, through a series of sintered glass filters so as to collect particles known to be between 1 and 5μ in diameter. Gold-198 was then adsorbed and reduced on to a sample of the final preparation. By this means a product could be obtained containing 50 mgm. resin particles of size 1–5μ, firmly labelled with 40 mc. of gold-198, having a total count of $1 \cdot 7 \times 10^{10}$ counts/min. The stability of the gold on the particles was checked by re-filtration through a No. 5 sintered glass filter. Only trace amounts of radioactivity came through into the filtrate, indicating firm labelling. This check was important, for in a preliminary experiment some loss of gold from the particles was observed.

Table 1

Lymph nodes	Counts/min./10 gm.	Tissue and fluids	Counts/min./10 gm.
Parotid	763	Tonsil	1,627
Mandibular	941	Pharynx	301
Suprapharyngeal	189	Lung	700
Mediastinal	2,483	Liver	189
Bronchial	794	Kidney	293
Hepatic	118	Spleen	242
Mesenteric	182	Muscle	56
Ileocæcal	361	Testis	246
Iliac	176	Blood	70
Precrural	1,718	Bile	25
Prescapular	2,052		
Popliteal	1,576		

The dose of particles was mixed with milk and fed to a calf six weeks old which was killed 72 hr. later and a variety of tissue samples removed and their radioactivity estimated in a well-type γ-scintillation counter. All counts were corrected for radioactive decay to the time of dosing. In addition, tissue sections were rapidly prepared by routine histological methods and covered with autoradiographic stripping film so that the precise localization of radioactivity could be determined. The results are shown in Table 1.

Radioactivity was relatively high in the tonsil and certain lymph nodes but low in the blood, muscle and bile. This result is, as would be expected if the particles were absorbed through the tonsil and alimentary canal, followed by distribution in the reticulo-endothelial system of the body. Confirmation of this was obtained by autoradiography, in which the localization of apparently individual particles could be traced in the tissues by the presence of tiny areas of dense blackening in the stripping film. By this means particles could be detected in the wall of the tonsil, pharynx (Fig. 1) and small intestine. Within the body they appeared to be associated with cells of the reticulo-endothelial system, particularly in lymph nodes (Fig. 2) and the spleen.

We conclude from these experiments that small numbers of particles of 1–5μ diameter can penetrate through the mucous membrane of the tonsil, pharynx and small intestine and be carried throughout the body, in apparently the same manner as bacteria. We suggest that the use of radioactive particles of this kind may prove to be a sensitive method for the study of various problems of infectious disease and possibly also in work on nutrition and nutritional allergy. Further details and results of experiments now in progress will be reported elsewhere.

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Influence of Tranquillizing Drugs on Phagocytosis *in vivo*

PHAGOCYTOSIS of invading micro-organisms has long been known to play a major part in the defence of the mammalian organism against infectious disease. In view of the widespread use and potent pharmacological activity of the tranquillizing drugs, it is not surprising that administration of such compounds has occasionally been associated with alterations in normal resistance to infection[1,2], and that such altered clinical responses have been linked to changes in the phagocytic activity of the reticulo-endothelial system[3].

Vinegar and Berger[4] have recently reported that, in high doses, chlorpromazine, hydroxyzine and reserpine slowed the clearance of carbon particles from the blood of mice, but did not do so in low doses. Carbon particle clearance was not altered by meprobamate in either high or low doses. On the other hand, at the low dose employed by Vinegar and Berger, Ludány[5,6] found marked inhibition by chlorpromazine of the phagocytic activity of leucocytes from peripheral blood of dogs and rabbits.

In an effort to approximate more closely natural conditions than either carbon clearance or *in vitro* phagocytosis, an *in vivo* bacterial study was undertaken. Large male Wistar rats in groups of four were injected intraperitoneally with tranquillizing agents suspended in 5 per cent acacia solution. Three doses, 8 hr. apart, were administered to the experimental animals while control animals received 5 per cent acacia solution on the same schedule. All food was withheld during the experiment since it has been reported that phagocytic activity is enhanced by starvation[7].

Eight hours after the last injection of tranquillizer or acacia solution, each animal received 20 ml. intraperitoneally of broth culture of *Staphylococcus aureus* filtered through sterile glass wool and diluted with sterile saline to give approximately 50 per cent transmittance on a Coleman 'Junior' spectrophotometer. After 3 hr., animals were killed by decapitation and the peritoneal cavity opened. Duplicate slides of the contents were prepared, stained and counted for phagocytic activity by the method of Kuna *et al.*[7].

Table 1. EFFECT OF PRETREATMENT WITH TRANQUILLIZERS ON THE PHAGOCYTIC ACTIVITY OF RAT LEUCOCYTES

Drug	Dose (mgm./kgm.)	Percentage of cells showing phagocytosis	Mean (per cent ± *S.E.*)	Significance of difference from control (*t* test)
5 per cent acacia (control)	—	32 38 24 31	31 ± 3	—
Chlorpromazine	25	63 71 86 70	73 ± 8	$P < 0{\cdot}01$
Reserpine	1	20 17 27 25	22 ± 2	$P < 0{\cdot}05$
Meprobamate	200	40 63 64 30	49 ± 8	$P > 0{\cdot}05$
Hydroxyzine	25	30 31 22 36	30 ± 3	$P > 0{\cdot}7$

Table 1 shows the effects of the four test agents on phagocytic activity as compared to acacia controls in a single run. It is apparent that pretreatment of rats with tranquillizing drugs resulted in marked alterations in phagocytic activity, with reserpine significantly depressing phagocytosis, chlorpromazine significantly enhancing phagocytosis, and hydroxyzine and meprobamate being largely without effect in this regard.

Analysis of variance[8] of the data obtained confirms the fact that the variation in phagocytic activity following drug treatment does not represent variation within a single population.

Repetition of the experiment at later dates gave comparable results, and the control values obtained by us are in agreement with reported values for untreated, starved rats[7].

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Influence of the Surface of the Small Intestine on Enzymatic Hydrolysis of Starch by Enzymes

THE classical conception of digestion as being the sum of processes occurring in the chyme under the influence of hydrolytic enzymes fails to explain many important physiological and clinical phenomena.

In previous papers[1,2] it was shown that cavital (chyme) digestion is probably not the sole or main mechanism underlying the hydrolysis of food. It was suggested that the surface of the intestine presents a living porous reactor (the pores being formed by microvilli), on the surface of which intensive hydrolysis occurs on account of enzymes (self-contained and adsorbed) on the external side of the cellular membrane. (The presence of microvilli was first demonstrated by Granger and Baker[3] and later confirmed by many authors.)

The enzymes form a rather strong layer, which possibly has an ultrastructure analogous to what is known about enzymes on the membrane of mitochondria.

This is of great importance and suggests an enzymatic conveyer ensuring continued splitting followed by absorption of the food.

The system of processes occurring on the surface of the intestine we have designated as membrane or contact digestion[1].

Previous experiments have revealed that hydrolysis of larger molecules occurs mainly under the influence of dissolved enzymes while intermediate products are better split on the intestine surface. Thus, membrane digestion seems to be the intermediate link between cavital hydrolysis and absorption. For the latter it is the main source of providing substances for resorption[2].

The comparison of amylolytic hydrolysis *in vitro* and in the intestine has shown that the considerably greater speed of starch digestion in the organism is due to the operation of membrane hydrolysis and the interaction of the latter with hydrolysis in the chyme. These results were confirmed by model tests *in vitro*. It was established that the addition of a piece of living intestine to a pancreatic amylase solution results in a sharp increase in the speed of starch hydrolysis, which considerably exceeds the sum of the amylolytic activities of the solution and the intestine taken separately. It was further established that not only living intestine but also that first treated with trichloracetic acid and then washed, that is, an intestine without any enzymatic activity of its own, considerably increases the activity of pancreatic amylase. A special analysis has shown that a certain amount of dissolved enzymes is adsorbed on the surface of the intestine, and thus a system is created in the test tube in which interaction of cavital and membrane hydrolysis occurs[1,2].

Judging by the increase of amylase activity following the addition of mucosa treated with trichloracetic acid, membrane digestion is practically absent in the œsophagus, is only slightly marked in the large intestine and the stomach, and is well marked in the small intestine. Taking into consideration that membrane digestion should be preceded by cavital digestion and the former is closely related with absorption, such a topography will not seem casual.

Yet the question of what groups of animals are characterized by membrane digestion remained uncertain as former investigations were conducted on albino rats only.

The present work presents an investigation of the ability of pieces of mucosa taken from the small intestine of various animals to increase the activity of pancreatic amylase *in vitro*. Pieces of mucosa (1–1·5 sq. cm.) from the upper portions of the small intestine were taken from albino rats, albino mice, rabbits, cats, pigeons and frogs. The pieces were quickly taken from narcotized animals, washed in cooled Ringer's solution and then placed into a 5 per cent solution of trichloracetic acid. The concluding stage of treatment consisted of continuous and repeated washing in Ringer's solution at the temperature of 2–4° C. (Methods of preparing trichloracetic acid models are described in greater detail elsewhere[1]. The amylolytic activity was determined colorimetrically by the reduction of starch iodine staining Smith-Roy's method, somewhat modified.) The concentrations of the pancreatic crystalline amylase were so selected that the starch hydrolysis was 30–50 per cent in 30 min. at 38° C. and *p*H 7·2.

Special tests proved the absence of substances activating the amylase in the trichloracetic acid intestine models.

As shown in Fig. 1, the mucosa of the small intestine of a pigeon, albino mice, rabbit and a cat possesses the ability to increase amylase activity *in vitro*, approximately to the same degree as the well-investigated small intestine mucosa of the rat. I consider

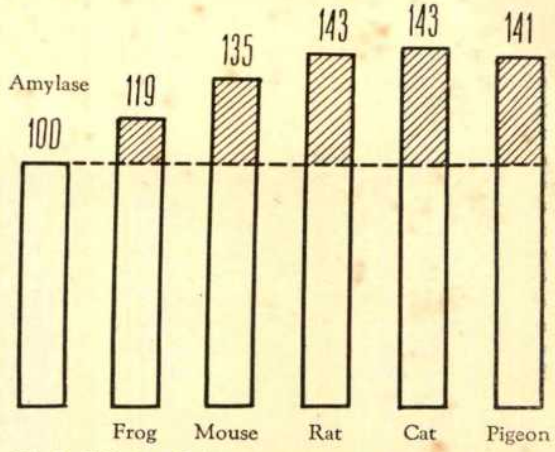

Fig. 1. Influence of pieces of mucosa from the small intestine on starch hydrolysis with amylase in various animals. Increase of activity is shown by the hatched part of the column above the background line. The activity of amylase solution is taken as 100 per cent; the trichloracetic acid intestine models possess no amylolytic activity of their own

this effect (with the reservations quite natural in such cases) to be a manifestation of membrane activity. The above experiments suggest the assumption that membrane digestion is inherent to all higher animals having various types of food ingestion. It is interesting that the same phenomenon, though to a lesser degree, is caused by the mucosa of the small intestine of the frog in which the typical villi are absent. Yet in Amphibia microvilli have been described which we are inclined to consider the structural basis of membrane digestion. If only this assumption is correct, membrane digestion must occur in the great majority of animal groups, for microvilli have been described even in roundworms[4].

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HÆMATOLOGY

Genetic Aspects of Two Different Minor Hæmoglobin Components found in Cord Blood Samples of Negro Babies

DURING work on the hæmoglobin types in the cord blood of Negro babies 70 samples were investigated by starch-gel electrophoresis[1]. The following results were obtained: 52 cases with HbA and HbF; 10 cases with HbA, HbF, and HbS; 3 cases with HbA, HbF and HbC; 3 cases with HbA, HbF, HbS, and a fast-moving component I; 1 case with HbA, HbF, and a fast-moving component II and 1 case with HbA, HbF, HbS, and a fast-moving component II. Using the carboxymethylcellulose chromatographic method[2,3], component I was found to be present for 3·2, 1·4 and 2·9 per cent respectively and component II for 5·6 and 6·5 per cent respectively. Work on the isolated fast-moving hæmoglobin fractions (prepared

by *CMC* chromatography) have shown that the two minor fractions were entirely different in structure[4-6]. These differences may be summarized as follows: (*a*) component I was slightly more resistant towards alkali than HbA, while the denaturation-rate of component II was intermediate between those of HbA and of HbF; (*b*) the ultra-violet spectrum of component I was similar to that of HbA, while the ultra-violet spectrum of component II was of the type found for HbF; (*c*) 'Amberlite *IRC*-50' chromatography of the globins prepared from the two hæmoglobin fractions at *p*H 1·9 with a urea gradient from 2 to 8 *M* revealed the presence of only β-polypeptide chains in component I and only γ-chains in component II; (*d*) sickle-cell hæmoglobin was formed as hybrid from a mixture of component I and normal HbA, and fœtal hæmoglobin from a mixture of component II and HbA. It seems, therefore, that component I (called 'Augusta I') consisted entirely of the β-chains of HbS, while component II is identical with Bart's hæmoglobin in being composed solely of the γ-chains of fœtal hæmoglobin.

Hæmoglobin studies of family members were possible for one family with the 'Augusta I' component and for two families with the Bart's hæmoglobin. The hæmoglobin samples were studied by starch-gel electrophoresis[1], by *CMC* chromatography[2,3] and by an alkali denaturation procedure[3]. In the 'Augusta I' family, the father and his sister, the mother, seven children (including the new-born baby) were available. In the blood of the new-born child HbA, HbF, 3·2 per cent of 'Augusta I', 0·8 per cent of HbS were demonstrable; the percentage of the fast-moving component being decreased to 2·1 per cent and the amount of HbS increased to 1·9 per cent[5], in a period of 45 days. Small amounts of an Hb-H-like component were also demonstrable in the cord blood sample. The mother and one of the children were completely normal; no increased percentages of HbF were detectable, while the HbA_2 component was present for 1·9 and 2·1 per cent. The father, his sister and three other children were heterozygous for HbS. Next to this abnormal hæmoglobin, however, minute amounts (about 0·1 per cent) of a fast-moving fraction were demonstrable. This fraction possessed electrophoretic properties similar to those of HbH (or β_4^A). It seems, therefore, that these family members were also 'heterozygous for the α-chain deficiency'[7], resulting in the formation of very small amounts of HbH. The two other children were heterozygous for the sickle cell hæmoglobin; no fast-moving fraction was demonstrable in the hæmolysates of their red blood cells. These results indicate that two genetically determined hæmoglobin abnormalities were present in this family[5], both being inherited independently.

In the first family with Bart's hæmoglobin, blood samples obtained from the father, the mother, and seven children (including the new-born baby) were available. The amount of Bart's hæmoglobin in the blood of the new-born baby (as determined by *CMC* chromatography) was 5·6 per cent, fœtal hæmoglobin was present for 60·7 per cent, while a small amount of HbA_2 (0·5 per cent) also was demonstrable. The hæmoglobins of both parents and of the six other children showed no abnormalities; the percentages of fœtal hæmoglobin were less than 1 per cent, while the amounts of HbA_2 ranged between 1·9 and 2·3 per cent.

In the second case, the percentage of Bart's hæmoglobin was 6·5 per cent, while next to HbA, HbF (68 per cent), small amounts of HbS (4·7 per cent) and of HbA_2 (0·2 per cent) were present. Blood samples of both parents were available for study. The hæmoglobin of the mother was completely normal (HbF less than 1 per cent, HbA_2: 1·9 per cent), while the father had the sickle-cell trait (HbS : 34·5 per cent, HbA_2: 2·1 per cent, HbF less than 1 per cent). No other abnormalities were demonstrable.

The results of these family studies are of some special genetic interest since in the first family an abnormality in the production of the adult hæmoglobin types HbA and HbS is present during fœtal and adult life, while in the other two families an abnormal fœtal hæmoglobin is formed during fœtal life without any visible alteration in the pattern of adult hæmoglobin. It is likely that all three new-born babies suffered from a 'heterozygous α-chain deficiency', resulting, however, in the formation of entirely different 'α-chain lacking' abnormal hæmoglobin types. These findings suggest a qualitative difference in the α-chain deficiency, to be explained by a suppression of the formation of the adult α-chain in members of the first family and of the fœtal α-chain in members of the other two families. Therefore my results offer evidence that the production of adult and fœtal α-chains is controlled independently by two α-genes, which, however, must be almost identical in fine detail since the α-chains of HbA and of HbF do not show structural differences by the finger-printing technique, or by hybridization[8-10]. The adult α-chain deficiency seems to be more pronounced during fœtal life, but is still visible after birth by the production of small amounts of HbH. The 'fœtal α-chain deficiency' is confined to the synthesis of fœtal hæmoglobin; thus, no abnormalities are detectable in adult life.

The possibility exists that a heterozygosity for both adult and fœtal α-chain deficiencies is present in one individual and results in the presence of an abnormal adult hæmoglobin (as 'Augusta I') and of the abnormal fœtal hæmoglobin (Bart's hæmoglobin) in the same cord-blood sample. Evidence for the existence of this double heterozygosity was obtained by demonstrating two fast-moving minor hæmoglobin components in the blood of a new-born baby next to HbA, HbF and small amounts of HbC. The fastest-moving minor fraction was electrophoretically similar to Bart's hæmoglobin, while the slowest-moving minor fraction ('Augusta II') was probably composed solely of the abnormal β-chain of HbC. Unfortunately, examination of the hæmoglobins of family members was not possible.

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The Diego Factor in Japanese

It is already known that the study of blood groups and types and their distribution and heredity are of great significance in anthropology.

Since the Diego blood group was originally reported[1] in 1954 the investigation of this blood group and its incidence in different races of various countries have been reported by several authors. At present, the Diego factor has been found in the blood of South American Indians, and mixed bloods in Venezuela, Brazil, North American Indians, and Chinese and Japanese residents in Canada and Venezuela. No Diego factor was discovered in Caucasians and Negroes; therefore it seems that the Diego factor is an anthropological characteristic of Indians and Mongoloids.

The first investigation of the Diego factor in Japanese in Japan was carried out by Furuhata, Yokoyama and Kuniyuki[2] in Tokyo, and they found 2 (2·3 per cent) Diego positive (Di(a+)) bloods in 88 samples. The anti-Diego serum was kindly supplied by Dr. Philip Levine, Ortho Research Foundation, Raritan, New Jersey, for this investigation. The serum showed activity and clear-cut results by indirect Coombs test.

We received another antiserum through the courtesy of Dr. Miguel Layrisse, Banco de Sangre, Caracas, Venezuela, for the second study. This time we used serum to test the blood of people in Tokyo and in Kumamoto located in the southern part of Japan. Tests were made by the indirect Coombs technique and the results were 6 (4·1 per cent) of Di(a+) bloods in 146 random samples in Tokyo and 17 (7·5 per cent) in 227 unrelated people in Kumamoto.

Masaki and Furukawa[3] reported the frequency of the Diego factor as 16 (3·2 per cent) in 500 Japanese living in the Gumma area. They used anti-Diego serum obtained from Dr. James F. Mohn, Buffalo University, Buffalo, New York.

The incidence of the Diego factor in Japanese from our investigation is approximately 3–4 per cent in Tokyo and is a little lower than the 8 in 65 cases (12·3 per cent) in Venezuela reported by Layrisse and Arends[4] and the 6 in 77 cases (7·8 per cent) in Canada reported by Lewis, Ayukawa, Chown and Levine[5]. However, the incidence of the Diego factor was found to be about 7·5 per cent in the southern part of Japan. Moreover, Dr. Paul J. Schmidt (personal communication), Blood Bank, National Institutes of Health, United States, found an incidence of nearly 10 per cent of the Diego factor in samples from Fukuoka located on the same island as Kumamoto. One of us (N. U., personal communication) examined samples in Kumamoto more recently and found 8·7 per cent Diego-positive bloods.

Table 1. Frequency of Diego Factor in Japanese

Authors	Tested No.	Diego factor	
		Pos. (%)	Neg. (%)
Layrisse and Arends (1956)	65	8 (12·3)	67 (87·7)
Lewis, Ayukawa, Chown and Levine (1956)	77	6 (7·8)	71 (92·2)
Furuhata, Yokoyama and Kuniyuki (1957)	88	2 (2·3)	86 (97·7)
Masaki and Furukawa (1959)	500	16 (3·2)	484 (96·8)
Yokoyama, Murakata and Ueno (1960)	146* 227†	6 (4·1) 17 (7·5)	50 (95·9) 210 (92·5)

* Tested in Tokyo. † Tested in Kumamoto. The number includes 5 (6·7 per cent) Diego positive of 74 random samples previously cited by Layrisse, M., *Amer. J. Phys. Anthrop.*, **16**(2), 173 (1958).

From our present results, there appears to be a lower incidence of the Diego factor in northern Japan, with the incidence gradually increasing and reaching the highest incidence in Japanese in the southern part of Japan. This frequency suggests that the Diego factor may be an Asiatic characteristic as are factors for group B, Rh_0, kk and Gm^a[6].

We are indebted to Dr. P. Levine and Dr. M. Layrisse for the sera used in the testing.

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RADIOBIOLOGY

Alkoxyglycerols as Growth-stimulating Substances

In connexion with experiments on irradiated rats, it has been shown that the alkoxyglycerols or their esters prohibit to a certain extent the decrease both of megakaryocytes and of nucleated cells in the bone marrow, a decrease which usually occurs after irradiation[1]. When radiomimetic substances (for example, leukeran and myleran) are given to rats, a diminution of the above types of cells is equally observed. This diminution is also partly prevented by alkoxyglycerols.

It has now been found that the alkoxyglycerols have an effect not only on the bone marrow, but they also influence the growth of the rats. In general, normal, non-irradiated rats increase in weight more rapidly than irradiated rats. However, when irradiated rats were prophylactically treated with alkoxyglycerols the increase in weight was higher than for the irradiated control group, which received no treatment. The normal non-irradiated group showed an increase of 1·7 gm. a day per animal, the prophylactically treated group 1·3 gm. and the control group 1·1 gm.

When the alkoxyglycerols were found to promote the growth of rats, it seemed desirable to try their effect on *Lactobacilli*, which have been used as test organisms for many growth-stimulating substances. Twelve strains of *Lactobacilli* were tested. Pure synthetic media were used as substrates. The growth was determined turbidimetrically. The best results were found for *Lactobacillus lactis* (Fig. 1). The cultures were transferred to two sets of tubes, one control set with synthetic substrates and one with substrates to which had been added selachyl alcohol (an unsaturated alkoxyglycerol). A very striking effect is observed at a concentration of 20γ per ml. of alkoxyglycerols, but even at a concentration of 2γ per ml. a clearly observable effect is obtained. (I am indebted to Dr. Lennart Enebo for the performance of these experiments.)

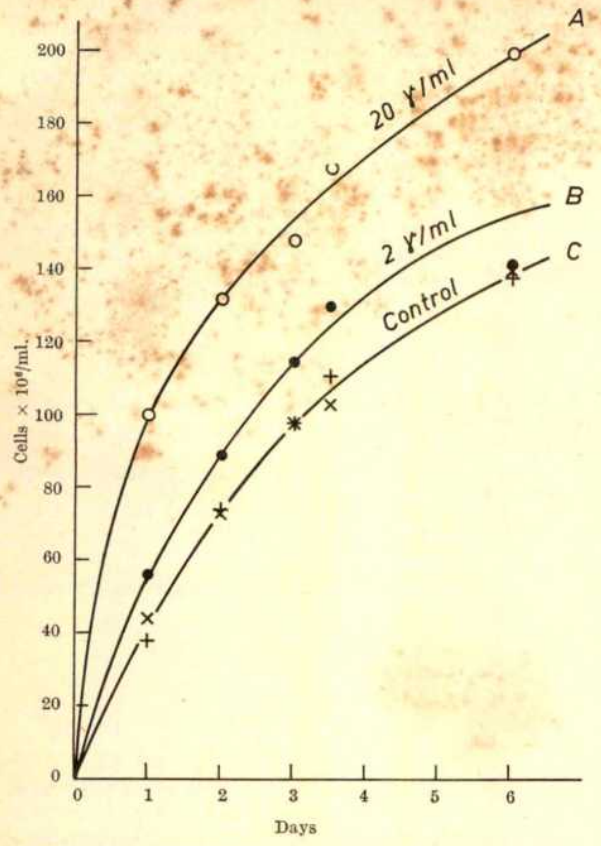

Fig. 1. Effect of selachylalcohol on the growth of *Lactobacillus lactis*. *A*, Synthetic substrate + 20γ selachylalcohol per ml.; *B*, synthetic substrate + 2γ selachylalcohol per ml.; *C*, control, synthetic substrate only

The observation that alkoxyglycerols stimulate growth is of interest since these substances are found in the blood-forming tissues (cf. ref. 2). From experiments on rats (*loc. cit.*) it was found that the alkoxyglycerols had an effect on both megakaryocytes and nucleated cells (from which derive several types of cells in the peripheral blood). The blood-stimulating factor vitamin B_{12} has an effect only on the red cells.

Very little is known of the formation of alkoxyglycerols in the body and of their presence in different foods. The effect of alkoxyglycerols in nutrition would be an interesting subject for further investigations.

A more detailed report of these experiments will be published elsewhere.

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An Apparent Difference in the Renal Clearance of Calcium-45 and Calcium-40 in Rats

IN investigating the comparative excretion of calcium-45 and strontium-89 in rats we have encountered evidence of unexpected variability in the renal clearance of calcium-45 and calcium-40. This finding may be significant in metabolic work employing radiocalcium as a tracer.

Weanling female Sprague–Dawley rats (group I) were injected intraperitoneally with 1·0 ml. of a solution containing carrier-free strontium-89, calcium-45, and 0·05 mgm. of calcium. Using methods previously described[1] urine was collected at the end of 30 min. and 60 min., and analysed for strontium-89, calcium-45 and total calcium. One hour after injection, blood was obtained from each rat by cardiac aspiration, and the concentration of strontium-89 and calcium-45 in the plasma was determined. A comparable group of rats (group II) was denied food for 12 hr. and the experiment repeated. The results are presented in Tables 1 and 2.

Table 1. CONCENTRATION OF STRONTIUM-89 AND CALCIUM-45 IN PLASMA

Group	No. of rats	Percentage of dose/ml. Strontium-89	Calcium-45	Sr-89/Ca-45
I	6	0·50 ± 0·03*	0·49 ± 0·02	1·01 ± 0·02
II	8	0·56 ± 0·02	0·56 ± 0·20	0·99 ± 0·01

* *S.E.*

Calcium-45 and strontium-89 occurred in slightly higher concentrations in the plasma of group II rats, yet these animals excreted considerably less of each during both collection periods. From the strontium-89/calcium-45 ratios in urine and in plasma it is further apparent that the renal clearance of calcium-45 was decreased more than that of strontium-89. This finding agrees with a previous report from this laboratory[1] which showed a progressive decrease with time in the renal clearance of calcium-45, relative to strontium-89, following the intraperitoneal injection of these isotopes.

Despite the markedly different excretion of labelled calcium, both groups of rats excreted equivalent amounts of total calcium. The reason for this is not apparent. It is unlikely that the short period of food denial would affect the total serum calcium. There is also no reason for believing that the renal clearance-rates of calcium-45 and calcium-40 differ intrinsically. While a slower absorption of the injected calcium-45 could account for its diminished excretion by group II rats, the results of a separate experiment would serve to rule out this possibility. Here it was found that the plasma of similarly starved rats contained a higher percentage of calcium-45 30 min. after injection than did that of non-starved controls, namely, 1·20 per cent and 0·89 per cent respectively. (Corresponding 1-hr. values were

Table 2. URINARY EXCRETION OF STRONTIUM-89, CALCIUM-45 AND CALCIUM

Group	No. of rats	Period (min.)	Percentage of dose excreted Strontium-89	Calcium-45	Sr-89/Ca-45	Calcium excreted (mgm.)
I	6	0–30	3·15 ± 0·60*	0·81 ± 0·26	7·2 ± 2·9	1·09 ± 0·07
II	8		0·31 ± 0·06	0·02 ± 0·001	13·0 ± 1·6	1·12 ± 0·09
I	6	30–60	1·31 ± 0·36	0·32 ± 0·14	5·4 ± 0·9	0·87 ± 0·05
II	8		0·17 ± 0·03	0·03 ± 0·008	6·2 ± 0·8	0·84 ± 0·03

* *S.E.*

0·52 per cent and 0·46 per cent.) An explanation for the disproportionate excretion of calcium-45 and total calcium under these conditions may possibly be found in a different partitioning of the injected label among the body calcium pools.

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Uptake of Phosphorus-32 by the Roots of *Lolium perenne*

PREVIOUS work on the ability of various portions of the root to supply the shoot with minerals has been carried out using the seminal roots of cereals grown in nutrient solution when the plants were a few days old. Weibe and Kramer[1] considered that in barley the most active zone of absorption and translocation of minerals was situated some distance behind the tip. The results of Lundegårdh[2], also working on barley, indicated that most nitrate was translocated from the basal portion of the root, that is, that nearest the shoot.

Young seminal roots grown in nutrient solution may not be directly comparable with older nodal roots. The present experiments were conducted with plants of *Lolium perenne* a few weeks old which had been grown in soil and possessed several nodal roots. Just before the experimental treatments the roots were washed free from soil. All plants the roots of which showed signs of decay were rejected.

The absorption and translocation of phosphorus were studied using phosphorus-32. This was received carrier-free in dilute hydrochloric acid, which was added as required to the Hoagland solution. The plants were allowed to absorb the phosphorus-32 from this solution for 6 hr. The amount in the shoot tissue after this period was estimated by drying the material, digesting it with concentrated sulphuric acid and then measuring the activity of the resulting liquid, after making it up to a known volume.

In the first series of experiments, the ability of one portion of a root to absorb and translocate phosphorus-32 was studied. A portion of 12 mm. of one root of each plant was isolated by passing the root through a cellulose test-tube which had two holes opposite each other in its side. The junctions between the root and the test-tube were made watertight with simple ointment. Radioactive Hoagland solution (2 ml. with an activity of 5 μc.) was put in the test-tube while the rest of the root system was bathed in normal Hoagland solution.

The results of one experiment with white unbranched nodal roots 10–12 cm. long are presented in Table 1. The basal region absorbed most phosphorus-32 which was translocated to the shoot. Similar results were obtained in other experiments.

Table 1. UPTAKE OF PHOSPHORUS-32 AND ITS TRANSLOCATION TO THE SHOOT FROM THREE PORTIONS OF THE ROOT

Portion	Base	Middle	Tip
Shoot weight (gm.)	0·0515 ± 0·0092	0·0614 ± 0·0068	0·0548 ± 0·0080
Counts per min.	2,855 ± 697	605 ± 105	462 ± 231
Counts per unit weight	6·3 ± 1·5	1·1 ± 0·3	1·0 ± 0·4
No. of plants measured	6	6	6

Table 2. EFFECT OF CUTTING OFF THE ROOTS AT 2 CM. FROM THE BASE OF THE SHOOT ON THE UPTAKE OF PHOSPHORUS-32 AND ITS TRANSLOCATION TO THE SHOOT

	Uncut	Cut	*S.E.*
Shoot weight (gm.)	0·0705	0·0728	0·0041
Counts per min.	1,447	1,055	140
Counts per unit weight	2·03	1·46	0·19
Total root weight (gm.)	0·0362	0·0337	0·0037
Weight of root cut off (gm.)	—	0·0259	—
No. of plants measured	12	12	—

The value of the basal portion of the root was confirmed by an experiment in which plants with intact root systems were compared with plants the roots of which had been cut off 2 cm. from the base of the shoot. The roots of both series of plants were immersed in Hoagland solution to which phosphorus-32 had been added to give it an activity of 100 μc. per litre. Although the 'cut' plants had 77 per cent of their roots removed, the amount of phosphorus-32 reaching the shoots was only reduced by 28 per cent.

These experiments strongly suggest that it is from the basal portions of the roots that the shoot receives most of its phosphorus. The top few inches of the soil would therefore appear to be most important for the mineral nutrition of the plant. Boggie *et al.*[3] found that grasses absorbed more phosphorus-32 from the upper 10 cm. of the soil than from greater depths.

According to Stout and Hoagland[4] the phosphorus-32 would have to reach the xylem before it could be distributed throughout the plant. It would seem, therefore, that the thickened endodermis found in this region of the root[5] was not an effective barrier to the inward movement of ions, as suggested by Weibe and Kramer[1]. Alternatively, there may have been considerable downward movement of phosphorus-32 in the cortex either to the younger regions of the root where the endodermis was not thickened, as suggested by Soper[5], or upwards to the junction of the root and shoot. If the thickened endodermis was an effective barrier, the plants with 'cut' roots in the second experiment must have absorbed the phosphorus-32 through the exposed xylem on the cut surface.

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BIOPHYSICS

Physico-chemical Properties of Purified Cytochrome a

THE enzymatic and spectral properties of purified cytochrome *a* isolated from animal tissues in soluble form have been studied by many investigators. However, a number of questions remain unanswered as to its physico-chemical properties. In previous

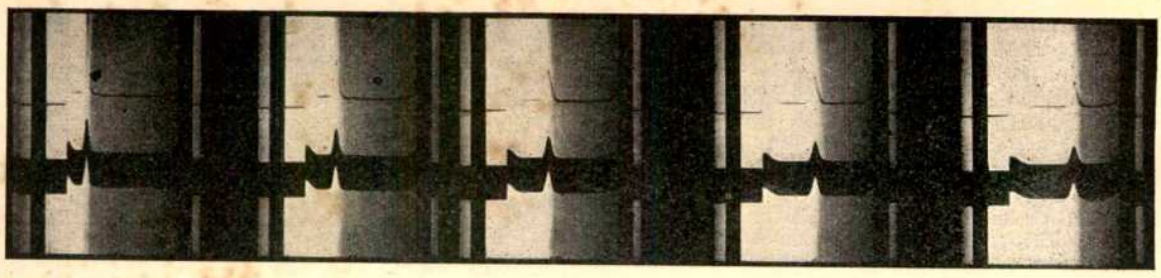

Fig. 1. Sedimentation pattern of cytochrome *a* in 0·1 *M* phosphate buffer containing 0·25 per cent 'Emasol 1130', *p*H 7·4. The direction of sedimentation is from left to right. The numbers under the photographs indicate the time in minutes after the rotor attained full speed (51,000 r.p.m.). The average rotor temperature was 16·4° and the protein concentration 0·54 per cent. (The small peak shown on the left may be due to detergent)

communications[1,2] we have reported that a synthetic non-ionic detergent effectively reactivated purified cytochrome *a* while an ionic detergent was inhibitory. To study cytochrome *a* in an enzymatically active state in the presence of a non-ionic detergent, we have carried out various sedimentation experiments by ultracentrifuge. The highly purified cytochrome *a* preparation used in these experiments was prepared from ox heart muscle as described in the previous communication[3]. Cytochrome *a* was dialysed against 0·1 *M* phosphate buffer containing 0·25 per cent 'Emasol 1130' at *p*H 7·4 for 12 hr. The sedimentation pattern of cytochrome *a* in the presence of the non-ionic detergent, 'Emasol 1130', showed a single homogeneous and symmetric monodisperse component, as seen in Fig. 1, whereas in the presence of the ionic detergent, sodium cholate, the protein behaved as a polydisperse, aggregated system.

The sedimentation constant was determined at different protein concentrations and found to vary slightly with the protein concentration. A corrected value of $S_{20,w} = 21 \cdot 9$ Svedberg units was obtained. Diffusion was measured on a preparation which had been dialysed overnight against the solvent system used for the sedimentation experiments. From results at different protein concentrations, the mean value was calculated as $D_{20,w} = 3 \cdot 58 \times 10^{-7}$ cm.^{2} sec.$^{-1}$. The partial specific volume was found to be 0·72 ml. gm.$^{-1}$. Combining these values in the familiar Svedberg equation, a molecular weight of 530,000 was obtained. The minimum molecular weight calculated from the hæm, iron and copper contents was 100,000. Based on these results it is concluded that cytochrome *a* has about five molecules of hæm and five atoms of copper per molecule of protein. However, Criddle and Bock[4] recently succeeded in obtaining monomeric cytochrome *a* by treating a preparation with sodium dodecyl sulphate and estimated the molecular weight to be 72,000. Therefore, assuming that cytochrome *a* contains only one hæm and one copper atom per molecule, it would be expected that some kind of polymerization takes place and a monodisperse pentamer of cytochrome *a* exists in the non-ionic detergent solution. To test this possibility ultracentrifuge experiments are now in progress in our laboratory. The frictional ratio f/f_0 was calculated to be 1·12. If the molecule is an unhydrated rotational ellipsoid, the axial ratio would thus be about 3 : 1. Further detailed results on the physico-chemical properties of cytochrome *a* will be reported elsewhere.

We wish to express many thanks to Messrs. K. Kakiuchi and T. Takagi of Isemura Laboratory of this University for helpful advice on the physico-chemical measurements.

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A Potentiometric Method for Observation of Osmotic Behaviour of Prawns

IN the course of work on osmotic regulation of estuarine invertebrates, it was found that cryoscopic and vapour-pressure methods do not yield reproducible results in a tropical place such as Madras. The potentiometric method outlined here, which is based on the predominance of chloride ions in the blood of animals and in sea water, facilitates a continuous picture of changes in the concentration of the blood of an animal in a given medium and helps us to measure the amount of energy involved.

A simple concentration cell containing 2 per cent sodium chloride solution immersed in 0·5–4 per cent sodium chloride solutions registers potential differences varying from 0·5 to 30 mV., the e.m.f. developed being proportionate to the ratio of the difference in concentrations When such a cell was used with sea-water of 16·2 per mille sodium chloride within the cell and sea-water varying from 4·05 to 32·4 per mille outside, it was found that in spite of the occurrence of other ions besides sodium and chloride, the silver – silver chloride electrodes used indicated potential differences varying in the same way as before. At the laboratory temperature (30° C.) the e.m.f. will be $60 \times \frac{87}{109} \times \log_{10} \frac{c_i}{c_o}$, allowing for the conductances of sodium and chloride ions and also the fact that the concentration and junction potentials are involved.

Table 1

Concentrations of outside media (per mille)		4·05	8·10	16·20	20·25	24·30	32·40
e.m.f. in mV.	Internal medium: sea water 16·2 per mille (observed)	27·24	13·68	0·30	4·86	8·12	13·56
	Internal medium: sea water 16·2 per mille (calculated)	28·40	14·38	0·00	4·65	8·34	14·38
	Internal medium: blood of prawn	23·60	11·70	3·01	0·31	2·10	7·60

Values calculated thus for the concentration differences are given in Table 1 along with values recorded by experiment. The e.m.f. increases by 14·5 mV. when the external concentration was doubled, as expected from the calculations.

In estimating the concentrations of the blood of the prawn in sea water of different salinities, a silver – silver chloride electrode is left in the container while the second electrode, shaped like a needle, is inserted in the heart of a live prawn, tied to a glass slide and left in the container. The results are given in Table 1. It will be seen that in spite of the blood having a protein concentration of 80 gm./litre[1], and is surrounded by different tissues as well as cuticular membrane, the e.m.f. values indicate the differences in concentration fairly closely. Since the e.m.f. recorded is lowest (0·31 mV.) when the prawn is left in sea-water of 20·25 per mille, the chloride concentration of the blood may be inferred to be the same as that of outside medium. It may be noted here that Panikkar and Viswanathan[2] found the chloride concentration of the blood of this prawn (*Metapenaeus monoceros*, Fab.) to be roughly 20 per mille, determined by the Volhard titration method as described by Wigglesworth. This method is now being used by one of us (O. R. R.) for work on osmotic behaviour of this prawn. Since the electrode is sharp and slender, the prawns can easily survive the injury in about eight out of ten cases even though they are used every day over a period of ten days.

We thank Dr. P. C. Caldwell, of the Marine Biological Laboratory, Plymouth, for his helpful criticism and Prof. O. Suryanarayanan, Department of Chemistry, Presidency College, Madras, for discussions on the subject.

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BIOLOGY

Different Types of Body Movement in the Hagfish, *Myxine glutinosa* L.

FROM the systematic and anatomical points of view, Myxinoids are well known[1-4]; but there are as yet only short notes about their living habits[2,4,5]. During the summer of 1959, I had the opportunity of examining living hagfishes at the Universitetets Biologiske Stasjon Drøbak in the Oslofjord, Norway. I observed about 200 hagfishes living in aquaria and also freshly captured specimens.

Observations on the habits of hagfishes will help in describing the life-history of these animals. I propose to report here particularly the movements of the animals when disturbed in their self-produced slime masses. There are to be distinguished complicated moving patterns of the body of the hagfishes, the result of which is the cleaning and liberation of the surface of the body from adherent slime. This cleaning seems to be of essential importance for a normally functioning respiratory stream from the nasopharyngeal duct to the gills.

The animals were captured by means of eel-pots furnished with fish as bait[5]. Most of the observations were made with hagfishes captured from a depth of about 50 metres in the Oslofjord near Drøbak, also some at the Biologiske Stasjon Espegrend near Bergen in western Norway. Freshly captured animals were put as quickly as possible into aquaria furnished with sea water of a medium temperature of about + 8° C. In the aquaria there was a continuous flow of new sea water taken from a depth of 30–50 metres.

Normally the hagfishes lie nearly the whole time at the bottom of the containers, most of them stretched out, some rolled up. Animals disturbed by touching with a stick move in lively fashion for some minutes but return shortly after the end of the stimulus to their usual motionless position. Hagfishes which have not been fed for some days become very active as soon as food is offered, for example, small herring, annelids, etc.

The hagfishes show normal locomotion movements comparable to those of eels, snakes or worms. The body of the animal makes sinuous swaying movements caused by alternate contractions and relaxations of opposite muscle segments of the body (compare Fig. 1). Usually the animals move forward with the head as the front pole. But often, especially if touching an obstacle, for example, the wall of the container or another animal, the movement may be reversed so that the tail end becomes the front pole of movement. Also under such conditions of backward swimming, snake-like swaying occurs. The plane of the swaying movement is often, but not always, horizontal. Locomotion is possible in all directions of space with the same accuracy. Sometimes a sort of rotation along the main body axis is observed, giving an impression comparable with driving a screw.

Fig. 1. Normal snake-like swimming movement in the hagfish

Excited animals—for example, after repeated stimulation by a stick, but also spontaneously in the case of animals disturbing one another by slime production (for example, in crowded containers)—show other types of movement besides the normal snake-like swaying. These special movements are in most cases connected with the liberation of the animals from slime masses covering their body surface.

Roughly two types of special movements can be distinguished: (1) The simpler one consists in a repeated rather narrow figure-of-eight movement of the body along the main body-axis. The general impression is similar to the usual snake-like type of locomotion, but the animal does not move forward or very little (Fig. 2). (2) The second type is more conspicuous and, I believe, is connected with a more intense excitement of the animals. At first the hagfish forms a loop by means of the end of its tail (Fig. 3). The loop remains close to the surface of the body and in the following stage of the movement the whole body is pulled through the loop, thus wiping away the slime from the surface of the body. The direction of this type of movement is from the tail towards the head. After passing the mouth and the nostril the loop opens again. The general impression of this type of movement is that of 'knotting' the body. The time necessary for one knotting movement is about 2–3 sec. Such knotting-movements are normally performed twenty times or more. After having finished with knotting, the animal swims off, moving then in the normal snake-like manner, and after some seconds or even minutes of swimming it comes to rest again in the usual manner at the bottom of the container.

Both types of special movements (figure-of-eight motion and knotting) are, according to my observations, always connected with intense excitement of the animals and are therefore to be regarded as 'excitement movements'. Intense excitement in most cases leads to the production of large amounts of slime. The types of movement described therefore serve to liberate the animals from self-produced slime, and also from slime produced by other members of the species or disturbing agents. Slime seems to be dangerous to the animals not only mechanically but also by the interruption of the water-stream from the nostril through the craniopharyngeal duct into the gills and thus causing cessation of 'breathing'. Before performing the special movements, the animals are often as it were exhausted; but after repeated 'knotting' and 'figure-of-eight motion' their bodies assume their normal motion.

The two types of special movements are performed in different positions of the body in relation to the bottom of the container, mostly of course in a general horizontal position.

It is obvious that these patterns of movement with their exact step-by-step decrease have a functional background in a central nervous mechanism released by special stimuli.

Fig. 2. Typical appearance during figure-of-eight motion

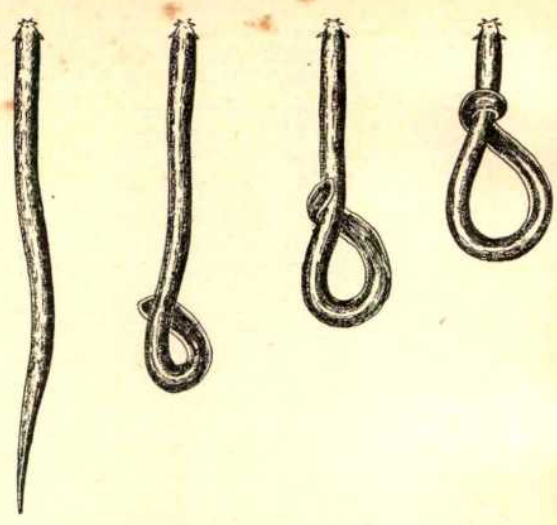

Fig. 3. Knotting motion in *Myxine glutinosa*. Succeeding stages from left to right, schematic

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Transplantation of Mammary Glands

I WISH to describe two methods I have used of transplanting whole mammary glands in goats. The work was undertaken so that mammary function could be studied in conscious undisturbed animals, by experimenting on one gland and comparing it with the control gland on the same animal. Anæsthesia reduces the rate of milk secretion, and it is not easy, for example, to make repeated flow measurements or arterial infusions in conscious goats because the main artery is difficult to exteriorize effectively. By transplanting one gland on to another site on the animal, the main artery and vein are made readily accessible. It is well known that mammary growth and milk secretion can take place after the nerves to the tissue have been removed, and it is generally

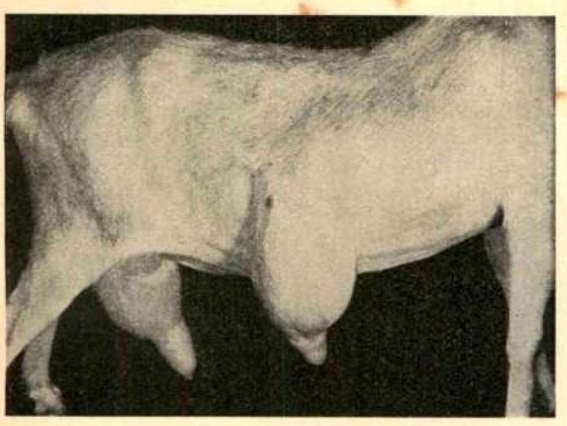

Fig. 1

believed that these processes are almost entirely controlled by hormones. Although Ribbert showed in 1898 [1] that small pieces of mammary tissue survive autotransplantation and show histological signs of normal growth and function, there have been no reports of the transplantation of whole glands nor of the quantitative measurements of growth and lactation of denervated tissue that are possible with the present methods.

The first results were unexpected since apparently successful transplants made in young kids failed to grow normally during pregnancy and yielded much less milk than the control glands in the normal situation. This was reminiscent of the long-term deficiencies following section of the spinal or sympathetic nerves to mammary tissue reported in some laboratories[2]. With modifications in technique, other transplanted glands have grown almost normally and the maximum yields have reached 70–90 per cent of the controls during lactation.

(1) *Transplantation in* 2 *or* 3 *stages*. By this method the gland was moved in stages to its new site (on the side or back) in such a way that it always retained a vascular link with the animal. It has been done in four virgin animals just before the first pregnancy, and in one animal at the end of the first lactation (Fig. 1). At the first operation one gland (half the udder) was separated from the body except for the skin at its front and the caudal superficial epigastric vessels ('milk' vein and artery) lying beneath this skin. These vessels were thus the only source of blood, and since they anastomose with the cranial superficial epigastric vessels emerging through the abdominal wall by the xiphoid, once they had enlarged, the result was a gland supplied by a readily accessible artery and vein each 25–30 cm. long. During this phase the gland was replaced in the normal position for 3 weeks and then again dissected out on this long pedicle right back to the xiphoid region. A piece of skin the size and shape of the gland was removed over the last rib and the gland was pulled into this space by tunnelling under the skin, and then stitched into place. Although it is almost certain that the entire nerve supply is cut by these two operations, in one goat the caudal superficial epigastric vessels were resected at a third operation three weeks later. In another the artery was exteriorized as a skin-covered loop which has remained patent for two years.

(2) *One stage transplant*. This has been done only in two goats, both in full lactation. In both cases one gland was removed entirely from its normal site and stitched on to the ventral surface of the neck (Fig. 2), the main artery and vein being joined to the carotid artery and the external jugular vein respectively. The control gland was pulled over to close the gap left in the inguinal region and now lies in the midline. In the first animal the caudal superficial epigastric vessels were joined to the omocervical vessels with polythene cannulæ within 16 min. and the main vessels were anastomosed within 100 min. to the carotid and jugular end-to-side by Phelan's trapdoor technique[3]. The carotid was tied above the join one month later. In the second animal the vessels were joined end-to-end in 36 min. using 1 cm. long stainless steel Payr cannulæ outside the mammary vessels and then stitched. This animal was then given one dose of heparin (1,000 U./kgm.). At both operations the main efferent lymph duct was cannulated and brought to the exterior. However, after the operation the lymph-flow slowed down markedly, probably associated with general anæsthesia[4], and to prevent clotting the cannulæ were removed. A defective lymph drainage may be why both transplants became more swollen than the controls. Whereas the milk yields of the controls recovered within 4 days, the transplants took 10 and 16 days and are still slightly œdematous 6 weeks after the operation. It should be possible to exteriorize the mammary vessels later.

Some observations made on all these goats may be mentioned. The 2-stage technique is easier to apply to virgin animals but, at best, glands transplanted in this way have given only 70 per cent of the expected milk yield. Furthermore, in one animal a decrease in yield was seen in the second lactation after the

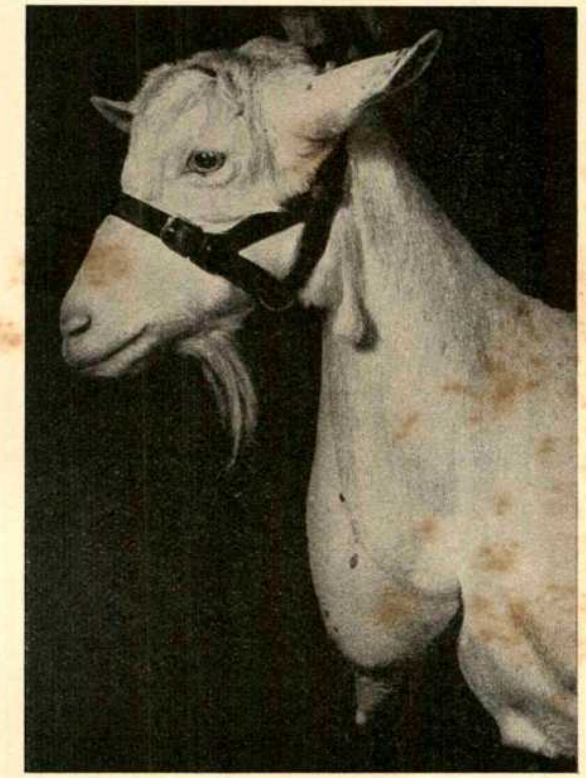

Fig. 2

transplantation and there is some evidence to suggest that the transplanted gland is affected by the presence or absence of the control. The newly acquired blood supply may well be inadequate. For this reason the one-stage technique would seem to be better and the milk yields of the two animals investigated are 75 and 90 per cent of that expected six weeks after the operation although the long-term results are not yet known. The operative technique could be improved by joining the blood vessels much more quickly and anastomosing the lymph duct to the lymphatics of the neck. In contrast to denervated glands or to those transplanted back into the normal site, when regeneration of sensory nerves has been fairly extensive during the course of pregnancy, the glands transplanted in two stages have remained completely anæsthetic for up to 2 years. In one animal tests made 2 years after transplantation showed that a small number of vasomotor nerves had entered the gland with a new artery that had grown in from the surrounding skin. In none of the animals has it been possible to initiate milk ejection or rumination by milking the transplanted teat. In cases where both glands were transplanted (1 animal) or the control gland was removed (2), lactation proceeded in the apparent absence of milk ejection. By injecting oxytocin intravenously (200 MU.) during each milking for a week at various stages of lactation it was possible to assess the importance of milk ejection; in this way it was found that 80–98 per cent of the milk may be obtained in the goat without it. Tverskoy[5] also noted that after complete denervation of both glands in one out of four goats the complete yield could be obtained without oxytocin.

Further work is in progress to try to decide to what extent the residual deficiencies noted may be due to impairment of the blood supply and lymph drainage.

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Inflation of the Neck Pouch of the Marabou Stork

THE pouch of the marabou stork (*Leptoptilos crumeniferus* (Lesson), was described by Peters[1] and its nature investigated by Chapin[2]. Chapin concluded that the pouch was inflated by means of air from the left nostril being driven into a pair of thin-walled sacs in the neck.

Detailed dissection of specimens collected in the Nairobi area have revealed a complicated valvular mechanism in the left nasal organ, which directs air from the lungs into the neck sacs during exhalation. The left and right air sacs are inflated through the left nostril, air being directed by a series of valves behind and below the eye-ball and through a narrow passage over the pterygoid. This passage leads into the left air sac, which in turn communicates with a smaller sac on the right side of the neck. The left nasal organ is divided into two chambers, one leading directly from the external to the internal nares, and a second inflation chamber which leads from the external to the internal nares and also to the orbital passage by means of a valvular opening. The right nasal organ is similar but bears no opening to the orbital passage. Although this opening is closed, the passage and the pterygoid duct are both present.

Inflation of the neck pouch is accomplished in the following manner:

(1) *Inhalation*. Air is drawn into the lungs through the external nares, passing through either the nasal or the inflation chamber.

(2) *Exhalation*. When the air sac is to be inflated, the nasal chamber and the entrance to the inflation chamber are closed by means of a sphincter and a small constrictor muscle. When air is exhaled from the lungs it enters the ventral opening of the inflation chamber; whence it is directed by a concave valve through the posterior opening to the orbital passage and the air sac.

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Isolation of Transplantation Antigens from a Cultured Lymphoblast *L*-5178*Y*

EXPERIMENTS designed to characterize the nature of the transplantation antigens have been greatly hampered by the difficulty of obtaining large amounts of a homogeneous starting material. We would like to report the successful isolation of transplantation antigens from a mammalian cell cultured *in vitro*.

Fischer[1] has shown that a lymphoblast, *L*-5178*Y*, that originated as a spontaneous leukæmia of thymic origin in a *DBA*/2 mouse can be grown in tissue culture. The cells do not stick to glass and can, therefore, be grown easily in suspension. In the medium reported by Fischer, yields of 2–3 gm. wet weight per litre are routinely achieved. The cells grow logarithmically *in vitro* and in the ascitic fluid of a *DBA*/2 mouse with an 11·4-hr. generation time, and can be transferred from one condition to the other with an adaptive lag in growth of less than 24 hr.

Adult C_3H mice immunized with 10,000 *L*-5178*Y* cells reject an intraperitoneal challenge of 2×10^6 *L*-5178*Y* cells, a dose that results in abundant growth of an ascitic tumour which is fatal to 23 per cent of the non-immunized controls. Such immunized C_3H mice also show an accelerated rejection of a graft of *DBA*/2 skin on the tail[4]. Test grafts of *C*57 *BL* skin on the tails of both immunized and non-immunized C_3H mice are rejected at the same time, 10–15 days, indicating that *L*-5178*Y* contains antigens specific for the *DBA*/2 strain.

The antigenic substances were isolated in a soluble form and attached to particulates from freshly harvested *L*-5178*Y* cells grown *in vitro*. The fractionation procedure is based on the methods used by Billingham, Brent and Medawar[2] with spleen and thymus cells. Cells were suspended in distilled water, and treated in a Raytheon 10 kc./sec. sonic oscillator

Table 1. RESPONSE OF C_3H MICE TO IMMUNIZATION WITH WHOLE CELLS AND CELL-FREE EXTRACTS OF L-5178Y CULTURED *in vitro*

Antigenic material	Tumour challenge			Skin graft test		
	No. of mice tested	No. of survivors: Showing ascitic growth	No. of survivors: No detectable ascitic growth	No. of mice tested	Median survival time of grafts (days) *DBA*/2	Median survival time of grafts (days) *C57BL*
Control	30	22	1	5	13	12
Whole cells	10	0	10	6	6	—
Crude suspension	12	1*	11	4	7	—
Deoxyribonucleoprotein fraction	10	4*	6	6	7	12
Microsome fraction	10	2*	8	6	6	12
Soluble fraction	17	4*	13	7	6	13
*p*H 5 precipitate	10	2*	8	6	7	12

* The amount of ascitic growth found in these cases was always much less than that seen with controls tested at the same time.

in the cold for 1 min. at full power. After centrifuging for 10 min. at 3,000*g* to remove debris, the crude suspension was made 0·15 *M* in sodium chloride, and allowed to stand for 1 hr. in the cold. The pellet obtained after centrifuging for 10 min. at 5,000*g* consisted mainly of deoxyribonucleoprotein of the cells. The supernatant suspension was centrifuged for 1 hr. in the Spinco ultracentrifuge, model *L*, at 105,000*g*. This precipitate (microsomal fraction) and the soluble fraction were tested separately for antigenic activity. Each fraction was injected intraperitoneally into adult C_3H mice, so that each mouse received the extract from $1 \cdot 5 \times 10^8$ cells. Five days later, the animals were challenged by each of the test procedures outlined above. Antigenic activity, that is, protection of C_3H mice from a challenge dose of L-5178Y and an accelerated rejection of *DBA*/2 skin (Table 1), was found in each of the three cell fractions to about an equal extent. Whether the antigenic material in each fraction is chemically different or whether equal amounts of the same antigen are distributed among the three fractions has not yet been elucidated. What is interesting to note is that we obtained an antigenic response to 1·5 mgm. of a soluble proteinaceous material in both tests. In several experiments the antigenic material was found to precipitate after 24 hr. in the cold when the soluble fraction was adjusted to *p*H 5. Castermans and Oth[3] have also reported the isolation of soluble antigenic material from the nuclei of mouse spleen and thymus cells.

A detailed report on the chemical properties of active fractions and the animal test procedures used will be presented at a later date.

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Gibberellin and Sex Differentiation of Flowering Plants

THOUGH work on the influence of gibberellin on flowering of plants has been given much attention, up to now very little is known about the relation of gibberellin to sex differentiation of plants.

My experimental work was carried through with hemp (*Cannabis sativa* L., var. Rastislavická). Gibberellin was applied in aqueous solutions containing 5, 10, 25 and 100 p.p.m. The seeds were allowed to soak in the solutions 24 hr.; controls were in distilled water for the same time. The number of individuals in the different variations of the experiment ranged between 400 and 500, all variations of experiments being repeated twice. When examining the results I noted first of all the relation of gibberellin (*a*) to sex differentiation, (*b*) to growth of female and male individuals.

As to the relation of gibberellin to sex differentiation, an increasing percentage of female individuals following treatment with gibberellin was observed. The highest increase by 113·9 per cent (with regard to control plants) was registered with concentration 10 p.p.m.

Proportions of male and females plants $\left(x = \frac{a♂}{a♀}\right)$ after application of gibberellin were as follows:

control plants		$x = 1 \cdot 07$
application of gibberellin at	5 p.p.m.	$x = 0 \cdot 99$
	10 p.p.m.	$x = 0 \cdot 82$
	25 p.p.m.	$x = 1 \cdot 05$
	100 p.p.m.	$x = 1 \cdot 04$

When comparing the average length of stems of female and male plants at the end of vegetative growth, different reaction of female and male plants to various concentrations could be traced, both with respect to stimulating (lower concentrations) and inhibitory (higher concentrations) effect. To a greater extent the stimulating effect was shown on female plants where the maximum of stem elongation was 107·8 per cent with a concentration of 5 p.p.m., the maximum elongation on male plants being 106·5 per cent at 10 p.p.m. (percentage given with regard to control plants). The inhibitory influence of higher concentrations (25 and 100 p.p.m.) was manifested in a greater measure with female plants. Induction of male sterility, however, was not observed; male plants showed normal development after application of gibberellin.

Because of the close relation of gibberellin to the synthesis of growth substances, as well as on grounds of observations made by Laibach and Kribben[1,2] and by others, according to which sex expression of female and male flowers depends on the concentration of growth substances in the organism, it may be presumed that the observed reduction of percentage and the higher growth inhibition in male plants and, on the contrary, the increase of percentage, the higher stimulatory and lower inhibitory effect in female plants, after application of various gibberellin concentrations is related in some way to the synthesis (to various concentrations) of growth substances in female and male plants. Their increased production (dissolution) from some precursor or their destruction after gibberellin treatment (especially at higher concentrations) is probably capable of influencing the biochemical processes of female and male plants considerably, which may find expression—as the observations mentioned show—not only in processes

of growth but also in the process of sex differentiation itself.

The gibberellin used in these experiments was obtained through the courtesy of the Kyowa Fermentation Industries, Tokyo, and Plant Protection, Ltd., Fernhurst Research Station, nr. Haslemere, Surrey, England.

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Effect of Growth Substances on the Osmotic Value of Pea Stem Sections

IT has been shown that gibberellin does not increase the extensibility of the pea stem, while auxin does[1,2]. It thus remains to show whether gibberellin increases the osmotic concentration in cells, so as to increase water absorption. As to the effect of auxin on the osmotic concentration, conflicting results have been reported[3-5]. The present communication reports some experiments which reveal that gibberellin causes catatonosis while auxin causes anatonosis.

Pieces of stem, 10 mm. long, excised from an apical part of the third internode of etiolated Alaska pea seedlings were weighed and soaked in 20 mgm./l. solution of gibberellin (composed of A_1 4·5 per cent and A_3 90·0 per cent), 10 mgm./l. solution of indole-3-acetic acid or distilled water. After being floated on the solutions or water for 3 and 6 hr. at 25·5° C., the stem pieces were lightly blotted and packed in weighing tubes to prevent loss and condensation of moisture during weighing and freezing (at about −21° C.) to follow. After melting, tissue juice was obtained using a hand press. Freezing point of the juice was measured using a copper-constantan thermo-junction and potentiometer to the nearest 0·01° C.

Freezing-point depressions measured are presented in Table 1. The molar concentrations (w/v) of mannitol solution corresponding to them were determined by using a standard freezing-point curve prepared experimentally, and given in Table 1.

Let the water content of stem pieces be H and βH respectively before and after the treatment; and let the virtual amount of the 'solute' contributing to the osmotic concentration of tissue juice be S and αS respectively before and after the treatment. Then, the osmotic concentration of press juice is $C_0 = S/H$ before the treatment, and $C_1 = \alpha S/\beta H$ after that. The solute change factor, α, is given by:

$$\alpha = \frac{C_1}{C_0}\beta \qquad (1)$$

C_0 and C_1 are represented by mannitol values. The water-absorption factor, β, is the ratio of the amounts of water (βH and H) which are determined by subtracting from the fresh weights the dry weight of the tissue. The last-named was estimated with the same stem pieces as used in the experiment.

The values of β in Table 1 show that pieces treated with indole-3-acetic acid absorbed more water than control, while those treated with gibberellin did not. On the other hand, the 'solute' contributing to the osmotic concentration of tissue decreased more conspicuously with indole-3-acetic acid and gibberellin treatments than water control. In these experiments, however, solutes may have diffused out of the tissue into treatment solutions. Hence, in order to determine if catatonosis is really caused by indole-3-acetic acid and gibberellin, stem pieces were kept in air of constant humidity, instead of being put in the solutions.

Air equilibrated with the saturated solutions of magnesium sulphate and potassium phosphate and with distilled water is considered to be of about 90 per cent (ref. 6), 96·8 per cent (ref. 7) and 100 per cent humidity, respectively, at 25° C. Pieces of stem were smeared at both ends with lanolin pastes of 1 per cent gibberellin and of 0·5 per cent indole-3-acetic acid, as well as with pure lanolin. They were incubated under slow circulation of the above-mentioned air for 3½ hr. at 25·5 ± 0·01° C. The fresh weight of these pieces (carrying the lanolin) were determined before and after the incubation, and press juice was obtained from the pieces after the

Table 1. Effects of gibberellin and indole-3-acetic acid solutions on freezing point depression of press juice, factor of water absorption, and factor of change in the amount of the osmotically effective solutes, when etiolated pea stem sections were floated on the solutions

	Freezing point depression (° C.)	Mannitol equivalent (M (w/v))	Water absorption factor (β)	Solute factor (α)
Before treatment	0·60	0·30	—	—
After treatment for 3 hr. with				
Water	0·48	0·24	1·14	0·91
Indole-3-acetic acid (10 mgm./l.)	0·38	0·19	1·36	0·86
Gibberellin (20 mgm./l.)	0·44	0·22	1·15	0·84
After treatment for 6 hr. with				
Water	0·44	0·22	1·18	0·87
Indole-3-acetic acid (10 mgm./l.)	0·29	0·15	1·57	0·78
Gibberellin (20 mgm./l.)	0·40	0·20	1·21	0·81

Table 2. Effect of lanolin pastes of gibberellin and indole-3-acetic acid on freezing point of press juice, factor of water absorption, and factor of change in the amount of the osmotically effective solutes, when etiolated pea stem sections smeared with the pastes were kept in air of constant humidity

	Freezing point depression (° C.)	Mannitol equivalent (M (w/v))	Water absorption factor* (β)	Solute factor (α)
Humidity (100 per cent)				
Control	0·60	0·30	0·996	1·00
Indole-3-acetic acid (0·5 per cent)	0·75	0·38	0·997	1·26
Gibberellin (1 per cent)	0·55	0·27	0·994	0·90
Humidity (96·8 per cent)				
Control	0·60	0·30	0·986	0·99
Indole-3-acetic acid (0·5 per cent)†	0·71	0·36	0·984	1·18
Gibberellin (1 per cent)	0·56	0·28	0·986	0·92
Humidity (90·0 per cent)				
Control	0·61	0·30	0·955	0·96
Indole-3-acetic acid (0·5 per cent)	0·76	0·38	0·957	1·21
Gibberellin (1 per cent)	0·56	0·28	0·947	0·88

* Water absorption factor less than unity represents loss of water.
† Elongation effect of indole-3-acetic acid was rather small in this experiment made in winter, as is usually the case.

parts smeared with lanolin were cut off. The results are shown in Table 2.

The moisture contained in the pieces decreased slightly even in air of 100 per cent humidity. This may perhaps be due to evaporation during the transfer to and from the container for incubation. The pieces treated with indole-3-acetic acid had high osmotic concentration, the solute increase being large. The gibberellin treatment, on the contrary, caused a decrease in the 'solute'. It is therefore suggested that anatonosis is caused by indole-3-acetic acid, and catatonosis by gibberellin.

It has often been shown that indole-3-acetic acid increases extensibility of the cell wall. Together with this, the fact that anatonosis is caused by indole-3-acetic acid presents a simple hypothesis which can explain the way this acid causes elongation. On the other hand, gibberellin rather causes catatonosis, and, as has been reported[1,2], makes pieces of stem elongate less under a stretching force. Hence the mechanism of action of gibberellin should be sought from some other point of view.

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Protein from Sugar Cane

SUGAR cane is a major crop in many areas of the world where there is also malnutrition, particularly a shortage of dietary protein, and a high birth-rate. It is important that these areas should exploit to the full any potential source of protein for human diets, either to be consumed directly or indirectly through animal feeding.

Pirie has canvassed widely for more attention to the potentialities of leaf protein extraction, but sugar cane leaves, in common with the leaves of all high-yielding crops, are very low in protein, containing only about 6 per cent on a dry-matter basis.

The basis of extracting leaf proteins is maceration, filtration and coagulation. This scheme is almost followed by sugar factories for preparing the cane juice prior to its concentration, the heat-coagulated protein being filtered off along with other solids to give filter cake which may be returned to the fields as a soil amendment or even dumped as waste.

The heat-coagulable nitrogen content of cane juice is very small, but nevertheless the quantities involved during a crushing season are high.

Mauritius, with an annual crop of around 550,000 tons of sugar, produces about 100,000 tons of filter cake with a nitrogen content of 1 per cent. In other words, about 6,000 tons of cane juice 'protein' are returned to the soil each year as a fertilizer in a country where protein-deficiency symptoms are common among the population.

In the laboratory it is simple to produce a precipitate containing up to 8 per cent nitrogen from cane juice; on a factory scale, however, the problem is more difficult.

Much work has been done in cane-producing countries on the separation of cane-wax, but no process has yet proved to be economical. As the coagulate formed in cane juice on heating carries much of the wax with it, a combination of protein and wax recovery may prove to be financially interesting.

Research work is in progress in Mauritius to study the amino-acid composition and nutritional values of the heat-coagulated precipitates and the technological aspects of their separation. The full results of this work will be published later.

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Microspectrophotometry of *Euglena* Chloroplast and Eyespot

A SIMPLIFIED microspectrophotometer developed in our laboratory was applied to obtain the *in vivo* absorption spectra for the chloroplast and eyespot of the algal flagellate *Euglena*. The optical and electrical characteristics of this instrument, which utilizes a Bausch and Lomb grating monochromator and a cadmium selenide photoconductive cell, have previously been reported[1].

Euglena gracilis Z strain (obtained originally from Dr. S. H. Hutner, Haskins Laboratory, New York) cultured in a chemically defined medium under continuous fluorescent light (300 ft.-candles) in a temperature-controlled room of 25° C. was used for this work. Samples of *Euglena* were taken, during their log-phase of growth, from the culture bottles, placed on a microscope slide with the edges of the cover-glass sealed with 'Vaseline' to prevent drying-out of the organism and pressure applied in order to immobilize them. No further preparation or staining was employed. The prepared *Euglena* slide was immediately placed on the microscope, a chloroplast or eyespot was selected and focused for scanning with the microspectrophotometer. The reference area was the suspending medium adjacent to the organism; the half-band width of the incident radiation was 4·6 mμ. The green chloroplasts measure about 1μ in diameter by about 10μ in length[2]. The orange-red eyespot is 1–2μ in diameter by 3μ in length; it consists of packed granules and is close to its effector, the flagellum[5,6].

In Fig. 1*a*, the absorption spectrum of an individual chloroplast over the wave-length range 250–340 mμ is illustrated. The results are presented as percentage absorption for intervals of 10 mμ. This spectrum is matched at 340 mμ with another chloroplast spectrum, Fig. 1*b*, extending to a wave-length of 700 mμ. Except for small changes in relative peak heights, the results were consistent from one chloroplast to another within the same organism as well as in different organisms under the same condition of time of growth and light intensity. These chloroplasts have two major absorption peaks, one in the region 430–435 mμ and the other in the region 675–680 mμ with minor peaks near 485, 585 and 620 mμ. The peaks were

previously noted from absorption spectra on cell suspensions of *Euglena*[3], although fine-structure details and the spectra from individual organelles were not obtainable. Among the absorption peaks listed above, the 485 mμ peak is known to be due to carotenoids, while the others are due mainly to chlorophyll *a*, which has peaks at 432, 480 and 665 mμ in methanol. In following the absorption peaks with culture age, changes in the 415–435 mμ as well as new peaks appearing at 685–690 mμ could be observed. In the ultra-violet region, an absorption peak in the region 265–270 mμ with lesser peaks at 290, 340 and 390 mμ would indicate that the chloroplasts contain proteins and lipids.

The eyespots of *Euglena* were investigated in the visible range, 400–700 mμ. The reference area in this case was the cell cytoplasm or the vacuole adjacent to the eyespot. The spectrum for an average eyespot is illustrated in Fig. 2. In contrast to the chloroplast spectra, the eyespot results exhibited appreciable variation in peak height from one eyespot to another. They show that the eyespot has a broad absorption maximum in the region 480–490 mμ, two sharper maxima at 510 and 530 mμ respectively, and lesser peaks at 430 and 630 mμ. An absorption peak at 450–460 mμ was noted for several eyespots, and is shown as a shoulder on the curve in Fig. 2. This spectrum is in qualitative agreement with that obtained by Gössel using a microbeam larger than the eyespot cross-section[4]. The eyespot therefore absorbs light throughout the entire visible range. The action spectra for *Euglena* phototaxis has peaks at 420 and 490 mμ, and for photokinesis (rate of swimming irrespective of direction) has peaks at 465 and 630 mμ[5]. The eyespot absorption spectrum therefore contains these same peaks as do the action spectra. The interpretation of Fig. 2 with respect to the identity of the pigments present in the eyespot is, however, difficult. Normal green strains of *Euglena gracilis* produce three main carotenoids: β-carotene, lutein and neoxanthin. In a non-polar solvent, carbon disulphide, the absorption range of these carotenoids is 450–510 mμ. These carotenoids could therefore account for a major proportion of the observed absorption. However, astaxanthin, which has a broad absorption band at around 500 mμ and has been found in red variants of *Euglena*, and not identified here, could be masked by the above carotenoids.

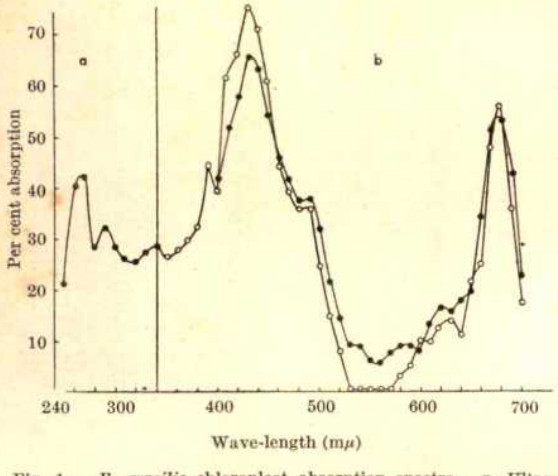

Fig. 1. *E. gracilis* chloroplast absorption spectra. *a*, Ultra-violet absorption over the range 250–340 mμ; *b*, visible absorption over the range 340–700 mμ of two different chloroplasts

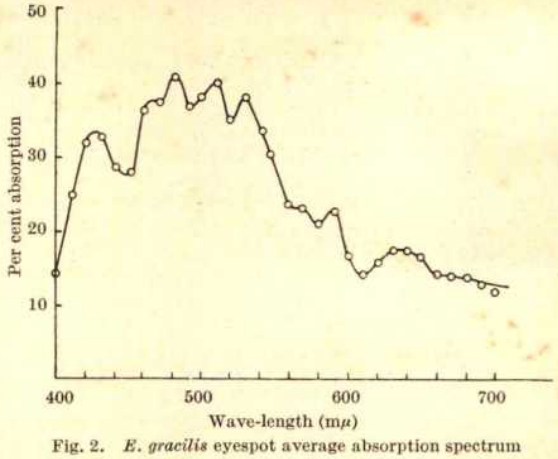

Fig. 2. *E. gracilis* eyespot average absorption spectrum

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MICROBIOLOGY

An Improved Method for photographing Superficial Microbial Colonies

THE lack of contrast in transparent superficial microbial colonies causes some difficulties during photography. The following method promises good results provided some precautions are taken. Suppose it is intended to photograph transparent, colourless colonies on nutrient agar plates. The surface of the medium is flooded with indian ink diluted in distilled water (1 : 100). The ink contains a pigment, carbon black, having a particle size of 200 Å. (Pelikan Tusche No. 541, Günther and Wagner, Hanover). When the upper layer becomes coloured (about 2–3 min.), the surplus solution is sucked off. As a result, in the weakly coloured medium the colonies remain colourless and in a photograph the distinction is clearly visible (Fig. 1). The principle of this procedure is founded on the slower penetration of coarse-grained colloid into the colonies and may be considered as the macro-adaptation of Burri's indian ink 'negative staining' method[1]. One must be careful to work

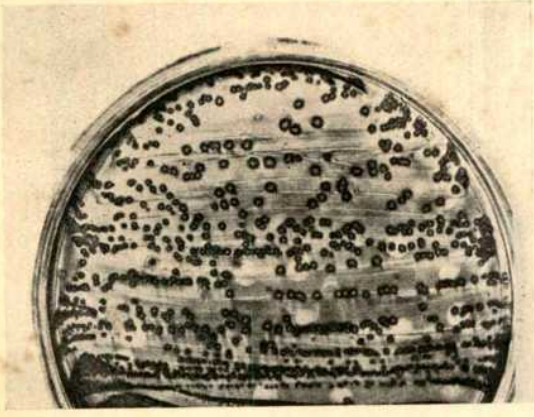

Fig. 1. Colourless and transparent colonies of *Salmonella paratyphi B* after treatment with diluted indian ink

quickly before the colonies become coloured and the dish should not be stirred because the colonies easily emulsify. The use of crossed 'Polaroid' filters or 'Polaroid *J*' film (Fisher Scientific) under and over the dish gives more contrasted pictures. As light source, an X-ray illuminator is suitable.

The advantages of the method seem to be at first in its application for the photographic documentation of colony counts, and for the visualization of small transparent colonies.

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CYTOLOGY

Determination of Sex in Granulopoietic Cells of Mice and Rats

WHILE examining Feulgen-stained sections of rat bone-marrow, it was observed that certain granulocyte precursors showed a body strongly resembling the sex chromatin described in other species[1] in that it occurred with much greater frequency in female than in male marrows.

In the initial work on the sex chromatin[1] it was not found possible to identify this body in rodents because of the coarse clumping of nuclear chromatin in the central nervous system, with which these studies were largely concerned. More recently, however, it has been shown that sex chromatin bodies may be demonstrated in those rodent tissues where the nuclear chromatin is sufficiently dispersed, for example, in liver cells[2,3], certain neurones[4], ameloblasts[5], amnion cells[3], cells in tissue culture[6] and a small proportion of peripheral blood leucocytes[7] in rats, and in neurones and liver cells in hamsters[3,8].

Accordingly, in view of the value a sex chromatin body could have as a marker in studies involving marrow transfer, the observations mentioned above were extended.

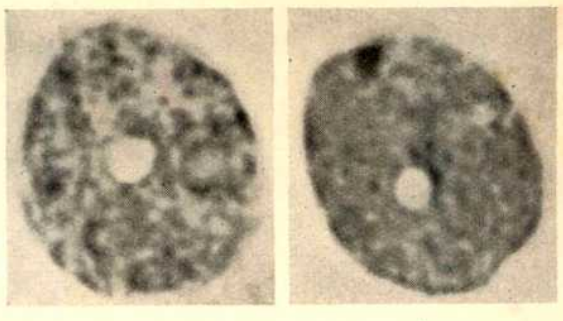
Colony-bred mice of *A2G*, *C57* and *AK* strains and rats of the *WAG* and *PVG* strains were used[9]. Femoral marrow was fixed in glacial acetic acid/ethanol (1:3) for 1 hr., re-suspended in water for 5–10 min., hydrolysed in *M* hydrochloric acid at 60° C. for 10 min., treated with Schiff's solution for 45 min. and transferred to chilled 45 per cent acetic acid. Permanent 'squash' preparations were made by the quick-freeze method[10].

A preliminary survey suggested that attention be concentrated on the cells classified by Harris and Burke[11] as 'typical metamyelocytes', large cells with ring- or doughnut-shaped nuclei, often with one or two nucleoli and showing, in Romanowsky-stained films, a few azurophil granules. In 'squash' preparations many of these cells show chromatin sufficiently dispersed to make observation of a sex chromatin body feasible. Only those cells were considered in which, apart from the bodies to be described, the chromatin was well dispersed, the nucleus showing a homogeneous lilac-stained background overlain by a finely condensed reticular or stippled pattern. Sometimes a few tiny splinter-like or nodular condensations were present, usually at the nuclear margins. Nuclei were excluded from consideration in which a sex chromatin body could not have been identified confidently had it been present, that is, the chromatin of which was coarsely reticular or nodular or that contained several small (less than 1μ in diameter) but deeply stained chromatin bodies, or more than one large chromatin aggregate or that were vacuolated. Nuclei which were damaged or overlapped by others, or were tilted or folded so that the position of a chromatin body could not be determined accurately, were also excluded.

Fairly conspicuous chromatin bodies were seen in some of the nuclei satisfying the above criteria; they stained with varying intensity and measured about 1/6–2/3 of the width of the nuclear sector in which they lay. They were usually solitary but nuclei were, for the purposes of this work, accepted as having such a body if they contained not more than one other appreciably smaller chromatin aggregate.

These bodies were either applied to the outer or inner aspect of the nuclear ring or lay free within the nucleus. In all positions their shape could be irregular, but usually they were triangular, trapezoidal or oblong if applied to the nuclear membrane and round or oval if lying free (Fig. 1). Peripherally situated bodies were sometimes bifid[12]. Bodies in other positions were often closely associated with a nucleolus.

Marrows were taken from three males and three females of each of the strains listed above, and all specimens were coded so that the sex of the animals was unknown until the results had been collected.



a *b*

Fig. 1. Metamyelocytes from marrow of a female *C57* black mouse. *a*, cell with no large chromatin body; *b*, cell with a large, peripheral chromatin body

Table 1. PER CENT INCIDENCE AND POSITION OF CHROMATIN BODY IN RAT AND MOUSE METAMYELOCYTES

Animal		Chromatin body			
		Peripheral	Central	Free	Absent
Male					
A2	1	2	4	24	70
	2	0	10	28	62
	3	0	6	22	72
C57	1	0	22	10	68
Black	2	0	22	20	58
	3	2	28	14	56
AK	1	2	20	30	48
	2	0	22	20	58
	3	2	6	12	80
WAG	1	0	2	26	72
	2	0	2	14	84
	3	0	2	32	66
PVG	1	0	0	28	72
	2	2	4	36	58
	3	0	0	30	70
Female					
A2G	1	52	12	18	18
	2	42	6	28	24
	3	30	22	28	20
C57	1	34	8	28	30
Black	2	34	24	10	32
	3	32	12	12	44
AK	1	52	8	18	22
	2	38	14	6	42
	3	34	10	16	40
WAG	1	40	2	38	20
	2	40	2	38	20
	3	48	4	34	14
PVG	1	34	10	28	28
	2	34	12	38	16
	3	44	6	16	34

Fifty nuclei were counted in each marrow and the presence or absence of a chromatin body and its position were recorded. Simple inspection of the results showed that marrows could be grouped into two non-overlapping classes: those in which the peripherally situated chromatin body occurred in 30–52 per cent of nuclei and those in which its incidence did not exceed 2 per cent. It was found that all the marrows in the former class were from females and all the latter from males. The results are summarized in Table 1. There was no clear sex difference in the incidence of chromatin bodies in other positions.

It can be concluded that the sex of mouse and rat metamyelocytes may be determined by the incidence of peripherally situated chromatin bodies, a finding that may be of use in studying the fate of inter-specific, inter-strain and intra-strain transfers of marrow.

The photographs were taken by Mr. D. F. Boxall.

M. C. BERENBAUM

Glaxo Laboratories, Ltd.,
Greenford, Middx.
April 13.

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Cytology of *Polygala*

COMPARATIVELY little is known of the cytology of the genus *Polygala*. Table 1 gives chromosome counts made on ten European and one South African species, together with previous counts for comparison.

The chromosomes of the *vulgaris–amara* group are very small but not uniform in size (about 0·5–1μ in somatic plates). Those of *P. monspeliaca* are yet smaller but seem more uniform, while those of *P. myrtifolia* are a little larger and not uniform. The chromosomes of section Chamaebuxus range from about $\frac{2}{3}$ to 4μ in length. The resting nuclei of the *vulgaris–amara* group are chromocentric, while those of Chamaebuxus have an abundant reticulum with some chromocentres[7].

In the *vulgaris–amara* group, apart from one rather larger bivalent in *P. calcarea*, individual chromosomes within the complement cannot usually

Table 1. CHROMOSOME NUMBERS OF *Polygala*

	No. of localities	British	Swiss	Other	Previous counts
Section X, Orthopolygala Sub-section 14 (Chodat (ref. 1)). the *vulgaris – amara* group					
P. alpestris Rchb.	6	—	$n = 17$ $2n = c. 34$	—	—
P. alpina Perr. and Song.	1	—	$2n = c. 34$	—	—
P. amara L.	—	—	—	—	$n = 14$ (ref. 2)
spp. *amarella* Cr.	9	$n = 17$ $2n = 34$	$n = 17$ $2n = c. 34$	—	—
P. calcarea Shultz.	6	$n = 17$	$n = c. 17$	$2n = 34$	—
P. comosa Schkr.	9	—	$n = 17$ $2n = 34$	—	$2n = 28$ (ref. 3) $2n = 28–32$ (ref. 4)
P. serpyllifolia Hose.	6	$n = c. 17$ $2n = 34$	$n = 17$	$n = c. 34$ —	—
P. vulgaris L.	23	$n = 34$ $2n = 68$	$n = c. 34$ $2n = c. 68$	$n = c. 34$ $2n = c. 68$	$2n = 28$ (ref. 4) $2n = 32$ (ref. 4) $n = 24–28$ (ref. 5) $2n = c. 56$ (ref. 4) $2n = c. 70$ (ref. 6)
Section X. Orthopolygala, other sub-sections					
P. monspeliaca L.	2	—	—	$n = c. 19$ $2n = c. 38$	—
P. myrtifolia L.	1	—	—	$2n = c. 38$	—
Section IX. Chamaebuxus					
P. chamaebuxus L.	6	—	$2n = c. 46$	—	$n = 23$ (ref. 7) $2n = 38$ (ref. 4)
P. vayredae Costa	1	—	—	$2n = 28$	—

'*P. oxyptera*' is included under *P. vulgaris*, and does not differ from it cytologically. The British '*P. austriaca*' (Kent) and '*P. amara*' (Yorkshire) are included under *P. amara* spp. *amarella*.

'Other' localities are as follows: *P. calcarea*, St. Andrews Botanic Garden (thought not British material); *P. serpyllifolia* (tetraploid), Corsica; *P. vulgaris* and *P. monspeliaca*, Portugal; *P. myrtifolia*, Antibes Botanic Garden; *P. vayredae*, horticultural, ex. Lausanne.

be picked out. Some of the larger chromosomes in Chamaebuxus can be recognized, however[7]. The largest two in the haploid set of *P. vayredae* have subterminal centromeres and resemble two in *P. chamaebuxus*, and a third nearly as large in *P. vayredae* has a median centromere and again could correspond to a chromosome in *P. chamaebuxus*, but two long chromosomes with terminal centromeres in *P. chamaebuxus* are not present in *P. vayredae* so that while *P. vayredae* may be a parent of *P. chamaebuxus*, a second parent must have contributed these latter chromosomes.

While previous work has suggested a less-orderly situation, the present work indicates that most species of the *vulgaris–amara* group are diploid with $n = 17$, *P. serpyllifolia* has both a diploid and a tetraploid race, and *P. vulgaris* is tetraploid with $n = 34$. Two less-closely related species of section X, *P. monspeliaca* and *P. myrtifolia* (a South African shrub), appear to have $n = 19$, which corresponds with Hagerup's[8] count on *P. erioptera*. In section IX (Chamaebuxus) two seemingly unrelated numbers have been found ($n = 14$ and 23).

Previous counts, except that by the Löves[6] ($2n = c.$ 70 for *P. vulgaris*), are all lower than those reported here. This is undoubtedly largely due to the extreme difficulty in counting the chromosomes of the *vulgaris–amara* group. Counts regarded as individually conclusive were obtained from only a small proportion of the localities examined in this work, though conclusive counts were obtained on each species other than *P. alpina* and clear cases of deviations from the numbers shown were extremely rare.

Baksay's[2] count on *P. amara* refers to a taxon not studied by me, but as her count was made on diakinesis, which I have found deceptive in that some chromosomes are not stainable until the very latest stages, the number could have been higher than she records. If some of the satellites recorded by Larsen[3] in *P. comosa* were independent small chromosomes his plant could be a $2n = 34$ form. Wulff[5], in recording $n = 24$ to 28 for *P. vulgaris*, spoke of difficulties in counting due to meiotic irregularities. Mattick's[4] finding of roughly diploid chromosome numbers in some of her *P. vulgaris* is interesting, but could be due to confusion with the closely related and very variable *P. comosa*. However, more work on European *P. vulgaris* is clearly needed.

Meiotic irregularities have been reported by Hagerup[8] and Wulff[5] in *P. vulgaris* from Denmark and Schleswig Holstein. In the present work they were found to be common in *P. comosa*, but rare in other species. The usual irregularity is the presence of univalents, leading to irregular tetrads. In *P. comosa* the degree of irregularity of the tetrads varied from bud to bud in the same spike (from apparent normality to about 40 per cent of the tetrads abnormal), suggesting that irregularities occurred in response to less favourable weather conditions. Most irregularities in other species could also be attributed to abnormal conditions. It is possible that at times the chiasma frequency may be so far reduced that some potential bivalents are not joined (cf. Elliott[9]).

Variation in the number of chromosomes in pollen grains of *P. chamaebuxus* has been established[7]; but it is not known if this reflects variation in the somatic chromosome number or is an immediate result of irregularities of meiosis. No irregularities in the meiotic process have yet been observed in this species, and more work is required.

A full account of this work, including observations on some interspecific hybrids, is in preparation.

Acknowledgment is made to the Department of Scientific and Industrial Research and to the Conseil d'Etat de Neuchâtel for financial support, and to Profs. D. H. Valentine of Durham and C. Favarger of Neuchâtel for their help and encouragement.

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PSYCHOLOGY

The Relativity of 'Meaning'

DR. W. ROSS ASHBY's communication on this subject[1] is very interesting and may prove to have much technical value, provided that it is possible to achieve a closed system of the outputs with which the brain may respond to the incoming message. This is the crux of the whole question. It is assumed that useful closed formalisms for this purpose are possible. In point of fact, every formalism that we know is made to work by unformalized human adjustments. Without these, the formalism would become so complex that it would lose its value as a shorthand. It would be uneconomical in practice.

It is necessary, then, in setting up a particular formalism to accept the limitation imposed by the practical use of the system and the resources available to use it. Ultimately, this means computing fast enough at an acceptable cost. I have no doubt that there will be invented successful schemes with limited applicability to handle the problem of meaning in translation and other processes that connect messages with action, but no useful purpose will be served by claiming to formalize all the possibilities of human behaviour.

It is very interesting to see recognized in a technical communication that application of a message shows its meaning in the context of the particular occasion, seeing that it is now some time since Wittgenstein first emphasized this thought, and the essential informality of behaviour in responding to ordinary language.

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[1] *Nature*, **187**, 532 (1960).

DR. W. ROSS ASHBY[1] has made the interesting assertion that the meaning of a message carrying information depends on the context of the message. Thus, if someone sends *A* of two possible telegrams, *A*, "How we wish you were here" and *B*, "The weather is fine", the meaning of the message is different from that of the same message chosen from three messages *A*, *B* and a third one, *C*, "Do come and join us". This may well be true in a coding

system as usable in mechanical information transfer, but it is not true of ordinary human assertions, messages and speech, except possibly in a few odd cases. If a radio message is sent, "The flowers are blooming", and it is the expected message instructing a submarine commander to release a torpedo, it is arbitrary that this particular sentence was prearranged as the message. It could have been a bell sounding, or a man blowing his nose that was the message. If I wish to convey the information that the cat is on the mat, in English, it is not arbitrary what message I use. As the corollary of this, it would be absurd to say that one of the possible meanings of the English sentence, "The flowers are blooming", is that it is an order to fire torpedos. It is similarly absurd to say, as Ashby does, that one of the possible meanings of "How we wish you were here" in English is "We wish to be cordial but do not require your company". The meaning of a simple assertion does not change when the speaker is a liar.

What does change according to the context is what it is possible to infer from the message, or in other words, its information content. Since, however, ordinary English meanings are determined by customary usage, and this particular usage is not at all necessary in constructing a means of communication, it is perfectly feasible, and simple even, to arrange a cipher where the significance of a symbol is altered according to its context among other symbols in the same cipher, as the figure 2 is of different significance in the figures 112 and 211. Thus, for constructing machines or other systems for conveying information by messages, it is possible, but not necessary, that the meaning of a message should depend on its context. It is a mistake to say that this holds for ordinary language.

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[1] Ashby, W. R., *Nature*, **187**, 532 (1960).

MR. WILLIAMSON points out that in most ordinary language the meaning of a sentence depends on its context only to a trifling or zero degree. Nevertheless, the recognition that the dependence is latent may be worth making. We all know how much Shannon and Wiener contributed by their recognition that the *quantity* of information in a message is a function both of it and of the unsent messages. They showed that a coherent theory can be developed only when the set of messages is regarded as a whole. It may be that a theory of meaning similarly must be based on consideration of the whole set. In such a theory, the sentence the meaning of which depends on context to only zero degree would be regarded as a special (though common) case, degenerate in the way that 'still air' corresponds to the wind that blows at 0 miles per hour.

W. ROSS ASHBY

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DR. ROSS ASHBY[1] is right (defining "right" as "what I think the best people think" and "best" as "tha class of people who think as I do") in his conclusions that no message has intrinsic meaning, and the meaning defined in terms of the set of messages from which it was taken (the sender's meaning) is relatively unimportant. In most cases the message is not consciously composed by an intelligent sender; in many cases our messages arise from non-living matter. The important meaning is the recipient-meaning and this meaning is very personal to the individual recipient (be it man, dog or computer), will vary with instant of reception and will generally decay after reception. It may be defined as the multiplex of correlates stimulated in the recipient by the input message. Even the most intelligent recipient will "know" only in part what this multiplex is. Much of it will not be accessible to his awareness, let alone his analytical senses. Even if he did "know" it, he could not convey it with any absolute certainty to a third person, for the establishment of a common language is a statistical process with a finite residual error-probability even for the most elementary conceptions; and this indeterminacy of meaning applies equally to communications between intelligent beings and to the raw information gathered by the absorption of electromagnetic or acoustic radiation or of vapours from, or contact with, the recipient's environment.

From this we see that no "fact" can ever be "true" in any absolute sense, and the definitions in my first sentence are not flippancies. Nor can any symbolic logic be designed to be absolutely true. Any attempt to reduce "facts" to "atomic" constituents, absolutely transferable, is doomed to failure from the outset, whether the atoms are simple conceptions (which never are simple), or the smallest perceptible increment of intensity (of light or sound) in a particular resolution-cell (of colour, position on the retina, sound-pitch, etc.). For the cross-correlation of such in two recipients will never be more than asymptotic to completeness. Our ability to affect, by intercommunication, each others' actions, and store of correlation patterns determining future actions, will always be on a probabilistic basis. The message transcribed into the memory will sometimes be quite different from the sender's intention, and his-truth will generally differ from my-truth and your-truth.

When we see clearly that there are no intrinsic meanings in words, then we are able to discount such words as 'mind', 'spirit', 'soul', 'psyche', 'freewill', as simply widely used poetic descriptions of some aspect of brain-function and to explain such words as 'truth', 'goodness', 'morality' and 'beauty' in scientific terms, and the conflict with Christian belief is resolved[2]. When we realize, with relief, that there is no intrinsic meaning in the whole, or any part, of the universe, we also see that the beauty of a universe governed by simple laws is no argument in favour of a creator. For the very existence of life (defined as a class of agglomerates of matter so formed as to take advantage, by prediction from stored information, of its environment to increase the probability of perpetuation of its own kind) is utterly dependent on the predictability of that environment. Were the universe not well ordered we could not be here; we can know no universes but beautiful ones, and as things we know not, do not exist, then all universes are inevitably beautiful.

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[1] Ross Ashby, W., *Nature*, **187**, 532 (1960).
[2] Lack, David, *Nature*, **187**, 98 (1960).

FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, November 14

INSTITUTION OF ELECTRICAL ENGINEERS, ELECTRONICS AND COMMUNICATION SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Discussion on "Tunnel-Diode Applications and Circuitry", opened by Dr. G. B. B. Chaplin and Dr. R. W. A. Scarr.

ROYAL GEOGRAPHICAL SOCIETY (joint meeting with the ANGLO-SWISS SOCIETY, at 1 Kensington Gore, London, S.W.7), at 8.30 p.m.—Mr. Max Eiselin: "The Ascent of Dhaulagiri".

Tuesday, November 15

INSTITUTE OF PHYSICS AND THE PHYSICAL SOCIETY, ELECTRONICS AND LOW TEMPERATURE GROUPS (at 47 Belgrave Square, London, S.W.1), at 10 a.m. and 2.15 p.m.—Meeting on "Electronic Devices at Helium Temperatures".

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C.1), at 1.15 p.m.—Dr. K. A. Kernach: "Fossils from Fissures".*

UNIVERSITY OF LONDON (at Birkbeck College, Malet Street, London, W.C.1), at 5 p.m.—Prof. J. Wyart (University of Paris): "Diffusion of Atoms (Na, K, Al, Si, O) in Felspars".* (First of two Special University Lectures in Crystallography. Further lecture on November 16.)

INSTITUTION OF ELECTRICAL ENGINEERS, MEASUREMENT AND CONTROL SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. T. Glucharoff: "Discrete Analogue-Computer Compensation of Sampled-Data Control Systems".

UNIVERSITY COLLEGE (in the Anatomy Theatre, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. E. E. Evans: "Environment and Society in the Atlantic Fringe".* (Further lectures on November 17 and 18.)

UNIVERSITY COLLEGE (in the Physiology Theatre, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. J. H. Gaddum, F.R.S.: "The Pharmacological Analysis of Tissue Extracts".*

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. K. S. Kirby: "Nucleic Acids and Cancer".* (Eighth of the fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

ROYAL INSTITUTE OF CHEMISTRY (at Shell Mex House, Strand, London, W.C.2), at 6.30 p.m.—Annual General Meeting.

Wednesday, November 16

INSTITUTE OF METAL FINISHING (in the Recital Room of the Royal Festival Hall, London, S.E.1), at 9.30 a.m.—Symposium on "Nickel-Chromium Plating".

UNIVERSITY OF LONDON (at the Postgraduate Medical School of London, Ducane Road, London, W.12), at 2 p.m.—Dr. A. L. Greenbaum: "Fat Metabolism".*

ROYAL METEOROLOGICAL SOCIETY (at 49 Cromwell Road, London, S.W.7), at 5 p.m.—Scientific Papers.

UNIVERSITY OF LONDON (at Birkbeck College, Malet Street, London, W.C.1), at 5 p.m.—Prof. J. Wyart: "Hydrothermal Synthesis and the Problem of Granitization".*

ROYAL STATISTICAL SOCIETY (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.15 p.m.—Prof. M. G. Kendall: "The Natural Law in the Social Sciences" (Inaugural Address).

INSTITUTION OF ELECTRICAL ENGINEERS, SUPPLY SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. E. H. Cox and Mr. R. E. Martin: "Radiocommunication in the Power Industry".

UNIVERSITY OF LONDON (in the Chemistry Lecture Theatre, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. R. J. Forbes (University of Amsterdam): "The History of the Petroleum Industry: Processing and Products during the Past Fifty Centuries".* (First of three Special University Lectures in the History and Philosophy of Science. Further lectures on November 17 and 18.)

BRITISH INSTITUTION OF RADIO ENGINEERS, COMPUTER GROUP (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6.30 p.m.—Lt.-Col. I. W. Peck: "Digital Computing Elements for Instructional Use".

Thursday, November 17

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Special General Meeting, followed by Dr. G. Herzberg, F.R.S.: "The Spectra and Structures of Free Methyl and Free Methylene" (The Bakerian Lecture).

INSTITUTION OF MINING AND METALLURGY (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Dr. Kun Li, Mr. R. W. Livingston and Mr. L. K. Lemke: "Flotation Conditioning of Iron Ore with Petroleum Sulphonate"; Mr. G. J. Brittingham: "Rehabilitation of Chang Hang Copper Smelter, South Korea".

LONDON MATHEMATICAL SOCIETY (at the Royal Astronomical Society, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Annual General Meeting. Prof. G. Kreisel: "Recent Work on the Foundations of Analysis".

UNIVERSITY OF LONDON (in the Physiology Theatre, University College, Gower Street, London, W.C.1), at 5 p.m.—Prof. R. A. Morton: "Ubiquinones and Related Substances—Nature and Biological Functions".* (Further lecture on November 24.)

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. J. C. Kendrew: "The Structure of Proteins".* (Ninth of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

SOCIETY OF CHEMICAL INDUSTRY, ROAD AND BUILDING MATERIALS GROUP (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Dr. L. J. Wood: "The Constitution and Properties of Tars and Tar-Polymer Mixtures".

Friday, November 18

BIOCHEMICAL SOCIETY (at the Middlesex Hospital Medical School, Mortimer Street, London, W.1), at 10 a.m.—Colloquium on "Histochemistry". Afternoon session—Original communications on histochemistry and other subjects.

INSTITUTE OF NAVIGATION (joint meeting with the BRITISH INTERPLANETARY SOCIETY, at the Royal Geographical Society, 1 Kensington Gore, London, S.W.7), at 10 a.m.—Symposium on "Navigation for the Early Exploration of the Moon".

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. M. Westergaard (Copenhagen): "Some Fundamental Concepts and Problems in Molecular Genetics".* (Further lectures on November 22 and 23.)

SOCIETY OF CHEMICAL INDUSTRY, FINE CHEMICALS GROUP (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Prof. J. F. Danielli: "Physicochemical Aspects of Chemotherapy".

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 9 p.m.—Mr. D. E. Broadbent: "The Perception of Speech".

Saturday, November 19

BRITISH INTERPLANETARY SOCIETY (in the Tudor Room, Caxton Hall, London, S.W.1), at 6 p.m.—Mr. D. Andrews: "British Participation in Space Research".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

LECTURER (with a degree and/or corporate membership of a professional institution, and preferably the ability to offer electrical measurements as a specialist subject) IN ELECTRICAL ENGINEERING at Brighton Technical College, to teach to final degree and diploma standard—The Director of Education, 54 Old Steine, Brighton, Sussex (November 19).

LECTURER (with a good honours degree in pharmacology or physiology, or a qualification in medicine, and a postgraduate qualification in pharmacology) IN THE DEPARTMENT OF PHARMACOLOGY—The Registrar, King's College (University of London), Strand, London, W.C.2 (November 22).

SENIOR LECTURER (preferably with a medical qualification) IN THE DEPARTMENT OF EXPERIMENTAL PATHOLOGY AND CANCER RESEARCH—The Registrar, The University, Leeds (November 22).

LECTURER (specially interested and qualified in the fields of petrology and mineralogy) IN GEOLOGY at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, November 25).

LECTURER or ASSISTANT LECTURER IN APPLIED MATHEMATICS—The Secretary, The University, Northcote House, Queen's Drive, Exeter (November 26).

ASSISTANT LECTURER (preferably qualified in physical chemistry) IN CHEMISTRY—The Registrar, The University, Leicester (November 30).

ENTOMOLOGIST, Scientific Officer or Senior Scientific Officer grade (with a good honours degree), to study the effect of insecticides on insect populations—The Secretary, Rothamsted Experimental Station, Harpenden, Herts (November 30).

LECTURER (with a good honours degree or equivalent and preferably teaching experience) IN THEORETICAL PHYSICS; and a LECTURER (with a good honours degree or equivalent and preferably teaching experience) IN PHYSICS at the University of Queensland, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, November 30).

READER IN ANALYTICAL AND INORGANIC CHEMISTRY; and a LECTURER or ASSISTANT LECTURER IN INORGANIC CHEMISTRY—The Clerk to the Governors, Chelsea College of Science and Technology, Manresa Road, London, S.W.3 (November 30).

SCIENTIFIC OFFICER (with a first- or second-class honours degree in mathematics with statistics, or a diploma in statistics) IN THE STATISTICS SECTION, for duties mainly concerned with the design and analysis of field experiments—The Secretary, The Macaulay Institute for Soil Research, Craigiebuckler, Aberdeen (November 30).

BIOLOGIST (with Ph.D., M.Sc., or B.Sc. in wildlife management or zoology, with experience in independent water-fowl research) IN THE WILDLIFE BRANCH, Department of Internal Affairs, Wellington, New Zealand, to carry out life-history studies of mallard and native grey duck populations or such other projects as may be assigned—The High Commissioner for New Zealand, 415 Strand, London, W.C.2 (December 1).

PROFESSOR OF AGRICULTURE AND DIRECTOR OF THE COLLEGE FARM—The Secretary and Registrar, University College of North Wales, Bangor, North Wales (December 1).

BEYER CHAIR OF APPLIED MATHEMATICS—The Registrar, The University, Manchester 13 (December 3).

LECTURER IN THE DEPARTMENT OF CLASSICAL ARCHÆOLOGY—The Secretary, The University, Edinburgh (December 5).

HEAD OF THE DEPARTMENT OF VIROLOGY, for duties which will include responsibility for the development of the Department for the study of animal viruses in close collaboration with the Departments of Pathology, Bacteriology and Biochemistry—The Secretary, Field Station, Agricultural Research Council, Compton, near Newbury, Berkshire (December 15).

LECTURER or ASSISTANT LECTURER IN PHYSICS at the University of Malaya, Singapore—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (December 15).

LECTURER (specialized, or prepared to specialize in the pre-history of South-East Asia and/or Oceania, and able to teach elementary physical anthropology) IN ANTHROPOLOGY at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, December 15).

LECTURER (with at least a first-class honours degree in chemical engineering) IN CHEMICAL ENGINEERING at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, December 19).

SENIOR LECTURER IN BOTANY and a LECTURER IN BOTANY at the University of Adelaide, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, December 20).

SENIOR TUTORS (2) IN PURE MATHEMATICS at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, December 20).

SENIOR RESEARCH FELLOW or a RESEARCH FELLOW IN THE DEPARTMENT OF NUCLEAR PHYSICS, Research School of Physical Sciences, Australian National University, to work either in the field of nuclear spectroscopy or on photonuclear problems—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, December 30).

CHAIR OF ZOOLOGY in the University of Malaya, Singapore—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (December 31).

TURNER AND NEWALL FELLOW (preferably under 28 years of age) at Newcastle or Durham, for research in Engineering, Inorganic Chemistry or Physics, or an allied science—The Registrar, University Office, 46 North Bailey, Durham (January 31).

IMPERIAL CHEMICAL INDUSTRIES LIMITED RESEARCH FELLOWS IN BACTERIOLOGY, BIOCHEMISTRY, BIOMOLECULAR STRUCTURE, BOTANY (PLANT BIOCHEMISTRY AND BIOPHYSICS), CHEMICAL ENGINEERING, CHEMISTRY, CHEMISTRY OF LEATHER MANUFACTURE, CHEMOTHERAPY, COLOUR CHEMISTRY AND DYEING, ENGINEERING (CIVIL, ELECTRICAL AND MECHANICAL), FUEL AND REFRACTORIES, GEOLOGY (including GEOCHEMISTRY), METALLURGY, MINING (SELECTIVE FLOTATION AND GEOPHYSICAL SURVEYING), PHARMACOLOGY, PHYSICS, PHYSIOLOGY OR TEXTILE INDUSTRIES (CHEMISTRY OF HIGH POLYMERS (KERATIN AND MAN-MADE FIBRES), TEXTILE TECHNOLOGY AND TEXTILE ENGINEERING)—The Registrar, The University, Leeds 2 (February 17).

ANALYTICAL CHEMIST (with an honours degree in chemistry or Associate Member of the Royal Institute of Chemistry, and preferably postgraduate experience in a public analyst's laboratory or veterinary research establishment), at the Veterinary Research Laboratories, near Nairobi, Kenya, to analyse animal food-stuffs for legislation purposes and carry out research in nutrition—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.67/7/017.

ASSISTANT LECTURER IN PHYSIOLOGY—The Secretary, Queen Elizabeth College (University of London), Campden Hill Road, London, W.8.

ASSISTANT VIROLOGIST (with previous experience in virological techniques) to undertake research on rubella and molluscum contagiosum, with particular reference to the isolation of their causal agents—Head of the Virology Department, The Lister Institute, London, S.W.1.

PRINCIPAL LECTURER (qualified to teach to final degree or diploma in technology standard) IN THE DEPARTMENT OF BIOLOGICAL SCIENCES—The Registrar, Bradford Institute of Technology, Bradford 7.

RESEARCH ASSISTANT (with a science degree in physiology, biochemistry or a cognate subject, and preferably experience in pharmacological or biochemical techniques) TO THE PROFESSOR OF PHARMACOLOGY, for work related to the assay of chemical transmitters in tissues and body fluids—Prof. G. Brownlee, Department of Pharmacology, King's College (University of London), Strand, London, W.C.2.

SUPERINTENDENT OF CHILDREN'S ZOOS in the L.C.C. Parks Department (preferably zoologist with some years practical experience)—Chief Officer, Parks Department (A.1/N/2736/11), County Hall, London, S.E.1.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Factors in Mental Evolution. By The Rt. Hon. Lord Adrian. (The Romanes Lecture delivered in the Sheldonian Theatre, 24 May 1960.) Pp. 19. (Oxford: Clarendon Press; London: Oxford University Press, 1960.) 3*s*. 6*d*. net. [48

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Société Jersiaise. La Cotte-de-Saint-Brelade, Jersey, British Channel Islands. Excavation of a Pre-Mousterian Horizon, 1950–1958. By Father Christian Burdo, S. J., Ph.D. Pp. 77+8 plates. (Jersey, Channel Islands: Société Jersiaise, The Museum, 9 Pier Road.) 7*s*. [48

Ministry of Housing and Local Government. Smoke Control (England and Wales): Summary of Programme submitted by Local Authorities for the Establishment of Smoke Control Areas. Pp. 19. (Cmnd. 1113.) (London: H.M. Stationery Office, 1960.) 3*s*. net. [48

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Other Countries

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National Museums of Ceylon. Some Sinhala Combative, Field and Aquatic Sports and Games. By P. E. P. Deraniyagala. Pp. 51+5 plates. (Colombo: Department of National Museums, 1959.) Rs. 2.00. [48

United States Department of Health, Education and Welfare: Public Health Service. Publication No. 779: Research Highlights in Aging. Pp. v+52. (Washington, D.C.: Government Printing Office, 1959.) 25 cents. [48

Universidade do Recife, Brasil. *Anais da Ascola Superior de Quimica*, Vol. 1, No. 1 (Dezembro, 1959). Pp. 105. (Recife, Pernambuco: Universidade do Recife, Instituto de Antibióticas, 1959.) [48

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Centro Brasileiro de Pesquisas Fisicas, Rio de Janiero. *Notas de Fisica*. Vol. 5, No. 20: Nuclear Interactions of Neutral K-Mesons of Long Lifetime–II. By V. Bisi, R. Cester, A. Debenedetti, C. M. Garelli, N. Margem, B. Quassiatt and M. Vigone. Pp. i+311–323. Vol. 5, No. 21: Phase Space Calculations. By G. E. A. Fialho. Pp. 327–362. Vol. 6, No. 1: Discrimination of Tracks of Photofission Fragments with Very High Background of Alpha Particles and Electrons in Nuclear Emulsions. By H. G. de Carvalho and A. G. da Silva. Pp. i+1–9. (Rio de Janeiro: Central Brasileiro de Pesquisas Fisicas, 1959 and 1960.) [48

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CO-OPERATION BETWEEN SCHOOLS AND UNIVERSITIES IN EDUCATIONAL DEVELOPMENTS

IN recent months the adequacy of university teaching both in chemistry and physics has been challenged by competent authorities, and some suggestions made that could make more time available for critical thought and for the more general education for which there have also been widespread and authoritative calls. The recent report of the Advisory Council on Scientific Policy (see *Nature*, November 5, p. 435) was mainly concerned with a review, undertaken at the specific request of the Minister for Science, of the balance of scientific effort in Britain, but the report also contains an important section on education in science. This likewise arose out of a request from the Minister for Science to consider the implications for science of the Crowther Report, and while the Council welcomed many of the recommendations in the Crowther Report, on questions of curricula, supply of teachers, and the raising of the school-leaving age in relation to the development of the proposed county colleges and the training of technicians, the experience of some of its members is at variance with the Crowther Committee's recommendations.

On the supply of teachers, the Advisory Council for Scientific Policy observes that on the figures at present available, the demand for teachers caused by reducing the size of classes is much greater than that consequent on raising the school-leaving age, and in either event the number of science and mathematics graduates needed for school teaching does not greatly exceed the number likely to be obtainable on the Council's present forecasts of scientific man-power. On the other hand, it points out that there may be difficulty in finding sufficient university teachers of quality in certain subjects, notably mathematics, to cope with the large increase in university population now proposed. Adequate provision in this respect is absolutely essential in universities if they are to produce the graduates required. Equally important, the Advisory Council points out that the desirability or otherwise of concentrating resources on raising the school-leaving age is intimately bound up with the needs of education for industry, and especially with the need for technicians. These will be required in large numbers if we are to get the full benefit from the increased numbers of scientists and engineers we are now producing, and it could be urged that it is the more important to increase the numbers of technicians quickly so as to secure the most effective use of the present limited numbers of scientists and technologists in industry, in Government service and in the universities. This point is borne out by the recent report from the Civil Service Commissioners for the year ending March 31, 1960; and as many of these technicians, and still more of the craftsmen on whom industry must depend, come from those who now leave school at fifteen, the Council suggests that a major extension of part-time education to the age of eighteen is more urgent than the raising of the school-leaving age.

There is a note of confidence and authority about the Advisory Council's whole report that should ensure that these suggestions are duly heeded, though it is surprising to find that the industrial members of the Council attach such value to evening classes as a component of existing part-time education. The Advisory Council emphasizes the importance of the development of county colleges, which, with the technical colleges, would be the main instruments of the part-time education it recommends, and it urges that this development should be more rapid than is envisaged in the Crowther Report. The system of day-release, however, is not mentioned by the Advisory Council; but in addressing the British Association for Commercial and Industrial Education at Cambridge on September 23, the Minister of Labour, Mr. John Hare, gave industry a clear and emphatic warning of its own responsibilities for industrial training and the urgency of a problem to which, in spite of the establishment of the Industrial Training Council, many firms are giving insufficient attention.

It is, however, on the question of the school science curriculum and specialization in schools that the Advisory Council is most forthright and authoritative. It has no doubt that school science curricula need a thorough re-examination. They tend at present to be unimaginative and to be overloaded with factual material, partly because new material is added without removing the old. It was suggested to the Council that up to 20–25 per cent of the content of the curricula in physics, chemistry and biology could be removed with advantage rather than detriment, and in particular a new approach is needed to the teaching of biology. The Advisory Council suggests it should be treated as a comprehensive discipline in its own right, with a bearing on the teaching of geology and geography, and so taught, with much more field-work than customary at present, it should be an integral part of the junior- and middle-school curriculum for all pupils.

The Advisory Council was, of course, fully aware of the extensive studies on the content of school science courses in the United States which the National Science Foundation has stimulated, and it understands that the Ministry of Education is already in touch with the Foundation. Science teachers at all levels could well support the Advisory Council in seeing that the closest possible contact is maintained, and in this connexion the possibilities offered by

sound broadcasting and television should be fully and authoritatively explored. To these possibilities the Organization for European Economic Co-operation has already directed attention in its report, "Teaching through Television".

The Advisory Council also considers that specialization in schools has gone too far, and that here is to be found the origin of the so-called 'gulf' between scientists and non-scientists. It deplores the segregation of children in the middle school into groups according to the subjects they are to study in the sixth form, and believes that with the revision of science and mathematics curricula all middle school pupils should be able to study science without making undue inroads into other subjects. In its opinion, all pupils in the middle school should have the same general education, in which science should play its full part. It urges, in fact, exactly what Sir Cyril Hinshelwood suggested in addressing the Manchester Literary and Philosophical Society; it rejects the idea that a few periods of general studies suffice as a leavening for the 'science sixth' or a few periods of general science for the others, and believes that curricula can be modified so that those who are primarily interested in science can continue a serious study of some other subjects and *vice versa*.

Beyond this, there are signs of over-specialization in science itself in the sixth form, and as things stand at present the Advisory Council agrees with the Crowther Committee's view that two science subjects may be all that a student should take at the Advanced Level of the General Certificate of Education examination. Reduction of the factual knowledge demanded in individual subjects and revision of curricula in the manner already indicated would, however, permit a corresponding increase in the breadth of sixth-form education, and the Council believes this should be done. Further, it stresses the urgent need for schools and universities to get together to devise some method of awarding scholarships which will avoid the over-specialization and disproportionate effect on school curricula which at present arises from college scholarship requirements at Oxford and Cambridge, and it points out that, in view of the present considerable overlap between what a student is taught in science in his first year at the university and what he has already learned in his last year at school, many professors would welcome a lower level of factual knowledge of their own subject in pupils entering the university if it were combined with a broader general education.

While the Crowther Committee endorsed the principle of specialization, or study in depth, it did not necessarily support all existing practice, and in fact it pointed out that syllabuses in science need reconsidering both subject by subject and together as the specialist curriculum of the science sixth. The Report, moreover, included some valuable suggestions for controlling premature specialization, and these have been welcomed by many headmasters. The present system of work has, however, since been challenged both in a report issued by the University of Oxford Department of Education based on an inquiry financed by the Gulbenkian Foundation into "Arts and Science Sides in the Sixth Form"*, and also in one issued by the Secondary School Examination Council entitled "The General Certificate of Education and Sixth Form Studies"†.

The Oxford report maintains that the present degree of specialization is greater than the Crowther Committee believed : it had evidence that nine-tenths of the working time of a sixth former is concentrated on either arts or sciences, and that in practice four-fifths of all pupils have to make an effective decision at 14–15 between a scientific and a literary education. Further, this degree of specialization is not found in any comparable country, and has arisen from local historical causes and not from educational principles. The Crowther Report itself pointed out that university entrance requirements should not determine the nature of sixth-form work, but at present they do; and the Secondary School Examination Council's report criticizes this university pressure even more strongly. In fact, it believes the pressure to show results in terms of examination achievement for such purposes as admission to a university has become so intense that specialization is carried to a point at which general education is in jeopardy.

The main source of pressure is, in fact, the keen and growing competition to enter a university, and it is estimated that by 1965 the number of candidates for the Advanced Level General Certificate of Education examination will have risen from 83,000 in 1959 to 150,000, although the planned expansion of university places in England and Wales for full-time courses is only from 22,000 to 32,000. The universities certainly need an examination which does not simply measure a pupil's achievement at school, but also offers some guidance on a pupil's potential for a university course, and especially for an honours course; and the Advisory Council, besides recommending the revision of Advanced Level syllabuses to reduce their factual and memory content, suggests that if a revised examination is introduced the universities might make it optional rather than obligatory to have three passes at Advanced Level. This pressure may well be the more serious if, as Prof. R. A. C. Oliver, for example, believes, the number of sixth formers not going on to universities greatly increases. Prof. Oliver himself believes that the present Advanced Level examination is detrimental to the university entrant, because it requires him to present his credentials exclusively in terms of his two or three specialized subjects. The whole implication of Dr. James Taylor's presidential address to Section B (Chemistry) at the Cardiff meeting of the British Association supports the argument of Prof. Oliver and those with him. The increasing scope of the scientist's work in industry means not simply that chemistry alone is not enough but also that an adequate broad general education is essential; and time must be found for this, both in school and

* Arts and Science Sides in the Sixth Forms. (Oxford Univ. Department of Education, 1960.) 2*s*. 6*d*.

† Examinations in Secondary Schools. Third Report. The General Certificate of Education and Sixth Form Studies. (London: H.M.S.O., 1960.) 2*s*. 6*d*.

in university, if men and women competent to meet the needs of industry itself are to be provided. Moreover, as already noted, it is not simply scientists and technologists who are needed, but also, and in even greater numbers, technicians and craftsmen, and one consequence of the present educational system is the tendency to under-value craftsmanship, or even, as Sir Cyril Hinshelwood has emphasized, to divert some with potentially first-rate manual skill into becoming second- or third-rate intellectual workers. Manual skill, Sir Cyril insisted, is in many ways as worthy of respect as mental agility. Technology involves both, and is not to be thought less liberal than fundamental science if approached in a liberal spirit, any more than the sciences are to be deemed less liberal than the arts.

In saying this, Sir Cyril had launched a devastating attack on the artificial barriers often set up between the arts and the sciences, urging that in all the arts, and in all the sciences, full satisfaction is only reached by the practice of creative effort, realized through the medium of a technique, painfully and elaborately acquired and involving natural aptitude. No educational system can be regarded as satisfactory which does not permit due account to be taken of such natural aptitudes, but the whole tenor of the address which Sir Cyril Hinshelwood gave to the Manchester Literary and Philosophical Society implies not simply the basic importance of a broad general education but also the practicability of such an education being given side by side to those seeking to specialize in the arts and in the sciences up to an advanced stage, provided the extent to which the arts and the sciences make similar demands on observation and experiment, imagination and creative powers is properly recognized. It is a matter for both school and university, and a solution will not be found except by close co-operation between them.

Unfortunately, this did not appear to be recognized adequately in the discussion on the education of scientists at a meeting of Section L (Education) at the British Association meeting in Cardiff, except possibly in Sir Patrick Linstead's address. Prof. M. W. Thring, it is true, challenged the idea that the humanities are superior to pure science, or the latter to technology, and maintained that the broadening of education by informal methods is a vital part of the training a university should give. He directed attention, moreover, to the influence which the school teacher has on the choice of a career, and the consequent handicap under which technology is placed since so few of those trained in technology teach in the schools. This is, in fact, a particular aspect of a problem on which a study group set up in 1958 by the Nottingham County Education Committee and the East Midlands region of the Institute of Personnel Management has commented strongly: the group was seriously perturbed by the danger of 'remoteness' of the student teacher and his/her tutor from the general industrial life of the community.

Prof. Thring was particularly concerned as to how we could show our ablest schoolboys that applied science is worthy of their talents, and could offer them a fascinating and satisfying career. This problem is not solved by the establishment of more colleges of technology, and it was not really considered by Dr. J. S. Tait in his paper, although he recognized the value of the time which the students are required to spend in industry and, like Prof. Thring, he referred to the importance of some research in technology. Dr. Tait's reference to the fostering of interest in the humanities was rather superficial, but Sir Patrick Linstead gave a preliminary account of the inquiry conducted by a special committee of the British Association, with the aid of a grant from the Leverhulme Trust, into the means of broadening the education of the graduate scientist, and this inquiry covers the whole range of education from school to university.

Both schools and universities have important but different formal parts to play, but Sir Patrick did not refer to co-operation between them or the way in which the adverse effect of university pressure on the schools could be reduced. More time for minority subjects in the sixth forms was recognized as one essential step, and once again the need for some reduction in the factual content of university courses and deflexion towards the study of general principles is recognized. Other suggestions at the university-level included greater attention to those non-scientific subjects which arise naturally out of the special subjects, such as the history of scientific thought and method and the use of English; the provision of a wide range of cultural events, on an organized but not compulsory basis; and the generous provision of amenities, such as libraries, halls of residence and beautiful surroundings.

The importance of early and decisive co-operation between the schools and the universities can scarcely be over-stressed, and there is no more important recommendation in the report of the Advisory Council on Scientific Policy than the one to that end. It is essential that the full implications of such a step should be faced, and appropriate measures devised to avoid the detrimental effects of the present system of awarding scholarships before and not after the present plans for university expansion are worked out in detail. It bears closely both on the question of general education and the quality of the graduates in science and technology which we produce, and on the use we make of them. In his recent book on American education, "The Child, the Parent and the State"*, Dr. J. B. Conant emphasized the way this question of effective use of the trained scientist or technologist determines the answer to the question of how many scientists and technologists we should be training, though it is only fair to recognize that the Crowther Committee also referred to it, particularly in respect of the use of sixth-form teachers.

Such questions are the more important in view of the mounting cost of education, and it may well be doubted whether all those who are advocating university expansion so strongly appreciate how much

* The Child, the Parent and the State. By Dr. James Bryant Conant. Pp. vi+211. (Cambridge, Mass.: Harvard University Press; London: Oxford University Press, 1959.) 28*s*. net.

it will cost and what is involved in willing the means. When Dr. Conant writes, of the American scene, that a climate of opinion must be created which brings forth in each young person a strong desire to do his or her best in school, he refers to a condition no less essential in Britain, as well as to what could well be another compelling reason for reform of curricula. He is equally aware of the importance of the technician, and, like Sir Cyril Hinshelwood, stresses the vital need for seeing that full opportunity is given for the expression of manual skills with intellectual skills in a whole spectrum of occupations.

Here, and when he refers to the need for an enlightened, public-spirited and stable electorate for fostering the development of a critical judgment regarding those who handle affairs of government, Dr. Conant touches on matters which need serious consideration in the planning of our educational institutions at the school- and the university-level alike. Indeed, he goes so far as to suggest that how to develop intelligent discrimination in future voters is one of the most challenging educational questions facing those responsible for social studies in schools. Be that as it may, Dr. Conant indicates a further decisive reason for a broad general education both in school and in university ; but it is difficult to imagine a more authoritative lead in that respect or firmer warning as to the dangers and waste which continued excessive specialization in schools is liable to cause than that which has now come from the Advisory Council on Scientific Policy. The Minister for Science can scarcely do less than ensure that the Minister of Education takes action on his side, and that the University Grants Committee takes any initiative required. There is indeed ample evidence that industry, the universities and other potential employers attach greater importance to this question of general education and look with disfavour on excessive and premature specialization. This, as the Crowther Committee recognized, is likely to be the decisive factor in leading schools and pupils to take seriously the work done in minority time ; but this by itself is not enough. It is to be hoped that the Advisory Council on Scientific Policy's recommendations may stimulate the coherent and properly phased programme of development, not simply for the schools but also for the universities, that is essential if educational expansion is to be adequate in scope and not to entail waste of precious resources.

THE COMPETITION FOR RURAL LAND

Agriculture and Urban Growth

A Study of the Competition for Rural Land. By Dr. G. P. Wibberley. Pp. 240+8 plates. (London : Michael Joseph, Ltd., 1959.) 21*s*. net.

FOR each head of population the land surface of England and Wales represents less than 0·8 acre—land of all sorts and for all purposes—against a world average of more than 12 acres. The figure is increased only to 1·1 if Scotland is included and Britain considered as a whole. Not only is the population in Britain continuing to increase by about 200,000 a year but also our standard of living is rising, and the movement is constantly to the towns. Back-to-back houses in our industrial towns have become almost a thing of the past : the demand is for a more spacious layout of homes. As we approach the ideal, questionable though it may be, of one car per family, the demand for bigger and better roads becomes more insistent. There is the growing clamour for recreational areas : the desire to get away from the noise and congestion of the city —with a consequent invasion of the countryside, which may easily destroy the very qualities that render it attractive. At the same time there is the growing realization of the need to preserve some rural areas inviolate if the native fauna and flora of Britain are to survive, hence the work of the Nature Conservancy and the establishment of a varied range of Nature reserves.

It would seem obvious that the whole cake is so small that few demands on it can be satisfied in full, and that the only solution is an overall town and country planning. This indeed was the reason for the establishment of a Ministry of Town and Country Planning in 1943, for the Town and Country Planning Act of 1947, and for the Acts which have followed. Despite the laudable objectives, it has proved very difficult to get a calm, objective view of land planning ; to some the very word is anathema, and arguments between the exponents of this policy or that are very liable to induce heat. It is precisely because Dr. Wibberley's book is a calm assessment of the facts, involving a very considerable amount of research by his team (especially R. H. Best and J. T. Ward, who might almost be named as joint authors) and himself at Wye College, that it is both a valuable and an opportune contribution. He has been accused by some as a 'master of brinkmanship' ; in reality that is praise indeed, for he brings his readers to the brink where they can see the whole position. Which way they plunge is then their decision, and it is interesting to note how the exponents of most diverse views are finding ammunition in Wibberley's figures.

The expansion of towns into the country and the consequent loss of rural land is inevitable, but the rate of loss is important. The only reasonably complete official statistics of land use that we have in Britain are those collected by the Ministry of Agriculture, based on the returns made every June 4 by holders of agricultural land exceeding one acre in extent. As the years have passed the returns have become steadily more complete and more accurate. Apart from the difficulty of definition, there have been no comparable statistics of urban land. The area of 'urban land' has been ascertained by subtracting rural land, for which returns exist, from total area. Thus, for obvious reasons, the loss of agricultural land during 1900–1950 is more likely of the order of 2,250,000 acres than the 1,130,000 acres which official figures suggest (p. 58). The only direct measure of 'urban land' is that carried out by the Land Utilisation Survey of Britain during 1931–33, when the use of every piece of land was recorded on 6-in. maps. The accuracy of the Survey's figures is only limited by the scale on which the calculations were made—on the published one-inch maps—since the question of definition does not arise. What was, or was not, included in the various categories can at once be seen

from the published maps; if necessary the original 6-in. maps can be consulted. Wibberley expresses some surprise that from other evidence he finds these figures reasonably correct! Such is the strict discipline of the map, they could not be otherwise.

In general Wibberley accepts the estimates that "new urban developments and special uses are likely to require between 500,000 and 700,000 acres . . . mainly on the better farmlands of the lowlands", before 1971 (p. 58) and he is concerned with the replacement of agricultural production thus lost. He writes as an economist, and although he finds the value added by the land alone in Britain—the input–output ratio—is only of the order of £4 per acre per annum, and would seem to suggest that farming as a whole is scarcely worth while, he has some interesting calculations. If land is worth only £30 an acre and is devastated by mineral working, any expenditure in excess of £30 an acre in restoration is not economically justified—so runs the old argument which conveniently ignores the lessons of two world wars. It is certainly an advance when Wibberley argues that a capital expenditure of up to £165 in 'general intensification of agriculture' (1955–56 values) for each acre lost to building is justified on economic grounds.

Undoubtedly, the real value of the book lies in the ammunition provided by an economist in favour of the conservation of the resources of the better types of land in the lowlands rather than in the attempt to replace acreage lost in the lowlands by heavy expenditure in the highlands. L. DUDLEY STAMP

CUSTOM AND MYTH

Folkways

A Study of the Sociological Importance of Usages, Manners, Customs, Mores, and Morals. By Prof. William Graham Sumner. Pp. vii + 692. (New York: Dover Publications, Inc.; London: Constable and Co., Ltd., 1959.) 2.49 dollars; 20*s*.

IT is not altogether easy to understand why this book has been reprinted. First published in 1907, it became a highly influential work in the United States and the basis of the author's "Science and Society" which, written with the help of A. G. Keller, did not appear until much later.

Prof. Sumner had a varied career. Educated both in the United States and in Europe, he was at one time an episcopal clergyman and then was appointed professor of political and social science at Yale. He became interested in the theories of Spencer and Lippert, and came to believe that what he called 'mores' and 'folkways' had had a far greater influence than had hitherto been believed. By 'mores' he meant that vast system of usages which cover the whole of life, containing within themselves their own justification of tradition and approved by mystic sanction, thus developing into principles of truth and right. They defined the limits which made anything 'right': they covered manners with a mantle of current custom. It is thus that the folkways arise and are gradually converted into the mores.

In developing his theories and illustrating his thesis, Sumner was making a systematic study of various anthropological and sociological records, and this book is in essence a collection of his notes and memoranda which were meant to be incorporated later into a more ambitious work. Strongly influenced by Darwinian teaching and the doctrines of *laissez-faire*, Sumner was a powerful exponent of individual effort, and he regarded all such ideas as those inherent in liberal socialism as an interference with natural laws. To Sumner the most important factors in the science of society are the folkways, which control both individual and social undertakings and nourish philosophical ideas generally. He does not consider them organic or material. Rather they belong to a super-organic system of relations, conventions and institutional arrangements.

As a work of interest to the historian of sociological research the book has long been esteemed in the United States, but its lack of sustained treatment and the date at which it appeared have now considerably lessened its value to the practical sociologist. E. J. DINGWALL

THEORY OF ELECTRIC CIRCUITS

Electric Circuit Theory

By Dr. F. A. Benson and Dr. D. Harrison. Pp. viii + 371. (London: Edward Arnold (Publishers), Ltd., 1959.) 30*s*. net.

THIS book will be welcomed by students of all colleges having a syllabus in electric circuit theory corresponding closely to that of the University of Sheffield, for here will be found all the material necessary for their examinations together with an adequate number of numerical problems and answers.

The authors cover d.c. and a.c. circuits, with a collection of useful network theorems, transformers, rotating machine circuits and thermionic valve circuits; and claim that their book is one of the few that covers light-current and heavy-current circuit applications in one volume. The space devoted to light-current applications is, however, very much greater than that allowed for the heavy-current problems, but in spite of this all reference to transistors has been omitted. The authors justify this on the grounds of the necessity to keep the book to a reasonable size, but to many readers it would have appeared preferable to omit some of the more advanced material to make room for at least an outline of transistor theory.

The book, although well written, is curiously uneven. No doubt this arises from the authors' efforts to base parts of the work on the standard required for first-year students and part on the standard for second-year students. This variation of standard is particularly evident in the circuit theorems, some of which are proved and others stated without proof. Yet by the end of the second year all students should be able to prove all the circuit theorems of which they make use. Thus, no proof is given that an active four-terminal network may have four independent parameters while a passive four-terminal network has only three, but the authors find space to give two proofs of the star-delta transformation.

There are a number of minor imperfections in the work, which are little likely to worry the average student, but could well be amended in a future edition. It would be wearisome to list all these, but

a few can be mentioned. The reference to superconduction should either be omitted or made more accurate, even at the expense of a few more lines of description. Resistance alloys should be described by composition rather than by trade names. Impedances should not be described as vectors, and the special interpretation of the meaning of vectors when applied to sinusoidally varying quantities should be stressed more heavily.

Students usually have considerable difficulty in dealing with the sign in problems involving mutual inductance. The treatment here is somewhat perfunctory, and an expansion together with a diagram showing clearly the direction of winding of coils, the direction of currents and of voltages, would be of great assistance to them.

The setting of the type is generally good and only a few errors, none of great moment, were observed. There is, however, an excessive use of the solidus in the equations throughout the book, and this makes reading difficult. A. H. M. ARNOLD

SCIENCE AND LIBERAL EDUCATION

Science and Liberal Education

By Dr. Bentley Glass. (Davis Washington Mitchell Lectures–Tulane University.) Pp. x+115. (Baton Rouge: Louisiana State University Press, 1959.) 3 dollars.

THIS book is based on the Davis Washington Mitchell Lectures given by Bentley Glass at Tulane University. Of the three lectures, one only, the second, deals with the subject the title of which is given above. Prof. Glass's primary research and teaching interests are concerned with genetics and especially with the influence of radiation on human heredity. In this connexion he serves as an adviser to the Atomic Energy Commission and as a member of the National Academy of Science's Committee on the Genetic Effects of Atomic Radiation. He is well known in the United States for his ability to interpret to the public significant aspects of genetic research.

His first lecture concerns genetics in the service of man. Prof. Glass's style is popular in the best sense of the word—he does not sacrifice the dignity and scholarship of the science for an easy, superficial appeal. The lecture is devoted to the genetics of plants in relation to their food value and the genetics of animals and man in relation to disease. After touching on the effects of radiation on mutation-rates, Prof. Glass considers the future of the human race in relation to population control and limitation, and he stresses the difficulties rather than the solutions of the matter.

His essay on liberal education in the scientific age is worth expansion into a whole book. It may be summarized in his own words: "Science, in ever greater measure, must permeate the study and teaching of each of the arts, humanities, and studies. These, on their side, must mollify, enrich and protect the sciences". This may appear to be trite, because it is so often said by educationists to-day; but, in an engaging manner, Prof. Glass is able to add some new and interesting ideas to this important and topical problem.

The third and last essay, which deals with Darwinian evolution and human values, is equally brilliant. There is a short, critical review of the present position of Darwinism in the larger sphere of evolution. There is much in common in these essays with Prof. Peter Medawar's Reith Lectures, and in the work here considered it is interesting to observe the different approach with its piquant American flavour. W. L. SUMNER

THE AGEING INDIVIDUAL

Handbook of Aging and the Individual

Psychological and Biological Aspects. Edited by James E. Birren. Pp. xii+939. (Chicago: University of Chicago Press; London: Cambridge University Press, 1959.) 12.50 dollars; 100*s*.

THIS enormous volume is symptomatic of the growing interest in and research on the topic of ageing in the United States. The first of three handbooks aiming at summarizing all that is known to-day about the problems of human ageing, the present work, edited by Dr. James E. Birren of the National Institute of Mental Health, Maryland, is concerned with the psychological and biological problems of the ageing individual. It is to be followed by two volumes on social gerontology.

Primarily a work of reference, and intended as a definitive secondary source of data, the handbook succeeds in compressing a vast amount of information on almost every conceivable aspect of human ageing —biological, morphological, neurophysiological, neurochemical, genetic, pathological, environmental and psychological (with perhaps a major emphasis on the psychological). The editing has been well done: there is no undue overlapping between the contributions of the thirty authors, and the standard is in general first rate. Although there is inevitably a good deal of padding in the form of general background material not specifically concerned with ageing, this can perhaps be justified in a work designed to be of use to workers trained in quite a variety of different disciplines.

In two respects the book is more than compilation, and is likely to be of first-hand interest to gerontologists. First, it discusses perhaps more thoroughly than has been done before the fundamental principles and methodology of the study of ageing. Secondly, by reason of the very completeness of its coverage, it points to gaps in knowledge and suggests areas urgently needing more research. The book, in any event in parts, has a stimulating and suggestive quality that is not too common in synthetic productions of this kind. No doubt the editor, Dr. J. E. Birren, is largely responsible for this, and his own contribution on "The Principles of Research on Aging" with which the book opens is a particularly valuable one, discussing both the special problems of research design encountered in the study of ageing, and some of the fundamental theoretical issues involved in the concept of ageing. Some of these issues are taken up in the two succeeding chapters on time and ageing by Reichenbach and Mathers, and biological periodicities by Landahl. Ageing is a process closely connected with the passage of time, and Birren and his collaborators may well be right in thinking that the systematic theoretical foundations of ageing research have their foundations in the theory of time.

L. S. HEARNSHAW

THE NATIONAL AVIATION MUSEUM, OTTAWA

By S. L. ROBERTS

Department of Northern Affairs and National Resources, Ottawa

THE story of Canadian aviation, an important chapter in Canada's national development which many Canadians have embellished with their distinctive contributions, is presented in the new National Aviation Museum at Ottawa.

The National Aviation Museum, situated in the new Uplands Air Terminal, was opened recently by the Hon. J. Angus MacLean, Minister of Fisheries. Through the displays, visitors can trace the progress of Canadian aviation from the experiments of the pioneers in the early 1900's to the complex jet and rocket developments of present time.

The basic theme of the Museum is "Canada's Contribution to Aviation, and Aviation's Contribution to Canada". To carry out this theme, reliance could not be placed on the display of historical items alone. These relics of the early days of the aviation have been placed mostly in the primary display area, which is concentrated on the pioneering days of flight in Canada. The rest of the displays are of the didactic type, using photographs, models and selected samples of actual aircraft and aviation parts, instruments, accessories and equipment to portray the story of civil aviation in Canada.

There are nine distinct sections to the Museum. From the pioneer section visitors pass to the area in which the development of piston-engines, navigation instruments and electronics is presented. The next area illustrates aviation's supporting services—air traffic control, airport construction, weather, aviation medicine, communications, maintenance and overhaul, search and rescue, and the radar detection chains in northern Canada. The operations section illustrates the development of commercial airlines and the use of aircraft in photography, mapping, geological survey, forest fire fighting, insecticide spraying, and communications.

The sections dealing with jets, rockets and research demonstrate the increasing complexity of aircraft design and the extent to which aeronautical research has expanded. Two other sections follow, one showing some of the development of the aviation manufacturing industry, and the other the extent that the demand of aviation for new techniques and materials has encouraged the development of Canadian industry and made the country less dependent on imports of manufactured articles.

One rather novel feature is a 'children's museum', where much thought has been given to making the displays interesting and attractive to children. Here young visitors can learn to identify the parts of aircraft and understand their function, and play with small plastic aircraft models on a toy landing field.

One full-sized aircraft, displayed in another part of the building, forms part of the Museum. This is a flying replica of the *Silver Dart*, the machine built on Cape Breton Island by the unique aeronautical research group of Canadians and Americans led by the inventor of the telephone, Alexander Graham Bell. The *Silver Dart* made the first flight in Canada—and the first flight by a British subject in the Commonwealth—in February 1909, with a Canadian pilot, J. A. D. McCurdy, at the controls. This historic aircraft was duplicated, with a few practical modifications, by L.A.C. Lionel McCaffrey and other airmen of the R.C.A.F. and flown by W/C Paul Hartman at Cape Breton Island in February 1959 in a re-enactment of the first flight.

Although space limitations prevent the display of other full-sized aircraft, models of Canadian aircraft types have been provided by British, Canadian and American manufacturers for display in the Museum. The 1/24 scale, as followed in the Science Museum at South Kensington, has been adopted as the standard for the aircraft models, though many of the models given or lent to the Museum are of other scales.

The Museum attempts to provide a clear and comprehensive presentation of aviation in Canada within the limitations of a small area. It is remarkably complete and contains many individual items of great interest. Among these are a 'mock-up' of the Canadian-developed *Velvet Glove* air-to-air missile,

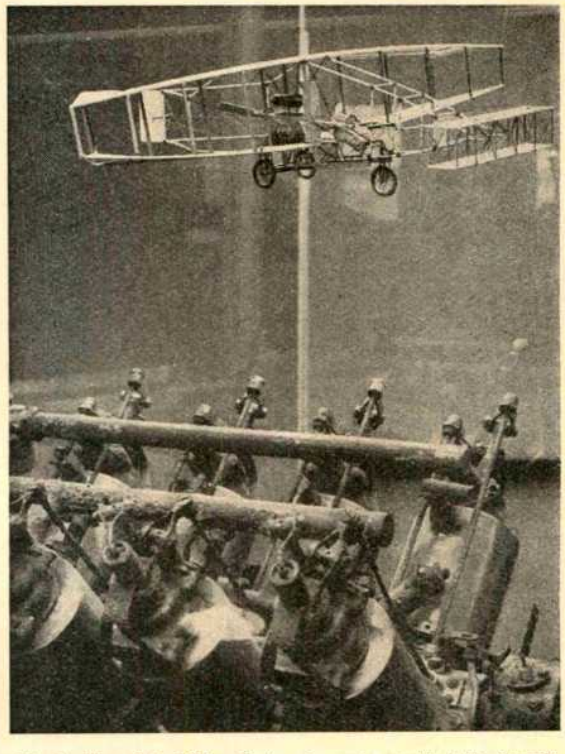

Fig. 1. The original *Silver Dart* engine and a model of the aircraft

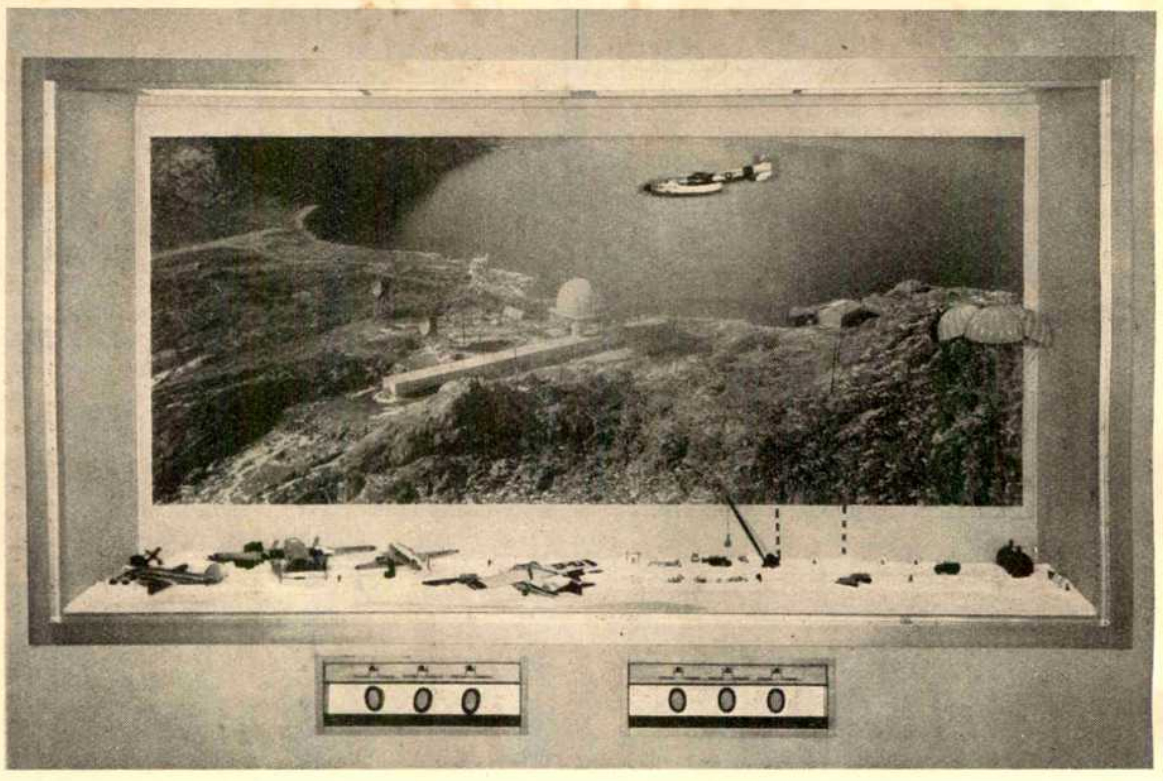

Fig. 2. Model of the *Dew* Line activities and aircraft used in supplying stations

controllable-pitch propellers invented by the New Brunswick pioneer Wallace R. Turnbull during 1923–27, an operating model of the early wind-tunnel used at the University of Toronto in the 1920's, and a steering wheel from the British airship *R*-100. In appearance, the Museum gains variety by using distinctive colours and surface textures to identify the display areas, and by arranging the walls in an irregular pattern.

In keeping with the technological atmosphere of the Museum, some individual displays can be set into operation by the public. Repeaters provide a recorded sound narration in French or English to explain the more technical aspects. Among these operating exhibits are demonstrations of the effect of changes in atmospheric pressure on sparking plugs, and of the contrast of photoelastic stress between large radii and sharp angles.

The National Aviation Museum of Canada has been a long time in the making. A start was made as early as 1929, when J. H. Parkin, now senior consultant to the Division of Mechanical Engineering of the National Research Council, brought a number of aircraft engines and models of wind tunnels to the National Research Council. In 1932 the Council set up a small aeronautical museum, devoted chiefly to engines, in the basement of one of its Ottawa buildings, but this museum was closed early in the Second World War.

Fortunately, the rare items from aviation history that had been collected were stored and well preserved through the years. In 1956 an Associate Committee of the National Research Council was formed, with General A. G. L. McNaughton as chairman, to study the problems of creating a National Aviation Museum. Much stimulus was provided by the National Co-ordinating Council for the Golden Anniversary of Flight in Canada, a group representing aeronautical and flying associations and organizations which planned the 1959 anniversary programme.

The National Aviation Museum was established with funds provided by the Canadian Government and with funds or displays given by many firms in Canada, Great Britain and the United States. The National Research Council collection served as the nucleus of the Museum, and this material was assembled with the new donations into an organized museum by the staff of the Engine Laboratory, Division of Mechanical Engineering, National Research Council, under the direction of its chief, M. S. Kuhring.

Although the National Aviation Museum is designated as the first unit of a Canadian Museum of Science, it will be some years before permanent accommodation is provided. As a temporary measure the Museum is suitably located at Ottawa in the new Uplands Air Terminal. From the windows of an observation room which occupies one corner of the Museum, aircraft can be observed landing and taking-off from one of the busiest of Canada's airfields. Air travellers may also enjoy the experience of visiting this unique aviation museum while waiting for their flights.

The National Aviation Museum is administered by the Department of Northern Affairs and National Resources, the Federal department which administers the National Museum of Canada, the Canadian War Museum, and a number of small historical museums throughout the country.

BIOLOGY IN THE TROPICS

AT the Cardiff meeting of the British Association for the Advancement of Science on September 1, Dr. G. S. Carter, of the Department of Zoology, University of Cambridge, set the stage in his presidential address on "Tropical Climates and Biology" to Section D (Zoology) for a session on the importance of the tropics to zoology. In the session Dr. Carter's address was followed by a paper on evolution within the tropical belt by Prof. J. E. Webb, of University College, Ibadan, Nigeria, and by another on tropical fish communities by Dr. Rosemary McConnell (*née* Lowe), lately of East Africa and now fisheries research officer in British Guiana.

Dr. Carter began by relating that when he was young he was told by his elders that a zoologist's education was not complete until he had visited the tropics and worked on a tropical fauna with its richness and variety of animal life. He believed that this is still true to-day although not, perhaps, for quite the same reasons that led our predecessors to think so. The richness and variety still remain largely unexplored, but we have come to realize that results of work in the tropics are frequently of great general interest to the biologist and may not be such as might be expected from knowledge of the biology of temperate climates.

Both Dr. Carter and Prof. Webb stressed the importance of climate in determining the fauna and flora of a region, and showed that the most unchanging of all land climates is to be found in the forests of the humid tropics. Temperate climates, although more moderate in regard to average temperature, in fact have greater seasonal and diurnal variation in this respect than the humid tropics, and thus present a more stringent environment for animal and plant life. In the tropics rainfall is more important than temperature in determining differences between environments, for the regions of high rainfall are covered by forest that gives way to grassland or savanna of increasing dryness in areas of low precipitation and this in turn to desert. Prof. Webb showed that the boundaries of the vegetational zones in Nigeria are related not so much to the amount of the rainfall but to the relative length of the dry period in each year. More accurately it may be said, as Dr. Carter pointed out, that the nature of the environment is controlled by the proportion (l/g) of the gain of water to the environment to its loss, not only in evaporation and run-off but also in transpiration from the vegetation and percolation into the soil. In the rain forests the value of l/g is of the order of 0·2, so that much of the water flows off the land and the environment is humid. In deserts, l/g may be as high as 200 and in savanna it is probably often near unity. This ratio l/g also controls the diurnal and annual ranges of temperature which are low in humid environments and high in the desert.

Dr. Carter mentioned several examples of work on tropical biology that has given results not to be expected from our knowledge of the temperate regions. In tropical swamps—an environment from which vertebrates and probably many other terrestrial animals almost certainly emerged from water on to land—the water is for all practical purposes stagnant. The content of nutrient salts in these swamps is often high, and at first sight it would be expected that the phytoplankton would be plentiful, but, in fact, both animal and plant plankton are sparse. It seems that the failure of the phytoplankton to grow is due partly to the shallow penetration of light into the shaded and highly coloured water, and partly to the low concentration of dissolved oxygen in the water at levels less than 5 per cent saturation. Dr. Carter suggested that the low concentration of oxygen might be a result of the absence of photosynthesis together with a lack of overturn of the layers of the water. Under conditions giving rise to a steep temperature-gradient from the surface downward with the surface 8–10 degrees C. higher than water at 12–18 in. depth, the water becomes permanently stratified, the lower layers receive no oxygen and in parallel come to contain a high concentration of free carbon dioxide, up to 70 c.c. per litre, which cannot escape by diffusion. This is, therefore, a very difficult environment for animals, and all the fauna shows adaptation to life in a deoxygenated habitat and has developed accessory breathing organs and the like. A study of this question of permanent stratification in shallow tropical waters is clearly important for their future economic development.

Equally unexpected results have been given by work on the sulphur content of tropical fresh waters in Africa by Beauchamp (*Nature*, 171, 769; 1953), where its lack appears to be a limiting factor in the growth of the aquatic fauna. It seems that the sulphur is absorbed from the water of the lake by the planktonic fauna and flora and carried down to the mud in their dead bodies so that the water becomes denuded of sulphur. In the mud the organic sulphur compounds are preserved without breakdown even for the several thousand years required for the deposition of 10–15 m. of mud. Plants rooted in the mud are able to absorb sulphur from this store, which is apparently the only means whereby the sulphur can be carried back into the water. Lake mud can thus be used to improve the fertility of tropical soils and fish ponds.

The control of seasonal rhythms of reproduction and migration in tropical animals is not easy to understand when the changes in climate are slight, yet periodicity of these kinds has been demonstrated in a wide range of equatorial animals. It may be that these rhythms are at least in part endogenous, but it seems there must be some environmental stimulus, physical or other, that controls their periodicity even though we cannot always define it. Clearly this is a subject on which further work is needed.

Dr. Carter ended with the problem of how small mammals are able to satisfy their needs for water under desert conditions without drinking and at temperatures as high as 54° C. This has been studied by B. and K. Schmidt-Neilson ("Biology of Deserts", Inst. of Biology, London, 1954). It is quite impracticable for the body temperature of a small mammal in the desert to be controlled by sweating, and accordingly sweat glands are reduced. In this case the water balance of the animal is achieved by a reduction of all forms of water loss from the body, utilization of metabolic water, the eating of plants absorbing dew deposited during the cold desert nights and

sheltering in a burrow during the day. It is evident that this is one complex physiological problem of which there are many in regard to tropical animals.

Prof. Webb remarked that for more than a century the distribution of animals had been viewed mainly from the point of view of the zoogeographical regions, none of which is exclusively tropical, and that the fauna and flora of the tropical belt as compared with the temperate and arctic regions had escaped detailed geographical analysis. The tropical belt, however, has a physical basis and unlike the zoogeographical regions must have existed for longer than life itself. An estimate based on the distribution of species in a representative sample of groups of land and fresh-water animals suggests that at least 70 per cent of the world's land species occur in the tropics and there is evidence that this is also true for land plants and marine organisms. Moreover, for tropical land animals and plants, an analysis of distribution suggests that not less than 50 per cent of these are found in the forest, most of the remainder being savanna forms. Relating these figures to the areas of the Earth's surface involved we find a density of species in the tropical forest at least three times as great as in savanna and six times that of the temperate region. Thus the number of species is high in the tropical forest and falls more or less progressively with increasing biological stringency of the environment through the tropical grasslands to the desert, on one hand, and from the tropics as a whole through the temperate to the polar regions on the other. This applies to species but not necessarily to higher taxonomic categories, such as the genus and the family where the numbers represented in the tropics may be less than elsewhere. Nor does it appear that the high number of tropical species is related to a greater biomass in the tropics, for there is evidence that this is not greatly in excess, if at all, of the biomass of the temperate region. The density of tropical species, therefore, is evidently due to greater speciation in the tropics than elsewhere, and the problem remains why this should be so.

When the distributions of the present-day families of the vertebrate classes between the tropic and temperate regions are compared, it is found that the most-recently evolved group, the birds, has a higher proportion of tropical families than the older group, the mammals, and that the proportion of tropical to temperate families falls steadily through the series reptiles, amphibians, fishes and lampreys. Moreover, the ratios of recent tropical to temperate families for these groups when plotted against the respective times of origin of the groups, as given by the age of the earliest known fossils of each, fall into two approximately parallel linear series. The first and earlier of these is the Anamnia and the second the Amniota, the break between them evidently representing the point when the reptiles achieved emancipation from water, which opened to them and their successors a new terrestrial path out of the tropics into temperate lands.

The evidence that the proportion of temperate to tropical vertebrate families has increased regularly with the age of the group suggests that each of the vertebrate classes originated in the tropics and that the rate of evolution of families has been virtually constant, first for the Anamnia and then for the Amniota, since the Ordovician for a period of 350 million years. Prof. Webb pointed out that if there is any truth in the speculation that evolution has been proceeding at a more or less constant rate for so long, then it becomes necessary to seek some physical change in the Earth which, by regularly affecting the tropical belt for this period of time, might have controlled the rate of vertebrate evolution.

The zone of transition from tropical forest to savanna consists of an interdigitation of areas of forest and grassland with inliers of savanna in the forest and outliers of forest in the savanna. Slow fluctuation in the extent of the forest in response to climatic changes over the centuries or millenia would result in the formation of new isolated areas of forest or savanna and their subsequent re-incorporation into the parent vegetational belt. The temporary isolation of these patches of vegetation could provide conditions favourable for speciation and perhaps account in part for the high density of species in the tropical forest. If in addition there was also a very much slower, constant and prolonged shift of the land masses through the tropical belt then, at its edge, outliers of tropical vegetation would move into the temperate zone, shrinking and finally disappearing. The isolation, together with the slow environmental change, that this would cause could be part of a mechanism leading to the evolution, at a more or less constant rate, of forms adapted to temperate conditions in proportion to their numerical representation in the forest.

Prof. Webb directed attention to the work of Prof. S. K. Runcorn in "Advances in Physics" in 1955, which postulated on palæomagnetic evidence a relative shift of the north magnetic pole from a point near the present equator west of America in the Pre-Cambrian through a wide arc crossing Japan and Siberia to its position at the present. As it is probable that the geographic pole has never been far from the magnetic north, this shift would also imply a corresponding shift of the equator. It is clear, therefore, that there may be some physical evidence for a constant and prolonged movement of the land masses through the tropical belt on which depends the suggested mechanism for the evolution at a more or less regular rate of temperate vertebrates from originally tropical forms.

Prof. Webb showed maps on which the equators of the different geological periods were drawn based on Runcorn's positions of the north magnetic pole and noted that the locations of the earliest known fossils of the vertebrate classes all lie within the tropical belts of their periods. He also pointed out that, on this evidence, the equator of the Triassic in which the Rhynchocephalia arose passed through the Bay of Plenty in New Zealand, where lives the tuatara lizard, the last survivor of that group. Moreover, the relative change in position of the equator, also on this evidence, has been about an axis between a point in the Pacific off the west coast of North America and the northern tip of Madagascar since the Silurian. These areas, therefore, may have lain continuously within the tropics for the past 330 million years and may have been the only regions on the Earth's surface to have done so. It may be significant that the Pacific location is near where the primitive mollusc *Neopilina* was recently found, while the seas off North Madagascar are the home of the living cœlacanths. Perhaps these areas are the nearest we shall find in fact to the fiction of Conan Doyle's "Lost World". (Recent work by Prof. P. M. S. Blackett, Dr. J. A. Clegg and Mr. P. H. S. Stubbs in *Proc. Roy. Soc.*, A, 256, 291; 1960, gives

palæomagnetic evidence for continental drift. A reassessment of the positions of the fossil equators relative to the land masses will need to be made in the light of this new evidence for drift.)

Dr. Rosemary McConnell ended the symposium with a comparison of the fish faunas of tropical Africa and tropical America. She commented on the great complexity of the tropical fish fauna which, combined with a lack of well-defined seasons, led to many of the difficulties experienced by ecologists in the tropics. The majority of the freshwater fish species of South America and Africa belong to relatively few family groups each of which has undergone remarkable adaptive radiation. The chief of these are the catfishes, the characids and the cichlids, which are common to the two continents and comprise about 70 per cent of the fish fauna. The main difference between the faunas of the two continents is the presence in Africa of numerous species of Cyprinidae and Mormyridae, families absent from South America, where their ecological positions are occupied by the Characidae and Gymnotidae.

The Amazon is by far the richest river system in the world with well over 1,000 known species of fish, and no doubt very many more await discovery. The fish communities there are very complex, many species, often closely related, living in one area as is shown by the fact that a large seine may net as many as 100 species of fish in a single haul in certain parts of the Amazon. A similar though less-extreme situation exists in Africa where, for example, Lakes Tanganyika and Nyasa both have about 200 species of fish, most of them endemic. The question, therefore, arises as to the reason for the complexity of these tropical fish communities. Dr. McConnell suggested that a factor contributing to this could have been profound weather changes of the Quarternary. Just as in the temperate zones the ice ages probably reduced the number of fish species there, so in the tropics the corresponding pluvial and interpluvial periods may well have promoted speciation. For example, in Africa, during a pluvial period, a rise in the level of the lakes would have made new niches for the fish which would afterwards become isolated during the interpluvial period when the lake-level fell, thus providing conditions favourable for speciation. This situation of fluctuating levels in the freshwater habitats is very similar to that proposed by Prof. Webb for the forest.

Dr. McConnell remarked on the extensive adaptive radiation achieved by the Cichlidae, Cyprinidae and Mormyridae in Africa and the Characidae and catfishes in South America, and outlined the astonishing diversity of form and habit found particularly among the catfishes. In such a complex of species the problems of how populations remain distinct and individuals of one species recognize one another for breeding purposes are not fully understood and certainly cannot be answered completely at the moment. The segregation of many of the species, particularly in the Cichlidae, has undoubtedly been maintained by differences in territorial behaviour, restrictions imposed by different food and breeding requirements and so forth. Recognition of each other by individuals within a species may be achieved again by their seeking similar environmental conditions for breeding purposes. In some cases the fish resort to sound signals for recognition and in this respect parallel many of the insects of the tropical forest. The characid of Guiana streams, *Prochilodus*, on a spawning run up river sounds like an outboard engine.

Eating and avoiding being eaten form the predominant theme in the tropics, the biotic relationships appearing to assume greater importance in the general ecology when physical conditions are stable, and much remains to be learnt about the balance between predator and prey. In the absence of well-defined breeding seasons, fish spawn at any time of the year so that young fish and fish at all stages of growth may also be found at all times of the year. The community is thus very uniform and some predators have been able to specialize in feeding only on young fish. In spite of this, however, a balance is maintained, for the food webs are too complex to allow certain species to multiply enormously and thus there is here, just as there is in the tropical forest, no species which can truly be considered dominant.

Dr. Carter remarked in closing his presidential address that, as tropical biology is at a much less advanced stage than that of temperate countries, it is less difficult in the tropics to find promising lines of work. Yet, when posts in tropical laboratories are advertised, it is not by any means always easy to find people to fill them. One reason for this may well be that the many advantages of work in the tropics are not sufficiently realized by the younger generation of biologists or, for that matter, by the older generation that advises them. Perhaps this session will have shown that the tropics offer new fields to conquer and the chance to view old problems in a new light.

J. E. WEBB

SPECIFICITY AND INHERITANCE OF ANTIBODY RESPONSE: A POSSIBLE STEERING MECHANISM

By DR. B. CINADER

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ANIMALS may be tolerant[1] to their own circulating antigens and hence to a very large number of antigenic determinants. An antigenic determinant of a heterologous protein could only induce an antibody response if it were different from any of the determinants of the autologous proteins. The specificity of the antibody response would thus depend on the relation between the structure of autologous and heterologous antigen. Furthermore, the determinant sites of autologous proteins are not always the same in individuals of the same species, and as a consequence the determinants of a heterologous protein which could elicit an antibody response would not be necessarily identical, in composition or number, in

two individuals of the same species. Since the structure and sequence of amino-acids of autologous proteins is genetically controlled, the antibody response which would depend on these would also be inherited and would be different for different antigens. The validity of this hypothesis depends on the following premises.

Immunological tolerance to defined antigens is as general a phenomenon as the antibody response itself. It depends on the individual chemical determinants of the antigen and not exclusively on the antigen as a whole. If two antigens share one or several determinants, tolerance to one antigen can affect the immune response to another. Since immunological tolerance to heterologous antigens is a general phenomenon, it may be assumed that it can also be induced by autologous proteins and that conclusions valid for tolerance to heterologous proteins apply equally to isologous proteins. Finally, autologous proteins of different individuals differ in amino-acid sequence (and tertiary structure) and these differences are under direct genetic control.

Before discussing the implications of these statements, their validity will be examined.

The injection of a heterologous protein into a newborn animal prevents antibody formation to this particular antigen during part or all of the adult life of the animal[1–13]. Acquired immunological tolerance to defined antigens has been induced in rabbits, calves, goats, mice and birds. The antigens used have been various serum albumins, globulins, ribonuclease, azo serum albumin, and yeast antigens. The variety of different species and of different antigens involved suggests that tolerance is as universal as the antibody response itself. Some experimental observations may appear to detract from this generalization. There are reports which indicate that tolerance in chickens[9,15], and possibly in rabbits[10] and in mice[11], may be of short duration and may require for its maintenance reinforcement by antigen during adult life. There is no need to consider the general significance of these reports (see ref. 16) here since, in the situation to be considered, antigen would be available during adult life. There are also several reports of failures to induce immunological tolerance, particularly when red cells are injected at birth, and these need to be considered in some detail since they affect the acceptance of tolerance as a general phenomenon.

Some failures to induce tolerance can, no doubt, be accounted for by the induction of tolerance being dependent on the quantity of antigen injected[17,18]. In order for tolerance to be demonstrated, every antibody-forming cell or its mother cell would have to be affected. If only a relatively small proportion of these cells has a tolerance-inducing encounter with antigen, the slight decrease in antibody production may be obscured by the wide scatter of the amount of antibody produced by normal rabbits. If, on the other hand, the dose injected at birth is such as to leave a very small proportion of antibody-forming cells unaffected, prolonged immunization would be required before the unaffected cells have multiplied sufficiently to produce a detectable amount of antibody. During the early stages of immunization it would, consequently, appear as if no antibody were being synthesized; after some time and after repeated challenge, formation of antibody would reach a level at which it can be detected.

Apart from failure to induce tolerance, experimental failure to prove its successful induction must be considered in this connexion.

The presence of antigenic impurities in the preparation used for injection at birth can lead to results which may be misinterpreted as failure to induce tolerance to the principal antigen. Tolerance to the principal antigen may have been induced, while an impurity may have been present in quantities too low to induce tolerance but sufficient to give rise to antibody during subsequent immunizations[14]. This source of error can occur with any purified protein and can only be excluded by a rigid demonstration that antibody found in an animal injected at birth is directed against the principal antigen injected.

This difficulty[14] occurs also, and in a very complex situation, when heterologous cells, not capable of propagation, are injected at birth. The cells consist of a large number of different antigens, all acting independently in inducing tolerance, all present in different relative quantities. The antigens which are present in very low concentration on the surface of such cells might not induce tolerance. More abundant antigens would induce tolerance. Subsequent immunization would lead to formation of antibody to the 'rare' antigens only. It might be concluded that tolerance had not been induced, which is correct on the cellular—though not on the antigen—level.

In the light of the foregoing experiments and considerations, it may be suggested that rigid criteria must be observed to demonstrate that animals injected at birth have failed to make antibody to the principal antigen injected. For this reason, negative reports—that is, reports of failure to induce tolerance—must be treated with caution, while the reports that tolerance can be induced to defined proteins can be taken at their face value and can be accepted as an indication that immunological tolerance is a general phenomenon.

The second question raised, as to the specificity of acquired immunological tolerance, has been approached by means of model experiments. The following experimental conditions may be considered[6,7].

Antigen injected at birth	Antigen injected during adult life
Human albumin	Azo-human albumin
Azo-bovine ribonuclease	Azo-human albumin

The system for examining antibodies has been based on agglutination inhibition[6,7,14].

Immunization with azo-human albumin of animals tolerant to human albumin does not elicit a demonstrable antibody response to azo-human albumin in most of the animals. However, 20–30 per cent of the animals tolerant to human albumin make antibody to azo-human albumin. This antibody cannot be inhibited by the prior addition of human albumin to serum, but can be completely inhibited by the prior addition of azo-human albumin. Such antibodies are thus essentially directed against the modified part of the molecule and are not directed against the protein moiety of the unchanged molecule. Animals injected with azo-ribonuclease at birth and afterwards immunized with azo-human albumin also show two different responses. All control animals and the majority of the animals injected at birth make antibody both against the protein moiety and against the modified part of the molecule, but a small number of animals make antibody directed against the protein

moiety and not against the modified part of the protein.

There is thus some evidence for tolerance being dependent on antigenic determinants. Consequently the immune response of an adult tolerant animal is not only inhibited with respect to the antigen injected at birth but is also reduced when an antigen is injected during adult life which shares determinants with the antigen injected at birth. This accounts for the observation[3] that rabbits tolerant to bovine albumin produce significantly less antibody to egg albumin (known to cross-react with bovine albumin[19]) than do animals not tolerant to bovine albumin.

The general conclusion that tolerance depends on antigenic determinants, though possibly in some way also on the molecule as a whole, seems justified.

If immunological tolerance[1] can be induced by heterologous proteins in general, it can presumably also be induced by autologous proteins; this would not only serve as a safeguard against antibody formation to circulating autologous proteins but would also have an effect on the specificity of the antibody response to heterologous antigens. Tolerance to one heterologous antigen can affect the antibody-response to another one if an immunological determinant is shared by both antigens. Assuming a similar effect as the outcome of tolerance to an autologous protein, an adult animal would not only be prevented from making antibody to the autologous protein as such but also to any determinant of the autologous protein. A heterologous protein could contain one portion consisting of an amino-acid sequence or determinant surface configuration which also occurs in an autologous macromolecule; this particular determinant would then be excluded, as an inducer of antibody, in a response to the heterologous antigen. Since a large number of different proteins circulates through the body, it would seem likely that a considerable number of determinants would be excluded from antibody induction, so that the specificity of the antibody response to proteins might be guided, to a considerable extent, by the tolerance developed to autologous proteins. Furthermore, the quantity of the antibody synthesized in response to a heterologous antigen might similarly depend on tolerance induced to autologous proteins, since the number of antibody-inducing determinants on a heterologous antigen would depend on the number of determinant sites not shared with autologous proteins of the responding animal.

The possible influence of tolerance to autologous proteins on the genetic control of the antibody response is perhaps the most interesting of the probable consequences of tolerance to isologous proteins; genes would act through an intermediary process.

In the model system already mentioned[6,7], azo albumin, which is normally a 'good' antigen, had become a 'bad' antigen in animals which were tolerant to human albumin. Naturally induced tolerance to an autologous protein could presumably act in the same way as experimentally induced tolerance to heterologous protein has been demonstrated to act. It is thus sufficient to assume that the inheritance of the extent of antibody-response is mediated through the structure of autologous proteins as a consequence of acquired immunological tolerance to autologous proteins, and it is not necessary to assume that the response to all antigens should be under direct and independent genetic control.

The amount of antibody synthesized would depend, among other factors, on the number of sites on an antigen which can give rise to antibody, that is, to the number of determinants which are not excluded by tolerance to autologous proteins. The determinant sites which would be excluded as antigenic determinants would be under genetic control in so far as the amino-acid sequences and structure of autologous proteins are under genetic control. Consequently, differences between the response of different individuals would be attributable to differences in the structure of their proteins. It is known that serum globulins in rabbits[20], guinea pigs[21], cattle[22] and man[23]; hæmoglobin in man[24], in cattle[25] and in sheep[26]; haptoglobin in man[27]; and albumin in man[28] are under individual genetic control and differ in different individuals. It is likely that this will be found to apply to other, if not all, proteins. Even if these differences should affect a very small portion of the amino-acids, it may still exercise a profound effect on tertiary folding. Thus antibody response to different amino-acid sequences[29] would be excluded in different individuals. As a consequence of this genetic variation between determinants, the determinants excluded as immunogens would vary from one individual to the other and a heterologous antigen might have many more determinants able to elicit antibody formation in one individual than in another. This would result in differences in the quantity of antibody produced by different individuals to the same heterologous antigen and would be inherited.

If the foregoing considerations are applicable, and if auto-immune disease can ever occur as a consequence of the breakdown of tolerance, it should be accompanied by a change, however small, in the specificity and nature of the entire antibody-response. This might permit an experimental discrimination between auto-immune disease caused by the release of a normally 'secluded' antigen to which tolerance had never been established, and auto-immune disease caused by breakdown of previously established tolerance.

There is suggestive, if not conclusive, evidence that differences in the antibody-response may be inherited. From an immunochemical point of view, a conclusive analysis has to be carried out with homogeneous, molecularly defined antigens.

An antigenic mixture can be used if one particular molecular species can be identified by its biochemical action, so that the antibody-response can be measured in terms of the inhibition of the biological or biochemical activity of the antigen.

Gorer and Schütze[30] have shown that the quantity of antibody produced in response to immunization with the *H* and *O* antigens of *S. typhi-murium* and *S. enteritidis* is different for animals of different strains and that the relative quantity of antibody made by each of these strains to each of these antigens is not the same. Similar observations have been reported by Ipsen[31] with respect to the response of inbred strains of mice to tetanus toxoid, the average response being different for each strain of mice and the relative quantity of antibody produced after primary and after secondary immunization being the same. Scheibel[32] has been able to produce, by inbreeding, two strains of guinea pigs differing in their capacity for the production of diphtheria antitoxin.

Sobey[33] measured the heritability of the rabbit's response to tobacco mosaic virus by assaying the

quantity of antibody produced by parents and their offspring to a secondary response to tobacco mosaic virus, and by measuring the regression of mid-parent offspring in a cross-bred population of rabbits. This regression gave a heritability $h^2 = 0 \cdot 876$, S.E. $0 \cdot 09$.

The experiments of Gorer and Schütze[20] have indicated that the antibody-response for different antigens may be inherited independently (see also ref. 34). This is also indicated by a recent observation with purified antigens. Bovine ribonuclease, a fairly 'good' antigen in wild-type rabbits, was found to induce practically no antibody in white Himalayan rabbits[8]. However, other antigens, for example, human albumin or azo-human albumin, elicited as high an antibody titre in white Himalayan rabbits as in wild-type rabbits. It would therefore seem that the genetic evidence is compatible with the prediction that the extent of the antibody-response to a given antigen is inherited, and also that the capacity for antibody-response to different antigens may be inherited independently.

On the basis of the considerations outlined, it is proposed that the antibody-response is inherited independently for different antigens, that the inheritance is not under direct genetic control, but that it is controlled indirectly by tolerance to autologous proteins; inherited differences in the antibody response of different individuals being attributable to the genetic differences between their constituent proteins.

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OBITUARIES

Dr. H. E. Wimperis, C.B., C.B.E.

On July 16 Harry Egerton Wimperis, first director of scientific research at the Air Ministry, past president of the Royal Aeronautical Society and a Crown governor of the Imperial College of Science and Technology, London, died at the age of eighty-three.

His was a full life, with perhaps more than a usual mingling of happiness and vicissitude and of reward and injustice. The death of his father while Dr. Wimperis was in his first year and the struggles of his mother to educate him, shaped his early life. At the age of fifteen he was apprenticed to an engineering firm, but his boyish love for astronomy led him to write to the Astronomer Royal, who must have been greatly attracted by the young Wimperis, for he spent several hours in showing him the Royal Observatory and advised him to seek entry into the Royal College of Science and thence to Cambridge. This advice was taken, and after happy years at the Royal College of Science, he was awarded, in 1898, a Whitworth Scholarship and a scholarship at Gonville and Caius College.

Academically, Wimperis did very well at Cambridge, for which he had a life-long affection; but his social life there was restricted by the need to provide a home for his mother. His debt to her, which he gladly paid until her death at a great age, led him to decline a fellowship of his College; this was the end of a dream of a life devoted to astronomy. Then followed a period with Messrs. Armstrong Whitworth until he was appointed, from hundreds of applicants, engineering adviser to the Crown Colonies. In London, close friendship with many men famous in the fields of the arts and humanities, and membership of the Athenæum (in his thirties) filled gaps caused by a forced life of specialization; these men must have helped him to develop an inherent lucidity of expression, for it was once said of him, "If you want something new, get Rutherford to invent it and Wimperis to explain it". His several books on technical subjects are indeed models of clarity.

Membership of the Royal Naval Volunteer Service, a fascination for aircraft and an inventive mind formed the pattern of his work during the First World War. Of his many inventions, the best known was his course-setting bomb-sight, which was introduced in 1917, and with various modifications remained the standard bombing aid until 1939. During the First World War, a small laboratory, known as the Air Ministry Laboratory, with Wimperis as its superintendent, came into being in a few rooms

provided by the Imperial College. Although the scientific staff under Wimperis was never more than half a dozen, the laboratory was no politician's plaything but one which for several years after the War continued to be an outstandingly virile centre of research on such diverse fields as aircraft engines, navigation aids and the effects of bombing on ships' structures.

When in 1925 the Air Ministry decided to follow the example of the Admiralty and create the post of director of scientific research, it was no surprise to those who had worked with Wimperis that he was asked to fill it; this he did until 1937. Much might be written of Wimperis in those years, for he was eager to pursue new and seemingly unpromising ideas while possessing a flair for detecting the bogus. He encouraged the Cierva autogyro, and in 1934 caused the formation of the Committee for the Scientific Survey of Air Defence, under the chairmanship of Sir Henry Tizard, the work of which was a major factor in transforming the whole picture of air defence. Wimperis also caused a revitalization of the Royal Aircraft Establishment of his day, and, most important of all, sowed much in defence science administration that others, with more imposing titles and more generous recognition, were to reap in the decades to come.

How much a man accomplishes for all to see must be judged in relation to whether wind and tide are for or against him. As the first director of scientific research at the Air Ministry, Wimperis had an unenviable task. Not all Civil servants were happy that a scientist should hold a responsible post; the fears of senior Royal Air Force officers led to the ridiculous edict that Wimperis was to have nothing to do with armament, that is, with the chief purposes of Service aircraft. Others caused a ban on concern with lighter-than-air craft, a restriction which did not prevent Wimperis from protesting against the premature and disastrous flight of the *R* 101. On a lighter note, it is amusing to recall that when Wimperis asked that a copy of *Nature* should be regularly provided for him, discreet inquiries revealed that it was not a salacious journal! By the exercise of patience, wisdom and courage, Wimperis gradually enhanced the respect for science in the Air Ministry and when he retired in 1937 the dictum was dying that "a scientist should be on tap but not on top".

On retirement, Wimperis accepted an invitation to Australia to advise the Commonwealth Government on aeronautical research. It was during this visit that the University of Melbourne conferred on him the honorary degree of doctor of engineering. Largely as a result of Wimperis' recommendations, a Division of Aeronautics was set up under the Australian Committee for Scientific and Industrial Research and a chair of aeronautics established at the University of Sydney, though Wimperis could not have foreseen that aeronautical research and development in Australia would be hindered by a reluctance in that country to manufacture aircraft.

During a stay in Singapore, Wimperis developed tropical sprue, which for twenty years was to call for fortitude on its victim's part and for devotion to his special needs by his wife, who survived him by only three weeks. In spite of a gradually increasing physical frailty, his range of interests widened further, and for several years he was convenor for the atomic energy study group at Chatham House.

One who knew him well, wrote these words of him: "Wimperis at the Air Ministry could be stern and biting, never suffering fools or the lazy or the self-deluded gladly but he was tender and helpful to the eager, the struggling and to those who showed courage in difficulties. He cared intensely for truth, honesty and intellectual and personal integrity and had a deep regard for some who stood for complementary values".

Add to these attributes a strong sense of humour and we have a fair picture of Dr. Wimperis, who survived many of his friends and is mourned by many more. A. P. Rowe

Mr. W. J. Chalk

Mr. W. J. Chalk, a member of the engineering staff of the British Broadcasting Corporation, died suddenly on September 24 at the age of sixty-one. His early interest in the field of communications led to his active service during the Second World War in the Royal Signals. He retired with the rank of lieutenant-colonel after having held a number of staff appointments as Radio Planning Officer in Europe and in the Middle- and Far-East. After the War he became a member of the Allied Control Commission in Germany; and, as the liaison engineer with the North-west German Broadcasting Organization, he represented the United Kingdom High Commission at the European Broadcasting Conference at Copenhagen in 1950.

Mr. Chalk joined the British Broadcasting Corporation in 1951, and, as a member of the Engineering Information Department, he became responsible for matters concerning frequency allocations and radio interference problems in the broadcasting field. His earlier experience in world-wide communications made him a valuable member of the United Kingdom delegation at international conferences. During recent years he had participated in the plenary assemblies of the International Radio Consultative Committee held at Geneva (1953), Warsaw (1956) and Los Angeles (1959). In 1959, also, he was a member of the British Broadcasting Corporation's delegation to the Administrative Radio Conference in Geneva, which established revised regulations and frequency allocations for the conduct of international radio communications of all types. His work in this field made him widely known both in Britain and overseas. He was very popular with both his British and his foreign colleagues, and had a reputation for exercising a sound judgment on all the problems with which he was concerned. R. L. Smith-Rose

Prof. E. W. Goodpasture

The death of Prof. Ernest W. Goodpasture at the age of seventy-nine is reported from the United States. He was a pioneer in the field of the pathology of virus infections.

Goodpasture was born in Tennessee, and there received his medical training at Vanderbilt University, Nashville, where he was for so long to hold the chair of pathology. He went to Yale and to Baltimore for postgraduate training; at Johns Hopkins he held a Rockefeller fellowship in pathology. In 1929 he was called to the chair of pathology at Nashville and here he remained until 1955.

His early work in the virus field was on herpes simplex, particularly on the progression of the virus along nerves. Turning to the pox group, he studied the inclusion bodies of fowl-pox, and in 1931, with

A. M. Woodruff, cultivated the virus on the chorioallantoic membranes of fertile eggs. Rous and Murphy had twenty years earlier used a similar technique in studies of tumours, including the Rous sarcoma; but Goodpasture and his colleagues really introduced the developing egg into virus research. Later, Burnet improved the method by showing how to make an artificial air-sac. In 1938 Goodpasture showed that viruses would grow after inoculation into the amniotic cavity of chick embryos; and this method, too, was taken up and developed by Burnet, and other workers. For many years Goodpasture worked with fertile eggs and used them for many purposes and to great advantage. He grew vaccinia on chorioallantoic membranes and advocated the use of such material for vaccination against smallpox. He grew 'difficult' viruses such as herpes zoster on grafts of human skin growing in eggs. He studied the behaviour in cells of egg membranes of some specialized parasites among the bacteria such as those of typhoid and tularæmia. The laboratory study of mumps really begins with his demonstration that monkeys can be infected by inoculation into their parotids.

Goodpasture held many important appointments, including that of scientific director of the International Health Division of the Rockefeller Foundation. On his retirement from Vanderbilt in 1955 he went to work at the Armed Forces Institute of Pathology in Washington. He was a member of the National Academy of Sciences and of the American Philosophical Society and received many honours.

C. H. ANDREWES

NEWS and VIEWS

Nobel Prize for Chemistry

PROF. WILLARD F. LIBBY has been awarded the Nobel Prize for Chemistry for 1960 in recognition of his work on the carbon-14 method of age determination. In a series of experiments carried out during the period following his appointment as professor of chemistry at the Institute of Nuclear Studies, University of Chicago, Prof. Libby demonstrated the presence of carbon-14 in Nature at a level close to that which he had predicted, and showed that its distribution throughout the world-wide carbon exchange reservoir is substantially uniform. He then pointed out that the death of an organism would prevent further exchange of its carbon atoms with those of the reservoir and that consequently a measurement of the residual carbon-14 activity of dead material could be used as a basis for an age determination. The practical application of the method necessitated the development of an experimental technique capable of measuring accurately, and on a routine basis, the extremely low levels of carbon-14 activity which are found in ancient materials. Libby's success in this direction can best be judged by the list of nearly a thousand dates produced by the Chicago dating laboratory during its period of operation. The importance of the method is incalculable, for it provides not only an absolute method of dating independent of hypothetical considerations covering the past 40,000 years or so, but also one which is of world-wide application to a variety of commonly occurring materials. Archæology, geology, oceanography and climatology have all benefited and will continue to do so in the future from the applications of Libby's fundamental researches.

Nobel Prize for Physics

THE announcement of the award of the Nobel Prize for Physics for 1960 to Prof. Donald A. Glaser of the Radiation Laboratory, California, has given pleasure to all who admire the way in which a young man not only conceived a brilliant idea but also, using commonplace physical ideas as a basis for his experimental work in an unexplored field, and working practically alone, presented the nuclear physicist with a powerful new tool—the liquid bubble chamber. The formation of bubbles along the track of an ionizing particle occurs in a medium of much greater stopping power than the gas in a cloud chamber, yet because of the short time (only a few milliseconds during which the liquid is rendered sensitive to such bubble formation it is possible to follow the various products of a particular nuclear reaction without the ambiguity, inherent in nuclear emulsions, caused by the presence of many other, extraneous, tracks. Chambers containing hundreds of litres of liquid, set up beside existing high-energy particle accelerators, can now produce photographs of nuclear events every few seconds and in this way not only has the existence of the neutral cascade particle been established but also new experimental data are being made available at such a greatly increased rate that only by the use of automatic measuring devices can the fullest advantage be taken of Prof. Glaser's great contribution to physics.

Royal Society: Award of Royal Medals

H.M. THE QUEEN has been graciously pleased to approve recommendations made by the Council of the Royal Society for the award of the two Royal Medals for the current year as follows: to Sir Roy Cameron, professor of morbid anatomy at University College Hospital Medical School in the University of London, for his distinguished contributions in the field of cellular pathology; to Prof. A. C. B. Lovell, professor of radio astronomy in the University of Manchester and director of the Nuffield radio astronomy laboratories, Jodrell Bank, for his distinguished contributions to radio astronomy.

Applied Mechanics at Nottingham: Prof. G. B. Warburton

DR. G. B. Warburton, who has been appointed to the recently instituted chair of applied mechanics in the University of Nottingham, studied at Peterhouse, Cambridge, and was awarded first-class honours in the Mechanical Sciences Tripos in 1944. As a demonstrator at Cambridge, he was attached to a research team investigating stresses set up in ships' plates due to welding. Later he became an assistant lecturer at University College of Swansea and, in 1947, joined the engineering staff at the University of Edinburgh. After varied teaching experience, Dr. Warburton was appointed head of the Postgraduate School of Applied Dynamics which was formed at Edinburgh in 1956, details of which appeared in *Nature*, 179, 1177 (1957). His research work at Edinburgh has

been in the field of mechanical vibration and his published work has been concerned mainly with the vibration of cylindrical shells and plates, and the propagation of ground vibration from machines to structures. The former work has been used in the determination of natural frequencies of aircraft, missiles and submarines.

Liverpool Observatory and Tidal Institute: Dr. A. T. Doodson, C.B.E., F.R.S.

DR. A. T. DOODSON has recently retired from the directorship of the Liverpool Observatory and Tidal Institute. After graduating from the University of Liverpool in 1912, Doodson spent a short time in the electrical industry. During the First World War, he worked with Prof. Karl Pearson on problems which included the trajectories of anti-aircraft missiles. The Tidal Institute was formed in 1919 on the initiative of Prof. J. Proudman, who became the director, with Doodson as secretary. When the Institute was combined with the Liverpool Observatory in 1929, Dr. Doodson became associate director of the joint institution, and later, in 1946, its director. A paper published by Doodson in 1921, giving a complete revision of G. H. Darwin's schedule of the harmonic constituents of the tides, provided the foundation for much of his later work on tidal analysis and prediction. In collaboration with Proudman, Doodson developed methods for the construction of co-tidal charts based on observed tidal elevations and currents. They also published a series of papers on the theory of tides in oceans bounded by meridians. Another line of research, started by Doodson in 1923, on the meteorological effects on tides, has led to important advances in methods of forecasting storm surges. At the same time as he was carrying out research, Doodson greatly extended the routine prediction work, and to-day the Tidal Institute provides tidal predictions for nearly all the countries of the Commonwealth. Dr. Doodson was elected a Fellow of the Royal Society in 1933, honorary Fellow of the Royal Society of Edinburgh in 1953, and in 1955 was made C.B.E. In addition to serving on several national committees, he has taken a prominent part in the activities of the International Association of Physical Oceanography and the International Union of Geodesy and Geophysics.

British Economic Growth

A RECENT broadsheet issued by Political and Economic Planning, entitled "The Growing Economy —Britain, Western Germany and France", discusses the main factors influencing the development of industrial production and is adapted from the findings of a group which over the past three years has been working on problems of adaptation and change in British industry (26, No. 445; 17th October, 1960. Pp. 281–308. London: Political and Economic Planning, 1960. 3*s*. 6*d*.). These findings are to be published in a forthcoming report which, assuming that economic growth is a proper object of policy, considers the conditions for achieving a rate of growth comparable with that of other Western industrial nations. After comparing levels of industrial activity and growth in the principal West European countries and the United States, the broadsheet examines the role of capital in economic growth and then considers the structure and achievement of the economies of Western Germany and France, respectively. In contrast to British policy, French and German economic policies have had marked success in stimulating economic growth, and the main conclusion of the broadsheet is that, in view of Britain's record since the War, priority must be given to the task of increasing the rate of growth. Specific suggestions include giving a high priority to measures which will encourage the release of workers from some industries and their rapid absorption by industries which need more labour. This involves stimulating industrial research into labour-saving methods, expanding educational facilities for scientists and technologists and participating in the organization of schemes to provide compensation for loss of employment, and to overcome obstacles to movement between jobs, such as housing difficulties, removal costs and re-training problems. It is urged that the trade union movement in Britain needs to be much more closely associated with the other organs of government and power in the attainment of the national economic objectives, above all, of economic growth. Publication of a more consistent series of plans governing the public sector would, it is suggested, go a long way towards providing private firms with the kind of assurance they need about the future growth of the economy, and it is probable that the economy would benefit if the Government exercised a more, rather than a less, positive influence over the investment planning of the private sector.

British Conference on Automation and Computation

THE rapid growth of automation in Britain led to a decision in 1957 (see *Nature*, 179, 948; 1957) by some twenty bodies having interests in this field to set up a central organization to provide more effective liaison between the interested bodies, to be known as the British Conference on Automation and Computation. The Conference was divided into three autonomous Groups, as follows: (1) the British Group for the Engineering Applications of Automation; (2) the British Group for Computation and Automatic Control; (3) the British Group for the Sociological and Economic Aspects of Automation Techniques. At meetings of the three Groups held on October 10, it was agreed that they should merge in a reconstituted organization. Sir Walter Puckey was elected chairman of the new Conference, with Messrs. L. T. Blakeman, J. F. Coales and H. G. Conway as vice-chairmen. Mr. S. M. Rix was elected honorary treasurer and Mr. W. K. Brasher (secretary of the Institution of Electrical Engineers, Savoy Place, London, W.C.2) as honorary secretary. The following representatives were elected to serve with the honorary officers as the Executive Committee: Dr. E. H. Bateman (Institution of Structural Engineers), W. J. Carron (Trades Union Congress), E. C. Clear Hill (British Computer Society, Ltd.), W. C. F. Hessenberg (Iron and Steel Institute), Prof. G. D. S. MacLellan (Institution of Mechanical Engineers), Prof. P. B. Morice (Institution of Civil Engineers), Sir Charles Norris (British Productivity Council), Prof. E. J. Richards (Royal Aeronautical Society), E. S. Sellers (Institution of Chemical Engineers).

The Wildfowl Trust

ALTHOUGH there were no major developments in 1958–59, the eleventh annual report of the Wildfowl Trust, by Hugh Boyd and Peter Scott, is once more a chronicle of satisfactory progress and development (Pp. 167+32 plates. (Slimbridge, Gloucestershire:

The Wildfowl Trust, 1960.) 10*s*. net.) The number of visitors increased during the year, finances are adequate and the scientific staff have extended their investigations by aerial surveys and other means. A valuable inclusion in this attractive report is the translation of a research article by Prof. S. M. Usjinski on the status of the Brent goose in the Soviet Union. The drawings and photographs are up to the standard expected from Slimbridge.

The National Research Council of Canada

DETAILS of the grants totalling 9·37 million dollars in 1959–60 from the National Research Council of Canada in its forty-third year in support of research at Canadian universities in science, engineering and medicine, show an increase of 2·62 million dollars on 1958–59 and of 6·25 million dollars on 1955–56; they are contained in a report issued by the Council, which includes also a Supplement to the 1958–59 report (Pp. ii+213+xi. Ottawa: National Research Council of Canada, 1960. 50 cents). Of this, 8,586,265 dollars were in direct support, 76·7 per cent being for scientific and engineering research and 23·3 per cent for medical research, while of the total, 84·6 per cent represented 958 research grants to members of university staffs and 15·4 per cent provided 450 postgraduate scholarships and fellowships. Of the indirect support, 39·4 per cent was for contributions, grants, etc., to scientific organizations and functions and 35·3 per cent for the publication of scientific periodicals. Besides a full list of grants and their recipients, fellowships and scholarships, the report includes an outline of the programme and particulars of the membership of the administering bodies.

Atmospheric Pollution

A RECENT publication entitled "The Investigation of Atmospheric Pollution" includes the thirty-first annual report of the Atmospheric Pollution Research Committee of the Fuel Research Board for the year ended March 31, 1958, and gives in synoptic form information regarding the research projects considered during that period (Department of Scientific and Industrial Research. Pp. iv+164. London: H.M. Stationery Office, 1960. 8*s*. net). Smoke from railway locomotives, which are responsible for one-seventh of all the smoke discharged to the atmosphere, has been investigated. Other subjects considered were, instruments for measuring air pollution, air pollution by fluorine compounds, fumes from coke fires, smoke abatement in the iron and steel industry, and air pollution and health. The second part consists of the report of the Director of Fuel Research on the investigation of atmospheric pollution. Here more details are given on the emission of pollutants to the atmosphere, with some indication of the sources of smoke and sulphur dioxide from various fuels. From the data available it would appear that there is a steady decrease in the amount of smoke emission to the atmosphere since 1955–56, and during the same time there has been no increase in the sulphur dioxide concentrations in the atmosphere. The report states: "This shows without any doubt that the concentration of sulphur in the air in this country [Britain] is not increasing". There is also some interesting information on the smoke and sulphur dioxide concentrations in the City of London. Some particulars are also given about the work of the Fuel Research Station on the production of reactive domestic coke, smoke elimination from boilers, combustion of oil fuel, exhaust gases from motor vehicles, and other topics. The third part summarizes the results of the observations taken throughout Britain by the co-operating bodies which take part with the Department of Scientific and Industrial Research in monitoring atmospheric pollution.

Water Pollution Research

ANTICIPATING a rapid rise in the demand for industrial water, an increase in the re-use of water, and the consequent need to improve effluents, the current report of the Water Pollution Research Board, Department of Scientific and Industrial Research, announces the imminent expansion of its Stevenage laboratory by nearly 50 per cent (Water Pollution Research, 1959. Pp. vi + 115 + 4 plates. London: H.M. Stationery Office, 1960. 7*s*.). The report contains much detailed and valuable, but necessarily esoteric, information about the progress made with diverse investigations into the design of waste treatment plants and the pollution of rivers.

Two particularly interesting advances may be selected for further mention. Previously, laboratory trials of a new synthetic detergent had shown that it was more easily decomposed during sewage treatment than the usual detergents. To test these observations, the whole town of Luton was supplied with apparently normal packages of detergent which contained the new active agent instead of those usually employed. Less synthetic detergent reached the sewage works, and the increase in the proportion destroyed during treatment agreed with the laboratory experiments. If it proves possible to extend the distribution of this new detergent to the whole country, the condition of many rivers and water supplies should be improved. Tests on the effects of suspended mineral pollution, often a subject for speculation, have shown that concentrations which are fatal to fish, during continuous exposures of about ten weeks, are higher than those commonly found in polluted rivers. Pathological changes of the gill tissues are apparent in the dead fish.

Biological Engineering Society

THE first meeting of the Biological Engineering Society was held on October 15 at the National Institute for Medical Research, Mill Hill. About 100 participants assembled in the morning to listen to a series of short papers, each describing a demonstration to be held during the afternoon. Sir Charles Harington, director of the Institute, opened the proceedings, and in his address drew a parallel between the state of biological engineering to-day and biochemistry half a century ago. Perhaps in the years to come a fusion of the two disciplines of biology and engineering might result in biological engineering becoming as acceptable as biochemistry to-day. In the meantime, advances in biological and medical science, he said, are very dependent on advances in engineering and instrumentation, and the Society is making a valuable contribution by enabling biologists and engineers to work more closely together and to understand each other's points of view. Prof. R. F. Woolmer, the president of the Society, replied to Sir Charles, and pointed out that it was appropriate that this first scientific meeting should be held at the Institute, which in its work and organization is a good example of the way in which engineers could work together with biologists. A number of demonstrations illustrating many aspects of the work of the institute, and that of members of the Society from other centres, was given. The honorary secretary of the

Society is Dr. A. Nightingale, Physics Laboratory, St. Thomas's Hospital, London, S.E.1.

Milk Hygiene

THE second report of the Expert Committee on Milk Hygiene, set up jointly by the Food and Agriculture Organization and the World Health Organization, amplifies and supplements an earlier one published in 1957 (W.H.O. Technical Report Series, No. 197. Pp. 55. (Geneva: World Health Organization.) 2 Swiss francs; 0.60 dollars. Also obtainable from H.M. Stationery Office. 3*s*. 6*d*. net. 1960). It deals first with some of the diseases that can be transmitted through milk, and refers especially to staphylococcal and streptococcal infections, and to tick-borne encephalitis. The nature of pasteurization and other forms of heat treatment, and their importance in reducing the danger of infection from milk itself and from milk products such as butter, cheese, fermented milk, dried milk and ice cream, are discussed. The fact is stressed that if in many countries of the world milk quality is to be significantly improved, information and exhortation about hygiene will not be enough; they will have to be accompanied by some system of payment for quality. A later section of the report describes some of the problems associated with dairying in warm countries, where the standard of nutrition is frequently very low and where dairy products are very badly needed to improve the diets of the vast populations that live there. Reference is made to the production of milk in these areas not only from cows but also from buffaloes, goats and sheep. The report contains two annexes. One is a code of principles for milk and milk products prepared under the auspices of the Food and Agriculture Organization. The other contains a description of some twenty of the less-well-known milk products such as 'yogurt' and 'ghee' which are much used in parts of Europe and Asia. The report should be of particular value in those areas of the world where more dairy products are urgently required, but where, for various reasons, the production of milk and its products is still somewhat primitive and relatively little is known of the science of dairy technology.

The Night Sky in December

FULL moon occurs on Dec. 3d. 04h. 25m. U.T., and new moon on Dec. 18d. 10h. 47m. The following conjunctions with the Moon take place: Dec. 3d. 01h., Aldebaran 0·5° S.; Dec. 6d. 06h., Mars 7° N.; Dec. 21d. 15h., Venus 4° S.; Dec. 30d. 07h., Aldebaran 0·4° S. In addition to these conjunctions with the Moon, Mercury is in conjunction with Antares on Dec. 13d. 08m., Mercury being 5° N. Mercury is a morning star, but conditions are not favourable for observation. Venus is an evening star, and conditions for observation are becoming favourable. Venus sets at 18h. 30m., 19h. 10m. and 19h. 55m. on December 1, 15 and 31, respectively, almost four hours after the Sun on the latter date. During the month its distance from the Earth decreases from 102 to 83 million miles, the visible portion of the apparent disk from 0·744 to 0·639, and its stellar magnitude from − 3·6 to − 3·8. Venus is visible in the south-west after sunset. Mars rises at 18h. 05m. and 16h. 50m. on December 1 and 15, respectively, and is above the horizon at sunset on December 31. It is retrograding in Gemini, and is at opposition on December 31. Mars is closest to the Earth on December 25, when its distance is 56 million miles and its stellar magnitude − 1·3. Mars is a very prominent object and can be seen all night. Jupiter and Saturn set shortly after the Sun, and are unfavourably situated for observation. Occultations brighter than magnitude 6 are as follows, observations being made at Greenwich: Dec. 3d. 0h. 57·2m., α Tau. (*D*); Dec. 3d. 2h. 16·3m., α Tau. (*R*); Dec. 7d. 3h. 53·8m., 5 Cnc. (*R*); Dec. 10d. 3h. 25·7m., 44 Leo. (*R*); Dec. 29d. 23h. 43·4m., γ Tau. (*D*). *D* and *R* refer to disappearance and reappearance, respectively. The Geminid meteors are active during December 9–14, but conditions for observation are unfavourable. The Ursids are active during December 20–22, and conditions are favourable; the radiant is near R.A. 14h. 28m., Dec. + 76°. The winter solstice occurs on Dec. 21d. 20h.

Announcements

AT the recent Inter-American Course of Physiopathology of Reproduction and Artificial Insemination it was decided to form a Latin-American Association for Animal Fertility. The following were elected officers of the Association: *Permanent Honorary President*, Prof. T. Bonadonna (Milan); *President*, Prof. A. Hernandez Prado (Venezuela). It is expected that sections in the different South American Republics will be established.

DR. M. R. POLLOCK, of the National Institute for Medical Research, London, will give the second Rapkine Memorial Lecture on "La Sécrétion d'enzymes par les Bactéries" at 5.30 p.m. on December 2 at the Laboratoire d'Evolution des Etres Organises, 105 Boulevard Raspail, Paris.

A MEETING on "Theoretical Rheology" is being organized by the British Society of Rheology at Reading during April 20–21, 1961. Further information can be obtained from Dr. M. F. Culpin, 8 The Broadway, Pontypool, Mon.

THE National Institute of Agricultural Botany is holding a Crop Conference at its headquarters in Cambridge during December 13–14. Further information can be obtained from the Assistant Director, National Institute of Agricultural Botany, Huntingdon Road, Cambridge.

THE eighth annual Western Spectroscopy Conference will be held at Asilomar, Pacific Grove, California, during January 26–27, 1961. Further information can be obtained from the chairman of the Western Spectroscopy Association, Roland C. Hawes, Applied Physics Corporation, 2724 South Peck Road, Monrovia, California.

THE fifth conference on "Carbon" is to be held at Pennsylvania State University during June 19–23, 1961. The conference is being sponsored by the American Carbon Committee and the Pennsylvania State University. Further information can be obtained from the chairman of the Executive Committee, S. Mrozowski, American Carbon Committee, Carbon Research Laboratory, University of Buffalo, Buffalo 14, New York.

A SYMPOSIUM on "Large Capacity Memory Techniques for Computing Systems" will be held during May 23–25, 1961, at the Department of Interior Auditorium on *C* Street, between 18th and 19th Streets, N.W., Washington, D.C. The symposium is sponsored by the Information Systems Branch, Office of Naval Research. Further information can be obtained from Miss Josephine Leno, Code 430*A*, Office of Naval Research, Washington 25, D.C.

THE PAINT RESEARCH STATION

NEW EXTENSION

THE Paint Research Station at Teddington has grown steadily in size and stature since its inception in 1926. A new extension to its already considerable premises was ceremonially opened and named the Jordan Laboratory on September 20 by Mr. E. B. Calvert, chairman of the recently formed Paint Manufacturers' Joint Executive Council. The new Laboratory is named, of course, after the founder-director, Dr. L. A. Jordan, whose outstanding service from 1926 until 1959 is commemorated on a plaque unveiled by Mr. Calvert. A further proof of the esteem in which Dr. Jordan is held was signalled by the presentation to him of the medal of the Research Association of British Paint, Colour and Varnish Manufacturers, of which the Paint Research Station is the instrument.

The opening ceremony, which was held in the new library in the Jordan Laboratory, was attended by about two hundred members and guests. At a luncheon preceding the opening ceremony, Sir Harry Melville, secretary of the Department of Scientific and Industrial Research, was the guest of honour and spoke of the continuing importance of the research association movement. Other distinguished guests at the luncheon included Mr. L. Farmiloe, president of the National Paint Federation; Mr. B. J. Nicholson, vice-president of the Society of British Paint Manufacturers; Dr. D. W. Hill, chairman of the Committee of Directors of Research Associations; Mr. P. J. Gay, president of the Oil and Colour Chemists' Association, and representatives of the Organic Coatings Division of the International Union of Pure and Applied Chemistry.

The Jordan Laboratory adds rather more than 10,000 sq. ft. of floor area to the 25,000 sq. ft. of the existing premises. The main feature of the new extension, which is a striking building of modern design, is a library of some 1,250 sq. ft. on the ground floor, with additional book storage in a semi-basement. The library—an attractive room furnished in African mahogany—and the adjacent staff common room may be combined for special occasions (the opening day, for example) to form one large assembly hall of nearly 2,000 sq. ft.

The first and second floors accommodate three large general-purpose laboratories, a section specially designed for microbiological studies, and eight smaller rooms (instrument rooms, balance rooms, dark room, stores, etc.). There are the usual chemical laboratory facilities and services, which are run in ducts along the external walls of the laboratories with access for further connexions. A feature is the storage of gas cylinders on the ground floor for easy access, oxygen, nitrogen and air passing to various points in the laboratories. The divisions between the pairs of large laboratories on each floor are formed with demountable partitioning to allow for future alterations if required. The working area has been considerably increased by designing the upper floors so that corridors have been almost eliminated.

An extension of the ground-floor area to the side of the old building includes a large room (800 sq. ft.) intended for paint application and related studies, while the sub-basement comprises, in addition to a library stock room, additional staff facilities, storage and service rooms.

After the opening ceremony, and for the remainder of the week, the entire Station was open to view. More than six hundred people used the opportunity to inspect the wide range of exhibits covering every aspect of the work of the Station.

The main displays in the physics section were of studies on electron microscopy, colour perception and measurement, adhesion, and accelerated weathering. The numerous striking electron micrographs of pigment particles and the sections of paint films aroused much interest, as did the many intriguing displays illustrating the physiological basis of colour perception. Methods of precise colour measurement, and their application to problems of colour matching, including practical field tests on industrial colour matches, were shown. Various methods of measuring adhesion, including the direct pull-off technique used at the Paint Research Station, were shown, together with results on the effects of the composition of paint and exposure to moisture vapour and water. Correlations (both positive and negative!) between natural and accelerated weathering for various types of paint films were displayed.

Physicochemical studies were centred mainly on the surface chemistry of pigments, although there were several examples of polymerization reactions, for example, the polymerization of organo-metallic systems and the formation of graft copolymers. Techniques for measuring particle size and shape figure largely in current activities, and examples of the use of these to elucidate such problems as the effect on pigment particles of micronizing were exhibited. Adhesion tension measurements, adsorption studies of polar substances on pigment particles, surface-active agents, radiochemical tracer techniques, electrode potential measurements on paint films—all these physicochemical techniques and many more were on show and served to demonstrate the range and depth of techniques currently used in studies on paint.

Such fundamental investigations are linked directly with practical issues such as milling studies, the protective action of paint films against corrosion, and the effect of atmospheric pollution on paint durability and staining. In the technical laboratories, work on these factors was prominently displayed, together with other features such as the relation between viscosity of a liquid paint film and brushability and how the porosity of a substrate affects the adhesion of the paint film.

The work of the organic chemistry section is naturally concentrated on the media used in paints, that is, the synthetic polymeric resins used as film-formers. Current technological interest in water-based finishes, whether of the solution or emulsion type, was reflected in numerous exhibits. Water-soluble resins present special difficulties, because the films formed therefrom have afterwards to be water-

resistant; the chemical features controlling such factors were illustrated. Practical studies were again included; for example, the effect on the wet abrasion resistance of emulsion paint films of using volatile coalescent agents to replace partially the plasticizer. Detailed studies of the structure and analysis of alkyd resins, carried out over the past few years, were comprehensively surveyed. Media incorporating drying oils suffer from a tendency to yellow; some of the factors influencing this tendency, such as the catalytic action of organic bases and the chemical reactions involved, have been uncovered.

As might be expected from the wide range of materials used in paint manufacture, the work of the analytical laboratory has to cover an extremely wide field. Work on display included analytical schemes for white pigments and protective colloids, the application (sometimes in modified form) of standard techniques, for example, chromatography, to problems of paint analysis and the special micro techniques developed to study paint blemishes and defects.

The growing interest in microbiological studies on paint has been reflected, as already described, in the provision of a special laboratory in the Jordan Laboratory. The display concerned identification of the various moulds, fungi or algae responsible for defects and assessments of the protective action of various chemicals against such microbiological attack. Special features appertaining to exposure under tropical conditions were also shown.

It is impossible in an article of this length even to list all the exhibits; the above will have indicated, however, the fascinating problems involved in paint manufacture and application, and the progress made at one research centre dedicated to their study.

L. VALENTINE

SELECTION AND TRAINING OF COMPUTER PROGRAMMERS

A SESSION of Sub-section A* (Mathematics) of the British Association at the recent Cardiff meeting was devoted to consideration of the selection and training of computer programmers. It took the form of an introduction followed by three short lectures and a very brief general discussion.

Introducing the subject, Dr. J. Howlett (Atomic Energy Research Establishment, Harwell) said that the electronic computer, although almost a household word, is really very new. Its rate of development has been remarkable, and it has put into our hands great and rapidly increasing logical and arithmetical powers; the use of computers is spreading widely in all fields, scientific and otherwise, but it is unlikely that their powers are yet fully appreciated or that the real nature of the task of programming them is completely understood. It is, therefore, only to be expected that there are sharp differences of opinion about the use and organization of computers and the types of person to be employed in connexion with them, how to select these people and how to train them.

When setting up a Computing Group, two important questions have to be settled: the relations with the establishment it serves, and the amount of stratification of the work within the Group. The first means deciding towards which of two extremes the Group shall tend: towards 'closed shop' working in which only the members of the Computer Group write programmes, or towards 'open shop' when anyone who wishes to do so may write his own programmes. The second concerns the extent to which the different kinds of tasks involved in going from the problem expressed in, say, the language of physics to a computer programme shall be performed by different people; these steps are formal mathematical analysis, numerical analysis, planning the flow or general structure of the programme and, finally, the detailed coding. The different tasks make quite different demands, and so if there is to be much division of labour, staff of several different types will be needed. Dr. Howlett suggested that scientific establishments tend to favour 'open shop' working and little stratification, while the reverse applies to commercial organizations and computer units tied to large engineering enterprises; and that the latter are more inclined than the former to use selection methods based on formal aptitude and psychological tests. Finally, he referred to the recent developments in efficient automatic programming systems which make it reasonably easy for the non-specialist to write the programmes to do his own work; in many computer units this has resulted in much work being put on to the machine by people who could not be called programmers at all. This possibility has been brought about by the production of more powerful machines in the past few years and is certain to continue as computer power and the appreciation of this increases.

Mr. J. J. Foody (Short Bros. and Harland, Ltd., Belfast) described the experience and practice in his own Company, the field of which is aircraft engineering. Its computer unit in Belfast uses an English Electric *Deuce*. The staff is grouped into three classes: systems analysts, programmers and operators. The first are honours graduates who do all the essential mathematical work on the problems, taking the development to the stage where it can be used directly as the basis of a computer programme. Those in the second group are generally of pass-degree standing; they take over the work of the analysts and turn it into a programme, doing all the work of flow-charting, coding and testing. The operators (for card punching and machine running) need have no academic qualifications; Mr. Foody said they had at one time tried to use pass-degree people as operators, but the results were unsatisfactory. This led the Company to adopt the principle of looking for the lowest grade of staff capable of doing any particular type of work—over-qualified people become dissatisfied and look for a change. Programmers should have the ability both to see the essentials of a problem and to attack it in a logical and orderly manner; the Company therefore uses in its selection process problems intended to test these qualities, as for example variations on the classical coin-weighing problem, questions on the connexions for a simple circuit or the analysis of some familiar numerical process such as the digit-by-digit method for extracting a square root. Experience in recruiting young people has suggested that failure to grasp fundamentals is often

a fault of the teaching rather than of the person. Mr. Foody commented that the search for suitable staff had been made difficult by the shortage of mathematicians, particularly numerical analysts, in Northern Ireland.

For training, new recruits are given first an introduction to the kind of work done in the computing group, which covers a very wide range; this is followed by instruction in the simpler techniques of programming, and they are then left for about two weeks to study the programme manual, working out examples so far as possible on their own. After this they are taught more about the logical structure of programmes, with particular emphasis on the ideas of loops and sub-routines and from then onwards take up progressively more difficult 'live' work. A lot of emphasis is put on the need to keep proper records of all work done and the importance of neat and orderly paper-work. Mr. Foody concluded by saying that he considers the quality of management to be of vital importance in a computing group. Good management will not only ensure that the group is well organized and run, but also that the power and value of high-speed computation are made clear to all those who might benefit.

Mr. P. V. Ellis (International Computers and Tabulators, Ltd.) described the method of selection and training used in his Company, which makes computing, data processing and accounting machinery on a large scale. Programming to them means a wide range of activities, including service to customers to help with the use of existing machines, provision of assembly, interpretative and related programmes, detailed appraisal of projected machines in advance of any construction and assistance in the logical design of new machines.

Primary selection is made by interview and formal aptitude tests. A candidate successful at this stage embarks on a training course, but may at any stage of this be declared unsuccessful if it has become clear that he is not going to reach the required standard. The tests, the form of which has been evolved over several years, are administered by a professional organization; they do not call on factual knowledge, but are intended to test observational powers and ability to think quickly and logically. They include problems in arithmetic, in the detection of faults in statements, in the application of selection rules, in logical inference and in logical deduction from sets of statements. Existing staff are used as a control, and Mr. Ellis said that the distribution of scores is satisfactorily stable. Candidates are assessed objectively by these tests and subjectively by personal interviews held before the results of the tests are known; agreement is usually good, and if there is any disagreement it is the usual practice to reject the candidate.

Training starts with a residential course lasting five weeks, new people being taken on in groups so that a class of ten or so can be formed. There are lectures, written papers and various co-operative activities. Those who complete the course satisfactorily move into different groups in the Company and continue training on 'live' work, each with an experienced member of the staff as mentor until they can stand on their own feet. The Company considers that the contacts made during the training course are of very great value in helping new people to acclimatize themselves to their new environment and to gain confidence.

Mr. H. Devonald (Ferranti, Ltd.) said that the comments he had heard during the interval suggested to him that many in the audience were unfamiliar with the ideas of programming and that he proposed, therefore, instead of further accounts of selection and training methods, to explain the essential points by means of a simple example. He then showed how one constructed a programme to solve a general quadratic equation, reading the coefficients from tape and printing the roots; he used the notation of the *Pegasus* auto-code.

In the brief discussion which closed the meeting, the principal speaker was Dr. A. D. Booth (Birkbeck College, University of London), who emphasized the importance of a constant mathematical awareness in all computing work. He instanced the difficulties one can get into by attempting to solve a partial differential equation by finite-difference methods without having a proper understanding of the mathematics of the process.

J. HOWLETT

PHYSICAL CHEMISTRY OF AEROSOLS

AIRBORNE clouds of small particles, or aerosols, are so widespread in Nature and arise in so many phases of modern industry that their study brings together a large group of physicists, chemists, meteorologists and engineers, each, of course, with his own special interests but all concerned with the generation, dispersion, sampling, counting, sizing, structure, composition, growth and aggregation of small particles. Such a heterogeneous ensemble aggregated in Bristol during September 13–15 to sample twenty-four well-dispersed papers at a discussion arranged by the Faraday Society, under the chairmanship of its president, Sir Harry Melville.

Broadly, there were four main topics for discussion: the nucleation of liquid and solid particles from the vapour phase; the coalescence, growth, evaporation and stabilization of liquid droplets; chemical reactions involving aerosols; and light-scattering by aerosols.

After some introductory remarks by Dr. R. Lessing, the symposium opened with a review by Dr. J. W. Dunning (University of Bristol) of the Volmer–Becker–Doring theory of homogeneous condensation and of various experimental studies of the phenomenon. Dr. Dunning was of the opinion that the results of expansion-chamber experiments had provided acceptable confirmation of the theory, but that condensation in expanding jets provided a more convenient and reliable technique of investigation.

Dr. B. J. Mason (Imperial College of Science and Technology, London) described some recent studies of homogeneous and heterogeneous nucleation of water aerosols involving vapour–liquid, supercooled liquid–solid and vapour–solid transitions. He underlined the limitations of the Volmer theory of homogeneous condensation and did not consider that this had been adequately tested and confirmed by experiment. He next discussed the growth of water droplets

on ions and on hygroscopic nuclei and their relevance to cloud physics. There followed a description of his recent work on heterogeneous and homogeneous nucleation of supercooled water droplets, of the efficiency of natural and artificial ice nuclei in relation to their crystalline and surface structure, and of the formation of ice crystals by direct sublimation from the vapour.

Dr. N. H. Fletcher (University of New England, New South Wales) had applied the Volmer theory of heterogeneous nucleation to calculate the conditions under which ice nuclei would form on a perfect spherical particle. Curves were presented showing the temperatures at which nuclei could be expected to form at the rate of one per second in a water-saturated atmosphere on particles of various radii and forming various angles of contact with the ice embryo. These results were then used to calculate the maximum number of silver iodide nuclei produced from 1 gm. of the material which would be active at various temperatures. In the discussion which followed, doubt was expressed concerning the validity of this treatment, which did not recognize that nucleation of ice on silver iodide and other substances occurs preferentially at surface imperfections.

Phase changes involving salt-vapours were the subject of a paper by Dr. E. R. Buckle (Imperial College of Science and Technology, London), who described his observations of condensation, growth and evaporation of liquid and solid particles of alkali halides in a high-temperature cloud chamber. It appears that for a wide variety of substances (for example, metals, ionic salts, water) condensing and crystallizing homogeneously, the maximum attainable degree of supercooling is almost exactly 15 per cent of the melting temperature. Interesting information on the structure and growth of particles formed by the vaporization of metals in air was provided by the electron- and X-ray diffraction and electron microscopy work of J. Harvey, H. I. Matthews and H. Wilman (Imperial College of Science and Technology, London).

In the final paper bearing on nucleation phenomena, Prof. F. P. Buff (University of Rochester, N.Y.) examined, from the point of view of molecular hydrostatics, the Gibbs theory of capillarity which calculates the higher terms in the asymptotic expansion of the free energy with respect to the geometrical parameters of the system, and provides a criterion for the breakdown of macroscopic thermodynamical concepts for small aggregates of molecules. In Buff's analysis there appear two tensions rather than a single surface free energy, and he argues that Gibbs's formulation is correct only in the (practically important) case when these two tensions are equal.

In the next group of papers, dealing with the growth, evaporation and coalescence of drops, Dr. D. P. Benton (Battersea College of Technology, London) and Dr. G. A. H. Elton (British Baking Industries Research Association, Chorleywood, Herts) presented experimental evidence for coalescence between micron-size water droplets colliding in highly turbulent air being affected by the addition of electrolytes and ionic surface-active agents to the water. The hypothesis is that these modify the structure of the surface electrical double layer, the existence of which is normally a barrier to the coalescence of two colliding drops. Discussion centred on the importance of this for the stability of non-turbulent water fogs where hydrodynamic forces prevent collisions between such small droplets, and on whether an appreciable electrical field would exist outside the surface double layer.

Dr. R. M. Schotland (New York University) had carried out experimental work on the coalescence of falling drops, 200–800μ in diameter, with large liquid hemispherical targets. He claimed that the coalescence mechanism was governed by two dimensionless parameters which, surprisingly, did not include the viscosity of the fluid separating the two liquid surfaces.

Measurements of the growth-rate of water droplets condensing on hygroscopic nuclei as a function of the humidity, temperature and velocity of the surrounding air stream were described by Dr. W. L. Dennis (Chemical Defence Experimental Establishment, Porton Down). Experimental results for drops of 0·3–1·0 mm. diameter agreed within about 20 per cent, with theoretical values derived from the standard equations for the growth of ventilated drops containing dissolved salts.

A remarkable experiment designed to measure the long-range diffusive forces between water drops and solid particles was described in a paper by Prof. P. S. Prokhorov and L. F. Leonov (U.S.S.R. Academy of Sciences, Moscow). The authors claim to have measured repulsive forces of order 10^{-6} dyne between a 1-mm. evaporating water drop and a glass sphere of similar size attached to one arm of a torsion balance, and to have shown that the magnitude of the force varies inversely as the square of the distance between them.

The influence of a foreign surface film on the evaporation of liquid drops, in particular its effect on the condensation coefficient, was discussed theoretically in papers by Prof. B. V. Derjaguin, S. P. Bakanov and I. S. Kurghin (U.S.S.R. Academy of Sciences, Moscow) and by Dr. P. G. Wright (University of St. Andrews). Some measurements on the stabilization of water mists containing droplets of 2–20μ radius by insoluble monolayers were presented by Dr. H. S. Eisner, B. W. Quince and C. Slack (Safety in Mines Research Establishment, Buxton). The addition of about 0·1 per cent of fatty alcohols to the water increased the lifetime of the drops several hundredfold.

The importance of aerosols in catalysing chemical reactions in the atmosphere was brought out in two papers. Dr. R. D. Cadle and Dr. R. C. Robbins (Stanford Research Institute, California) had applied chemical kinetic theory to calculate the rates of heterogeneous chemical reactions involving aerosols, and compared the theory with experimental results for the systems nitrogen + ammonia + sulphuric acid and air + water + nitrogen dioxide + sodium chloride. A. C. Chamberlain, Dr. A. E. J. Eggleton, W. J. Megaw and J. B. Morris (Atomic Energy Research Establishment, Harwell) had investigated the rate at which radioactive iodine vapour in concentrations of less than 1 μgm./m.^{3} was adsorbed on atmospheric nuclei, and demonstrated that this must be allowed for in the design of systems for removing radioactive iodine from reactor shells.

The next three papers, on light scattering by aerosols, provoked a lively discussion. E. Matijević, Prof. M. Kerker and K. F. Schulz (Clarkson College of Technology, New York) described how, using silver chloride aerosols, they had obtained excellent agreement between the polarization ratio from light-scattering measurements and that calculated from

the particle-size distribution and theoretical scattering functions. Since the light-scattering itself was insensitive to particle-size distribution over the range studied (r = 200–800 mμ) the particle size could not be determined from light scattering, but there was an optimum size-range around 55 mμ for which this was possible. Prof. F. K. Gucker and R. L. Rowell (Indiana University) had succeeded in determining the light-scattering diagrams of single aerosol droplets by first charging and suspending them in an electric field, illuminating them with monochromatic light and measuring the light scattered into a photometer over the arc 40–140° from the direction of illumination. Good agreement was obtained with calculations based on the Mie theory. The effect of particle separation on the light-scattering properties of monodispersed spheres was investigated by Prof. S. W. Churchill (University of Michigan), G. C. Clark (Continental Oil Co., Ponka City, Oklahoma) and C. M. Sliepcevich (University of Oklahoma) by measuring the transmission of light through a hydrosol of latex spheres as a function of the particle concentration. According to their measurements, optical interference between the particles is negligible when their average separation exceeds 1·7 particle diameters.

The wide scope of the conference was epitomized in the last two papers, representing meteorology and fuel technology. Dr. C. L. Hosler and Dr. R. E. Hallgren (Pennsylvania State University) described how the aggregation of small ice crystals was affected by their shape, and particularly by the air temperature; Dr. R. H. Essenhigh and Dr. I. Fells (University of Sheffield) presented a mathematical theory of the combustion of liquid and solid aerosols.

The conference enjoyed the generous hospitality of the University of Bristol and the excellent facilities of the new Queen's Building. One's main regret was that the Russian contributors were not there to present and discuss their four papers. B. J. MASON

PHYSICS OF SEMICONDUCTORS

AN international conference on the physics of semiconductors, sponsored by the International Union of Pure and Applied Physics and arranged by the Czechoslovak Academy of Sciences, was held in Prague during August 29–September 2. In recent years this has become a biennial conference, the previous one having been held in Rochester, New York (*Nature*, 108, 1067; 1958), in August 1958, and it is proposed that the next of the series should be in Britain in 1962. The present conference showed clearly that semiconductor physics still represents a very active and indeed an expanding field of research. It is, of course, unwise to judge only by the numbers of papers submitted or by the number of physicists attending the conference; but this gives some indication, and was supported by the fact that new ideas emerged and many new and exciting developments were reported. Indeed, the chief problem which had to be faced by the organizers was that of selecting from the large number of papers submitted. Approximately 265 papers were selected for inclusion in the conference proceedings, of which only about half were actually read. The geographical division of these papers is of some interest; approximately 110 originated in the United States, 40 in the U.S.S.R., 22 in Germany, 20 in Great Britain, 15 in France, 14 in Czechoslovakia, 9 in Poland and 7 in Japan, the remainder being distributed over a large number of participating nations.

The number of physicists attending was much larger than for any previous conference of the series, being nearly 750. As a result, it was necessary to divide the conference into four parallel sessions, three of which were run on the normal pattern of papers followed by discussions and one using *rapporteurs* followed by discussion. In the former, translations into Russian, Czech and English were available, though the English translations were frequently very difficult to follow. The chief drawbacks of the conference arose from its large size, there being many overlapping papers of interest, and it is hoped that future conferences will revert to a smaller and more intimate form.

It is impossible in the space available even to mention all the interesting topics discussed at the conference, and only a few of the highlights can be selected that left the most vivid impressions in the memory. Introductory papers were given by (the late) A. F. Joffe and by W. Shockley. The former stressed the urgent need for a new theoretical approach to the problem of low-mobility semiconductors for which conventional theory based on a nearly perfect crystalline lattice is clearly inapplicable, the mean free path for current carriers being comparable with the lattice spacing. Various discussions based on 'electron hopping' were later given; but it is clear that a lot more work is required before these processes are as well understood as transport phenomena in high-mobility semiconductors. Later in the conference Joffé discussed some of the difficulties associated with the understanding of thermo-electric phenomena in semiconductors. In his introductory paper Shockley discussed a wide variety of phenomena associated with avalanche breakdown in p–n junctions induced by high electric fields, and introduced some new theoretical ideas which might lead to a better understanding of these complex phenomena.

Discussion of transport phenomena again dominated the conference, there being no less than 48 papers submitted on this subject, dealing mostly with silicon and germanium, which remain the basic semiconductors for the study of fundamental phenomena. C. Herring (United States) reviewed developments in the theoretical formulation since the Rochester conference and directed attention to some recent clarification of the difficult problems associated with multi-phonon scattering, and of scattering of carriers in the presence of strong magnetic fields. Two interesting new experiments on transport stood out. The first was described by W. Shockley and K. Hubner (United States) in which an n–p–n structure was used to demonstrate phonon drag on electrons. Some electrons given momentum by an electric field applied in one n-type region pass into the p-type region where they are scattered, producing phonons with a preponderance of momentum in

the same direction; these diffuse into the second n-type region producing an observable e.m.f. through making collisions with electrons. The second experiment, described by T. P. McLean and E. G. S. Paige (Great Britain), consisted of demonstrating by means of measurements of drift mobility at low temperatures an important drag effect of the majority carriers on the minority carriers. A number of papers dealt with the variation of mobility with temperature and it was clear that in spite of the large amount of work carried out in this field there are still aspects of it which are not properly understood. A considerable number of papers dealt with 'hot' electrons produced by strong electric fields.

Perhaps the outstanding new development reported at the conference was the use of the phenomenon of quantum-mechanical tunnelling, discovered by L. Esaki, as a tool for the study of some of the fundamental properties of semiconductors. By a combination of theory with the study of the voltage-current characteristics of 'tunnel' diodes, it was shown by R. N. Hall (United States) that much valuable information may be obtained on the phonon energies associated with the band edges of semiconductors such as germanium, and also possibly on polarons in partially polar semiconductors such as the 3–5 compounds. There was, however, some doubt cast, particularly by E. O. Kane (United States), on some aspects of the interpretation of the experimental data.

The optical properties of semiconductors again gave rise to a considerable number of papers (45 if we include photoconductivity), and, as at Rochester, a discussion of excitons played a prominent part. The experiments of S. Nikitine (France) and of E. F. Gross and his colleagues (U.S.S.R.), particularly with cuprous oxide, seem now to be well understood in terms of the theory of R. J. Elliott (Great Britain), an excellent example of international co-operation. The paper by Gross and his colleagues stressed, however, that there is still no convincing direct evidence for exciton transport though its deduction from theory is beyond doubt. They described various optical effects which they have observed in cuprous oxide and which are a consequence of the fact that an exciton is free to move. (The form of the exciton spectra in indirect transitions in germanium and silicon reported at Rochester are also a consequence of the freedom of the exciton to move.) Optical effects in magnetic fields discussed by B. Lax (United States) and others have continued to provide a powerful tool for the investigation of the band structure of semiconductors. Work on the lattice vibrational spectrum of semiconductors is becoming of first importance, and interesting new results were reported by F. A. Johnson (Great Britain). In particular it is of considerable theoretical interest that the $T.A.$ mode in 3–5 compounds such as indium antimonide has a low energy at the zone edge as for silicon and germanium. Surprising new effects in the absorption associated with the *reststrahl* band in gallium arsenide were also reported by Johnson. Emission of radiation due to inter-band transitions with various phonon combinations reported for silicon by J. R. Haynes, B. Lax and W. F. Flood (United States) and for germanium by Benoît à la Guillaume and O. Parodi (France) threw new light on these processes, especially when taking place by means of an impurity centre, and also provided very accurate values for various energies associated with the phonon spectrum. Further information on the band structure of germanium–silicon alloys and of a number of 3–5 compounds was obtained from the accurate measurement by J. Tauc (Czechoslovakia) of optical reflectivity in the visible and near ultra-violet regions of the spectrum. In particular, fine structure was observed which could be interpreted as due to the spin-orbit splitting of the valance band at the zone edge. At the other extreme, photoconductivity was reported in indium antimonide in a magnetic field at 1·7° K., by R. A. Smith (Great Britain), extending throughout the far infra-red spectrum to wave-lengths beyond 2,000μ.

A considerable number of papers was devoted to the study of ionic crystals and this widened considerably the scope of the conference. In the sessions on new materials, the 3–5 compounds received a good deal of attention, but organic semiconductors were also discussed by C. G. B. Garrett (United States) and an interesting group of defect compounds such as In_2Te_3 by V. P. Zuze and his colleagues (U.S.S.R.).

Perhaps the most mysterious phenomenon discussed without reaching a satisfactory explanation was the occurrence of oscillations in n-type germanium and indium antimonide carrying a current in a longitudinal magnetic field. These appear to be due to plasma effects and were described by P. Aigrain (France) in terms of 'helicons'. Such topics for argument gave spice to what was in any event a very stimulating and thought-provoking conference, which was concluded by an excellent summary of the highlights by J. Tauc. This summary was of the greatest help in preparing this report. The conference papers will be published by the Czechoslovak Academy of Sciences in due course.

R. A. SMITH

ERGONOMICS IN INDUSTRY

A CONFERENCE on ergonomics in industry, organized by the Department of Scientific and Industrial Research, was held in the Connaught Rooms, Great Queen Street, London, during September 27–29. It was attended by more than three hundred representatives of some two hundred industrial firms. The purpose of the conference was to explain the features of ergonomics, to describe some of the ways in which it has already been applied to industry, and to discuss the possible ways in which further use of ergonomic techniques and ideas could be promoted.

Sir Harry Jephcott, chairman of the Council for Scientific and Industrial Research, introducing Lord Hailsham, Minister for Science, who formally opened the conference, said that it was the logical development of a meeting held in March 1959 in Zurich organized by the European Productivity Agency, and entitled "Fitting the Job to the Worker". At Zurich there were three groups, representing manage-

ment, trade unions and research workers. In the present conference, he said, industry had provided by far the largest group, although the trade unions were also represented. The research workers were there to present papers and to answer questions, but it was not primarily a scientific congress with discussion between scientists; the scientists' job was to tell their story, and the industrialists on their side were required to comment and to criticize, to try to find out how far the findings and the ideas of the research workers were useful or potentially useful to the industrialists.

In addition to a series of papers, there was a number of exhibits demonstrating application in particular fields provided by the Medical Research Council, General Post Office and several research associations and centres of the Department of Scientific and Industrial Research, notably the British Iron and Steel Research Association, the British Boot, Shoe and Allied Trades Research Association, the Road Research Laboratory, and the Building Research Station. An exhibit on seating had been arranged by the Physiological, Anatomical, British Psychological and the Ergonomics Research Societies, together with the Furniture Development Council.

The papers at the conference were presented under the headings of "What Ergonomics Means", "The Place of Ergonomics in Industry", "Ergonomics and Production", "Ergonomics in the Post Office and in the Steel Industry", "Ergonomics and Products" and the "Future of Ergonomics".

The term 'ergonomics' means the study of the laws of work, and more specifically the study of the relationships between the worker and his environment. Such a study embraces a very wide field, and involves research derived mainly from physiological, psychological and anatomical studies. Up to the present, the Armed Forces have provided the chief field of study, although the term 'personnel research' has been used to describe the work. Although many of the problems affecting the worker can be described as primarily physiological, such as extremes of heat or cold, or psychological (namely, the presentation of information), or anatomical (namely, the anthropometric data required to design a work space), there are very few cases in which a single-discipline study is adequate. This means that a multi-disciplinary approach is necessary, and the techniques and methods required to develop such an approach are one of the basic problems of ergonomics. However, the problem does not end at this point, since it is clear that engineering aspects are equally important. Without a knowledge of the engineering problems involved, a solution can be put forward which is either impracticable or exceedingly expensive. At the conference a number of speakers, both in presenting papers and in discussions following papers, emphasized the need to view the problem and its proposed solution in the total setting of industry, that is, to include the worker relationship and trade union views, management and economic aspects. It was generally agreed that there is a need to bring biology into industry, but this requires that a proportion of engineers, especially those concerned with the design of equipment, and production engineers, should have some undergraduate instruction in biology. Equally, biologists require a knowledge and understanding of the complex nature of industrial problems.

Dr. A. Y. Wisner, who is head of the Physiological Section of the Renault Factory in France, illustrated many of these points. He has had to become familiar with the problems of design of motor-cars, with the engineering and production difficulties involved, as well as the economic aspects. He regards himself as an adviser who must not overlook the fact that important and decisive design or economic consideration must have their place in considering requirements for the comfort and safety of the driver. Furthermore, unless the biologist is involved at the beginning of a design study, it is unlikely that he can make a useful contribution, as even apparently small alterations in, for example, the position and angling of pedals can involve expensive re-tooling and extensive re-design.

The importance of engineering was also brought out in a paper by Mr. W. T. Singleton, who was until recently head of the Ergonomics Department of the British Boot, Shoe and Allied Trades Research Association. The sewing machines used in the shoe industry have a simple mechanism for starting and stopping, using a clutch and a continuously rotating fly-wheel. This type has been in use for fifty years or more; but details of the operator's work have changed, becoming in general more complicated. Experiments showed that this form of power transmission is not suitable for producing controlled speeds other than the maximum, and with the more complex tasks the machinists could not always stitch at maximum speed. This apparent paradox was solved by the skill of the machinist in achieving slower than maximum speeds by flicking the clutch on and off at about 3 cycles/sec. The skill required to do this to produce a particular speed was considerable and took time to learn. A variable-speed power transmitter was required, and this needed considerable engineering development before it could be produced in large numbers. A laboratory model was made and a comparison made with the standard machine. The results showed that operators with no machinery experience performed better using the variable-speed control than did skilled machinists using the orthodox control. In the factory there was an improvement in speed of 10–15 per cent. This information made it possible to calculate the financial benefit of the new system, an essential factor, as there are about 100,000 machines of this type in Britain. The improvement was clearly worth while, and hence it was considered justifiable to embark on the engineering study needed to produce a new machine.

Three industries in which ergonomics already plays a considerable part are the General Post Office, London Transport and the steel industry. Papers were given describing the effects of heat in a steel mill, essentially radiant heat which, as Dr. R. F. Hellon said, cannot be cured by ventilation, as one cannot blow away radiation. There are three ways in which a severe heat situation can be combated: by reducing the level of work so that heat-loss balances heat-production, or by working at a normal rate and taking frequent rests to cool off, or by reducing heat stress so that normal working is not impeded. The last is clearly the desirable method, but the usual practice in industry is to combine the first and second. Dr. Hellon then outlined possible ways of relieving the heat stress.

Dr. L. G. Norman described the way in which the cab of the new 'Route Master' bus has been designed by a team which included medical officers, trade

unionists and engineers. Others joined the team at different times to advise on seating, ventilation, position of controls and the muscular forces required to operate them. Among the problems was the lack of anthropometric data relating to bus drivers, so calculations had to be based on published measurements of National Service recruits. The need to increase the range of anthropometric data was stressed by other speakers, including Dr. J. S. Weiner, assistant director of the Medical Research Council's Unit on Climate and Working Efficiency.

The discussion after the papers was in general lively, and there were many useful criticisms. The now familiar problem of communication was frequently mentioned as one of the reasons for the delay in applying biological research to industry. The biologists were advised that industry must not be led to expect that solutions to all its problems are within immediate grasp, and the industrialist was advised that research workers are not good salesmen, but that did not mean they did not have valuable services to offer.

There is, therefore, a strong probability that there will be a considerable demand from industry for biologists and biological advice. The difficulty will be in supply. O. G. EDHOLM

ULTRACENTRIFUGATION OF BIOLOGICAL MACROMOLECULES

THERE were about a hundred participants from several countries at the informal meeting on ultracentrifugation organized on behalf of the Faraday Society at Birmingham during September 14–15. Prof. K. O. Pedersen (Uppsala) gave a stimulating historical introduction. Papers by Dr. J. M. Creeth (Lister Institute, London) and Dr. H. G. Elias (Zurich) considered thermodynamical aspects of the sedimentation of multicomponent systems, while Dr. M. Gehatia (Frankfurt am Main) discussed various methods of evaluating S and D constants from the shape of the gradient curve of ultracentrifugation. Dr. G. A. Gilbert (Birmingham) described his theory concerning the analysis of moving boundaries in reversibly aggregating systems; examples of its application being provided in papers by Drs. S. N. Timasheff and R. Townend (Philadelphia) and by Mr. K. A. Cammack (Medical Research Establishment, Porton). A paper by Drs. A. J. Rowe and Dr. P. Johnson (Cambridge) considered the interaction of actin and myosin by ultracentrifugal studies.

Dr. P. A. Charlwood (Medical Research Council, Mill Hill) reviewed trends in the determination of molecular weights of macromolecules from transient state measurements in the ultracentrifuge and Dr. H. G. Elias (Zurich) discussed the various methods of determining the experimental values used in the Archibald expression. Dr. G. Träxler (Munich) considered various ways of using the analytical ultracentrifuge in the measurement of diffusion constants of macromolecules. Papers on the sedimentation of charged macromolecules were presented by Prof. K. O. Pedersen and Dr. R. G. Wallis (Medical Research Establishment, Porton).

A new recording device for the ultra-violet absorption was discussed by Drs. J. B. Th'Aten and A. Schouten (Rijswijk, Netherlands), while Dr. I. Wiedmann (Basle) described a new schlieren optical system. Drs. P. A. Bianchi and K. V. Shooter (Chester Beatty Institute, London) considered the study of the sedimentation characteristics of deoxyribonucleic acid by the ultra-violet system.

Application of zone-centrifugation to the analysis of human serum proteins was described by Dr. D. R. Stanworth, Prof. J. R. Squire and Mr. K. James (Birmingham). Drs. P. Johnson and A. Albert discussed the sedimentation characteristics of human serum macroglobulins.

A suggestion by Prof. K. O. Pedersen that sedimentation coefficients should be referred to 25° C. rather than 20° C., as is becoming the practice in the United States, evoked considerable discussion, but no final decision was taken.

Prof. K. O. Pedersen, Dr. A. S. McFarlane (Medical Research Council, Mill Hill) and Dr. R. A. Kekwick acted as chairmen and Dr. P. Johnson summed-up at the end of the proceedings. D. R. STANWORTH

MIGRATION OF MARINE ORGANISMS

A LATIN American symposium on migration of marine organisms was held at Guayaquil, Ecuador, from June 27 until July 1. It was organized jointly by the Unesco Science Co-operation Office for Latin America and the University of Guayaquil.

It was the fifth of the series of meetings on marine sciences which the Office has held since its foundation in 1949. The previous meetings had, like the Guayaquil one, the double character of symposium and working-party session. They were held at Concepción, Chile, in 1954; São Paulo, Brazil, in 1955; Montemar, Chile, in 1956; and Montevideo in 1957.

Dr. Enrique Rioja (Mexico) was elected chairman of the symposium and Dr. Hugo Ferrando (Uruguay) acted as secretary. Thirteen marine scientists participated, from the following countries: Argentina, Brazil, Chile, Cuba, Ecuador, Mexico, Peru, Uruguay. The Unesco Science Co-operation Office for Latin America was represented by Dr. Angel Establier.

The programme of the meeting was as follows: (1) migration of marine organisms, namely (*a*) fish, (*b*) invertebrates, (*c*) cephalopods, (*d*) birds, (*e*) other vertebrates; (2) study of environmental factors causing migration, (*a*) oceanographic factors, (*b*) biological factors; (3) standardization of methods for studying migratory phenomena, with the view of comparing results; (4) establishment of regional programmes for work on migration of aquatic populations; (5) general discussion of other problems related to migration of marine organisms.

At the conclusion of the symposium, six recommendations were unanimously approved by the participants. First, considering that the study of the migration of marine organisms by its very nature requires a joint effort on the part of the countries concerned, regional action was recommended. The following delimitation of problems common to a number of countries was made with a view to their being undertaken regionally: Argentina, Brazil and Uruguay: Thunnidae, Scombridae, Clupeidae (*Sardinella* sp.), Galeorhinidae (*Galeorhinus vitaminicus*) and Mugilidae (*Mugil* sp.); Chile and Argentina: Merluccidae (*Merluccius* sp.), Decapoda (Macrura—"Langostinos"—Shrimps and "Langosta" de Juan Fernández); Peru and Chile: Thunnidae (*Neothunnus macropterus*), Engraulidae (*Engraulis* sp.), Scombroidae (*Sarda* sp.) and Decapoda (*Munida* sp.); Peru, Ecuador and Colombia: Thunnidae (*Katsuwonus* sp.) (*Neothunnus macropterus*), Decapoda (Macrura—"Langostinos"); Mexico, Caribbean and coast of Venezuela: Thunnidae (*Katsuwonus* sp., *Thunnus* sp.), Centropomidae (*Centropomus* sp.), Decapoda (Macrura—*Panulirus* sp. and Penaeidae–*Penaens* sp.).

Secondly, it was recommended that information be exchanged between Argentina and Chile covering research results and methods used in work on the principal species of *Merluccius*. Thirdly, marking trials should be held in conjunction with studies on the biological cycle of the species (growth, reproduction, alimentation, etc.) with the view of relating migration and the different phases of life of individuals. Similarly, the importance of the study of environmental conditions emphasized at the meeting of the Unesco Marine Sciences Working Party, held at Montevideo during May 22–24, 1957, was underlined.

In view of the importance of movement and mixture of different bodies of water, it was expressly recommended that Argentina, Brazil and Uruguay should study the northern and southern limits and fluctuations respectively of subantarctic and subtropical waters and also the origin of the water of the coastal region. It was hoped that similar work might be undertaken for the south-east Pacific area in the fairly near future.

Unesco was also asked to interest the Governments of Latin America in helping this type of scientific work, which is an indispensable basis for a proper knowledge of the renewable resources of the sea. Finally, it was recommended that the next marine sciences meeting to be organized by the Unesco Latin American Science Co-operation Office should be divided into two sections: 'abiotic oceanography' and 'marine biology'.

ABSOLUTE DATING OF THE MIDDLE ORDOVICIAN

By PROF. J. A. S. ADAMS and J. K. OSMOND*
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AND
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A NUMBER of recent papers have amply emphasized the need for absolute dating of geological samples which meet two essential requirements: (1) occupy an unambiguous position in the classical stratigraphic column; (2) contain unaltered mineral conducive to age determination by the well-established stable-isotope methods.

This communication presents additional results from our work[1,2] on the dating of the Middle Ordovician and discusses the factors which must be considered when sufficient data become available to consider revision of existing geological time-scales.

Several years ago, G. Hamill[3] made a petrographic and geochemical study of bentonites, particularly of the fine, euhedral zircon found in low concentrations (one part in 20,000–40,000). This work and the results of further experiments have consistently led to the belief that the zircon was indigenous to the volcanic ash falls which gave rise to the bentonite beds. The bentonites occur as beds in fossiliferous marine deposits, and hence their positions in the stratigraphic column are usually unambiguous, so that zircons in bentonite clearly offer an excellent possibility of ascribing absolute ages to the geological time-sequence of marine deposits.

The bentonites also contain biotite, generally in greater concentration than the zircon. In 1958 we published preliminary age determinations by the rubidium–strontium method on biotites of Devonian and Ordovician age which were later cited by K. I. Mayne, R. St. J. Lambert, and D. York[4] in an article in which they proposed a much more radical revision of the Holmes time-scale than was suggested by our results. In our original publication, we stressed the fact that these measurements were of a preliminary nature and that the experimental error could probably be reduced by a study of the zircon in bentonites.

During the past year, samples of pure zircon and of zircon with small amounts of monazite and apatite, in quantities of about 1 gm., were obtained from several bentonites. Zircons from four bentonites were chosen for age determination because they occurred in relatively high concentration, and because the stratigraphic position of occurrence was well established[3].

Microscopic examination showed that the zircons were euhedral, and none exhibited rounding of the crystal edges or overgrowths that would be inconsistent with a pyroclastic origin. The zircons were commonly associated with subhedral biotite flakes, euhedral apatite, sanidine and euhedral quartz. The appearance of the quartz was consistent with a high-temperature morphology (positive and negative rhombohedra with little or no development of prism

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faces). In no case was a mineral (for example, garnet or kyanite) observed that was inconsistent with a pyroclastic origin.

The results of isotope measurements on lead and the amount of uranium in the zircon from the Ordovician bentonites are shown in Table 1.

Table 1

Sample number, location, and stratigraphic position	Concentration* (10^{-6}gm /gm.) Pb	U	Lead-isotopic composition (per cent) 204	206	207	208
GH-22 Alexandria, Tenn., Carters Limestone, Stones River group	34·5	320	0·387	64·680	9 585	25 347
GH-7 Vonore, Tenn, Bays Formation	29 7	314	0 277	70 762	8·239	20 722
GH-24 Dowelltown, Tenn., Carters Limestone, Stones River group	26·7	317	0 157	75·317	6·855	17 670
GH-17 Nashville, Tenn., Carters Limestone, Stones River group	27·2	335	0 219	72·220	7 396	20 165

* Lead and uranium by isotopic dilution

In all cases, the amount of common lead present as indicated by the presence of lead-204 was more than 11·5 per cent of the total. 1 gm. of zircon was used for each experiment, and repeated experiments have shown contamination by common lead in the laboratory to be consistently less than 0·8 μgm. All the zircons contained more than 26 μgm. lead, and hence the experimental contamination is thought to have contributed about one quarter of the common lead observed to be present in sample *GH*-24 and a lower fraction of the common lead in the other experiments. It is reasonable to assume that at least the major portion of the common lead observed was incorporated in the zircon at its time of crystallization.

On the basis of isotope data for oceanic lead by T. J. Chow and C. C. Patterson[5] and with computation in the way described by C. B. Collins, R. D. Russell, and R. M. Farquhar[6] for the rate of change of the lead isotopes with time, we estimate average ratios of the isotopes of common lead in Middle Ordovician time as:

204	206	207	208
1	18·260	15·675	38·490

Lead in sanidine present in the bentonites may ultimately yield more pertinent information than this approximation of the actual isotopic composition of common lead in these zircons.

The above estimates, together with the isotopic data of Table 1, were used as described by A. O. Nier, R. W. Thomson, and B. F. Murphey[7] to obtain the ages shown in Table 2. Radioactive decay constants of $1·537 \times 10^{-10}$ and $9·72 \times 10^{-10}$ yr.$^{-1}$ were used for uranium-238 and uranium-235 respectively.

Table 2. Isotopic Ages in Million Years

Sample number	Uranium-238/lead-206	Uranium-235/lead-207
GH-22	452 ± 10	483 ± 20
GH-7	453 ± 10	471 ± 20
GH-24	446 ± 10	478 ± 20
GH-17	438 ± 10	452 ± 20

Subtraction of the isotopes of common lead from the measured isotope concentrations involves 4–11 per cent of the total 206 isotope and 36–64 per cent of the 207 isotope. The uranium-238/lead-206 ages are consequently less affected by the assumed common lead isotope ratios than are the uranium-235/lead-207 ages. The discordance in ages based on uranium-238 and on uranium-235 may be accountable in this way, but may represent one of the forms of discordancy discussed by G. W. Wetherill[8].

As is common, when the uranium-238/lead-206 age is not in close agreement with the uranium-235/lead-207 age, the lead-207/lead-206 age is still more discordant. In the absence of more accurate information on the composition of common lead in these zircons, we regard the uranium-238/lead-206 age as the best approximation of the mineral age.

Recently, H. Faul and G. R. Tilton carried out age measurements on zircon and biotite from a bentonite in Alabama beds which were stratigraphically very close to those of the Tennessee samples reported here. We are greatly indebted to them for permission to include their data (Table 3) in this article. The uranium-238/lead-206 age computed by them is within 0·5 per cent of the average of that for the Tennessee samples. In all respects their measurements are, within experimental limits, corroborative.

Table 3. Age Determinations on Zircon and Biotite from Carters Limestone Bentonite, Alabama

Zircon*

Concentrations in 10^{-6} gm./gm.

U-238	U-235	Pb-206	Radiogenic lead Pb-207	Pb-208
313	2 24	19 24	1·124	3·103

Isotopic composition of lead

	Pb-204	Pb-206	Pb-207	Pb-208
Observed	1 000	391	37·27	97 57
Correct for blank	1 000	667·3	53·35	141·7

Isotopic ages in m.y.

U-238/Pb-206	U-235/Pb-207	Pb-207/Pb-206
446	464	550 (± 40)

Biotite†

Rb-87/Sr-87 age is 475 ± 40 m y. (Rb-87 = 86·0, Rb-85 = $217·8 \times 10^{-6}$ gm./gm.; radiogenic Sr-87 = $0 568 \times 10^{-6}$ gm./gm. with radiogenic Sr-87/total Sr-87 = 0·149 and half-life = $5·0 \times 10^{10}$ years).

Biotite‡

Age in m.y.	K per cent§	Radiogenic¶ A-40	Radiogenic Ar-40 / Total Ar-40	Locality
420	6·94	0·232	0·81	Pyne Mine
		0 233	0·90	
	6·23	0 209	0·77	Wenonah No. 8 Mine
		0 207	0·85	

* G. R. Tilton (private communication); thorium determination failed; the corrections and calculations are as made by George R. Tilton, Geophysical Laboratory, Carnegie Institution of Washington.

† G. R. Tilton (private communication).

‡ H. Faul (private communication).

§ Potassium determined on Perkin-Elmer flame photometer by W. W. Brannock and P. L. D. Elmore, U.S. Geological Survey.

¶ In 10^{-6} gm./gm. as determined by isotope dilution by H. Faul and H. H. Thomas, U.S. Geological Survey.

Shortly after the preliminary rubidium-87/strontium-87 ages referred to previously were published in 1958[1], several authors made use of these and other data to interpolate and extrapolate to other geological periods in an effort to establish substitutes for the Holmes scale. The premature proliferation of various time-scales is unfortunate, because it confuses the many persons who are interested in the results, but who are not conversant enough with all the geological and experimental details to choose among the various scales or to reject them all. These proposed scales all assign ages to the beginning of each geological period.

Samples suitable for age measurement seldom occur at the boundaries of the geological periods, and interpolations of the experimental data to yield period dates involves the additional uncertainty of estimating the rate of sedimentation in the various periods and localities. As more data become available, interpolation of boundary ages of the geological series will become more reliable Of the data discussed here, we

regard the average of the consistent uranium-238/lead-206 ages (447 ± 10 m.y.) as the most reliable for the Middle Ordovician (Stones River and Bays formation) time in Tennessee and Alabama, for both experimental and stratigraphical reasons.

We are of the opinion that only after many measurements have been conducted on samples from the various geological periods and have proved to be consistent will it be prudent to try to devise a new geological age-scale.

Two of us (J. A. S. A. and J. K. O.) received financial support from the Robert A. Welch Foundation in all the geological and mineralogical aspects of this work. One of us (J. K. O.) received financial support from the Petroleum Research Fund of the American Chemical Society. We repeat our indebtedness to Drs. H. Faul and G. R. Tilton for their permission to publish their results in this article.

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OBSERVATIONS OF EARTH–IONOSPHERE CAVITY RESONANCES

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IN 1952, Schumann[1,2] published a detailed description of the resonant modes to be expected for the concentric spherical cavity bounded by the Earth and the lower region of the ionosphere. For such a cavity with perfectly conducting walls, the resonant frequencies should obey the relation:

$$f_n = f_1\sqrt{\left\{\frac{n(n+1)}{2}\right\}} \qquad (1)$$

with a fundamental-mode frequency $f_1 = 10{\cdot}6$ c./s. to be expected for a cavity the size of the Earth.

The ionosphere is, however, a rather poor conductor, and it is furthermore quite difficult to estimate the losses to be expected for oscillations of these extremely low frequencies, because of the tremendously varying ionospheric conditions of electron density and collision frequency in the regions penetrated by the field[3]. These losses result in a relatively low value of Q (the ratio of resonant frequency to frequency separation of the half-power points) for the mode, and the question has been raised as to whether it is indeed so low that it would be difficult to measure the spectrum at all. Another effect of the low value of Q is a shift in the resonant frequency. A general result in the theory of resonant cavities[4] gives:

$$f = f_0\sqrt{\left(1 - \frac{1}{Q}\right)} \qquad (2)$$

as an approximation to the peak frequency f of a mode which would have a resonant frequency f_0 in a perfectly conducting cavity. This expression would no longer be accurate for the very low values of Q to be expected in the Earth–ionosphere cavity, but should serve to indicate that the actual peak frequency of the fundamental mode may be considerably lower than 10·6 c./s.

It may be assumed that the cavity is continually being excited by lightning strokes all over the world. To the extent that radio noise at these frequencies is a result of such excitation, the power spectrum of the noise should show peaks with frequencies and values of Q corresponding to the various resonant modes. There has been some indication that variations in the vertical electric field below about 20 c./s. are largely local in origin[5] (for example, moving clouds, pollution of air by combustion products), which would further inhibit the observation of cavity effects.

An earlier attempt[6] to observe cavity effects of modes of higher order with frequencies greater than 60 c./s. produced some suggestive results, but they were not statistically significant. It was therefore decided, despite the problems just mentioned, to attempt to observe the cavity effects on the spectrum of radio noise at and just above the fundamental frequency.

As in the previous attempt[6], it was planned to produce the final results by simulated spectrum analysis on a digital computer. For this and other reasons, it was decided to record the raw data digitally in such a format that the original tape recorded at the field site could be read directly into the Lincoln Laboratory IBM 709 computer for processing.

The equipment used to record the radio noise was assembled at a field site in Ipswich, Mass. A block diagram is shown in Fig. 1. The (receiving) antenna was a 120-ft. metal tower which, of course, responded to variations in the vertical electric field. The signal was passed through a low-pass filter which cut off at about 75 kc./s. to prevent strong radio-frequency fields from overloading succeeding stages. A cathode follower was then used to reproduce the signal at a lower impedance-level. This was followed by an audio filter which cut off at about 35 c./s. and was designed to have a minimum at 60 c./s. to minimize interference by power lines (none was ever observed following this filter). The filtered signal was then fed into an audio amplifier. All this equipment was powered by batteries and was located directly at the base of the antenna. The frequency response of the system, measured by replacing the antenna with a signal generator of like impedance, is shown in Fig.

The signal was conducted into the building which contained the recording equipment through an insulated shielded cable. In order to eliminate ground return currents which would result from the small potential difference between the ground at the antenna and the ground at the building, an amplifier with unity

* Operated with support from the U.S. Army, Navy and Air Force.

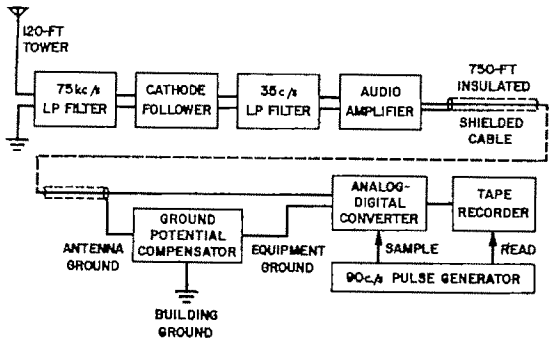

Fig. 1. Recording equipment

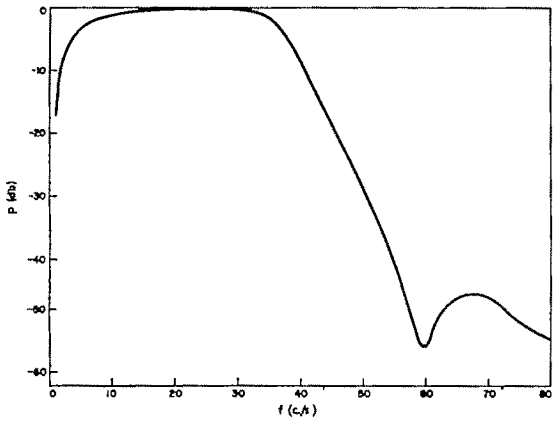

Fig. 2. Frequency response of recording equipment

gain was used to sense this potential difference and maintain the recording equipment ground at the potential of the antenna ground. Finally, the signal was sampled 90 times per sec. and the voltage was then converted to a six-bit number, that is, one of 64 levels, and recorded on IBM magnetic tape. Since the highest effective frequency in the signal was less than 45 c./s., no information is lost in the sampling process except for the small quantization error.

The day which was chosen for making these observations, June 27–28, 1960, appeared to be most favourable for minimizing undesired effects. The sky was absolutely clear, the humidity was low (for New England), and the air was fairly calm (straight, sharp jet-vapour trails indicated that this was also true at higher levels). Atmospheric interference in the high-frequency band seemed quite low for the summer-time.

Recordings of the extremely low-frequency radio noise of duration slightly longer than 12 min. were taken on an average once every 2 hr. around the clock for the day indicated. Also recorded for test purposes were sine waves of various frequencies in the pass-band, produced by an oscillator which was substituted on those occasions for the antenna.

During parts of the recording periods the analogue signal that was presented to the digital apparatus was also recorded on paper tape, and it was always monitored on an oscilloscope. A typical sample of the recorded noise is given in Fig. 3. The only exceptions to this apparently random wave-form were large impulses (which corresponded to nearby lightning disturbances heard on high-frequency) which saturated the pen recorder and the digital recorder for periods of up to a second. These increased in frequency of occurrence and intensity during the night and diminished again the next day, although not quite to the level of the previous day. Apart from these bursts, no wave-forms different in character from that shown in Fig. 3 were ever seen. (This contrasts with findings of Schumann and Konig[7,8], who have reported observing signals of sinusoidal character with frequencies near 8 or 9 c./s. on similar paper recordings. Some differences in the shape of their pass-band (principally due to a notch filter they used to eliminate 16⅔ c./s. interference) may help explain the disparity in observed wave-forms.)

The filtered radio noise signal was compared on an oscilloscope with a calibrated 10 c./s. oscillator, and the root mean square noise voltage was estimated to be about 20 mV.

A programme was written for the IBM 709 computer (largely adapted from the one written for the earlier attempt[6]), which read in a 12-min. block of noise signal from the original tape and, in effect, passed it through a 1 c./s. filter, then squared and integrated the output to give the power in that 1 c./s. band. This was done for all integral frequencies between 5 and 34 c./s. and the results were multiplied by a correction factor to compensate for the system response of Fig. 2.

In mathematical terms, the computer simulated a narrow-band filter the impulse response of which is given by:

$$h(f,t) = \sin \omega t \qquad 0 < t < 1 \qquad (3)$$
$$= 0 \qquad \text{elsewhere}$$

where $\omega = 2\pi f$ and f is an integral frequency between 5 and 34 c./s. The frequency response of this filter is given by:

$$\left| H(f') \right|^2 = \frac{\sin^2 \pi (f' - f)}{\pi^2 (f' - f)^2} \qquad (4)$$

and is shown in Fig. 4 as the solid curve. The peak at the centre would be at the frequency f, and the nulls occur at all other integral frequencies. If we

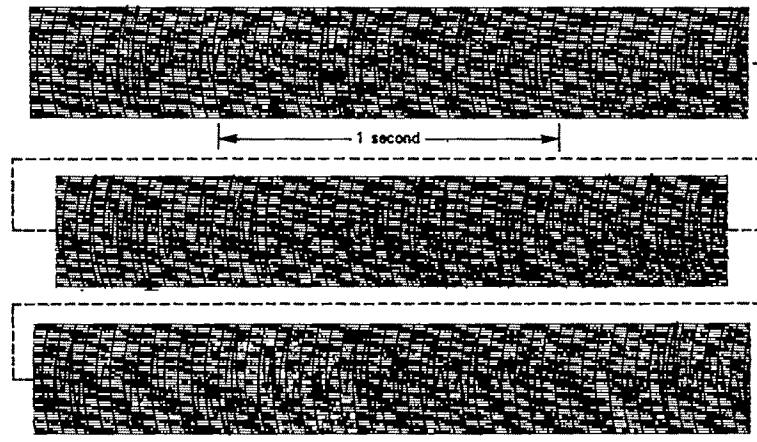

Fig. 3. Sample of recorded extremely low-frequency radio noise

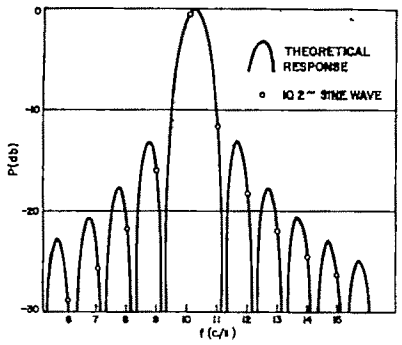

Fig. 4. Theoretical frequency response (solid curve) of 1 c./s. filter used in processing. Points are results of processing a sine wave of about 10·2 c./s.

call the input signal $x(t)$, then the output of this filter is :

$$y(f,t) = \int_{t-1}^{t} x(\tau) \sin \omega(t - \tau) d\tau \qquad (5)$$

$$= \left(\int_{t-1}^{t} x(\tau) \cos \omega\tau d\tau\right) \sin \omega t - \left(\int_{t-1}^{t} x(\tau) \sin \omega\tau d\tau\right) \cos \omega t$$

The power in this band is then estimated from :

$$P(f) = \int_{0}^{T} y^2(f,t) dt \qquad (6)$$

where $T = 720$ sec. The computer performs all of the operations indicated on the input tape, substituting sums over the sample points for integrals.

The integration process just outlined reduces the fluctuations in the estimate of power $P(f)$, which is a random variable derived from the sample function $x(t)$, so that smaller differences in mean power may be discerned. By a calculation analogous to that presented in ref. 6, it can be shown that the standard deviation $\sigma(P)$ is given by :

$$\frac{\sigma(P)}{E(P)} = \frac{2}{\sqrt{3TW}} \qquad (7)$$

where $E(P)$ (the quantity we seek) is the mean value of P, W is the 1 c./s. band-width of the filter, and T is the integration time of 720 sec. (This equation was erroneously given as being smaller by a factor $\sqrt{2}$ in ref. 6.) It can therefore be expected that random fluctuations slightly larger than 4 per cent of the mean power ($\pm$ 0·18 db.) will appear in the computed spectra, and considerably larger deviations may be accepted as significant spectral structure.

In order to test the system, a sine-wave signal of about 10·2 c./s. was recorded and processed. The results are the points shown in Fig. 4. (More accurately, each point is the result of centring the filter on the frequency indicated below it and finding the response at 10 2 c./s. Due, however, to the symmetry between f and f' in equation (4), the points should all lie on the response curve centred at 10·2 c./s.) It can be seen that the system operates as expected. A further result of these tests indicates that the recorded radio noise is nearly 30 db. above the system noise, so that the latter should not be a consideration in the results.

Ten records of noise were obtained which could be properly processed. Two representative spectra resulting from this processing are shown in Fig. 5. The power, as stated earlier, is computed only at integral frequencies. These points are joined by straight-line segments for ease in reading them, not to suggest the actual shape of the spectrum.) The records were taken around 4.20 p.m. E.S.T. and 3.50 a.m. E.S.T. The mode structure of these spectra is immediately obvious (as it is on all the remaining records processed), with the power differences being much larger than the predicted statistical fluctuations. The only systematic difference that could be observed among the records is the behaviour below the lowest mode frequency. As already observed, the night-time records were characterized by more frequent and stronger lightning bursts. These would saturate the recorder for periods of a fraction of a second to a second, and would naturally appear as strong enhancements of the spectrum in the region of a few cycles. The very large enhancement observed in Fig. 5 (broken line) at 5 c./s. (and undoubtedly down to about 1 c./s.) is representative of the regular increase and subsequent decrease in close correspondence to the previously noted lightning activity.

Fig. 6 is a composite of all ten processed records. It therefore represents two hours of integration, although the individual 12-min. periods are taken from all parts of the day rather than continuously. The random fluctuations are smoothed out even further, and in this case the points are joined by a smooth curve that is an attempt to suggest the probable shape of the spectrum. No attempt is made to follow the points below the dominant mode where the behaviour is systematically variable, as discussed in the preceding paragraph, and where the sum therefore does not constitute further smoothing.

The resultant spectrum is smooth enough to be read to $\pm$ 0·1 c./s. on the original curve, and the peak frequencies were determined for each of the five modes in the range. These are listed in Table 1. Estimates can also be made of the Q of the cavity for each of the modes. The fundamental mode has $Q = 4$, and the value increases regularly (although it is difficult to obtain accurate estimates) until for the fifth mode, $Q \approx 6$.

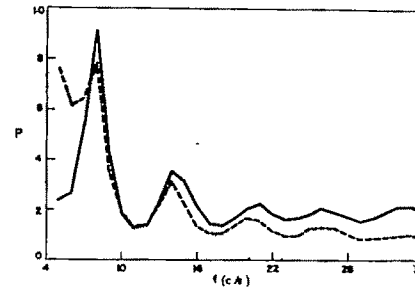

Fig. 5. Typical spectra of recorded noise (scale of P is linear). Full line, day-time record ; broken line, night-time record

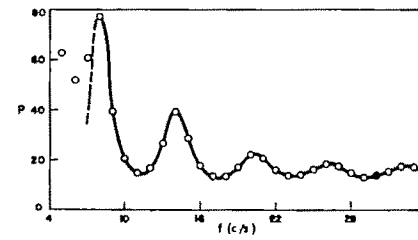

Fig. 6. Composite spectrum of ten 12-min. records of extremely low-frequency noise (scale of P is linear)

Table 1

n	f_n (c/s.)	$\sqrt{\left\{\frac{2}{n(n+1)}\right\}} \times f_n$ (c./s.)
1	7 8	7·8
2	14·1	8 14
3	20 3	8·29
4	26·4	8 35
5	32 5	8 39

Note added in proof. The frequency 7·8 c./s. for the first peak was actually obtained from a more detailed examination of the results, carried out after the submission of this article, in which the simulated filters had a bandwidth of 1/3 c./s. and were separated in frequency by that amount. The points in Fig. 6 are insufficient to determine the first peak to within 0 1 c./s., and an earlier estimate of 8·0 c./s. was obtained from some of the individual records relatively free of corrupting impulse noise at the lower frequencies.

Except for the low value of f_1, the results seem to be quite consistent with the predicted behaviour. The frequency progression is about what is expected from equation (1). The quantity $\sqrt{\left\{\frac{2}{n(n+1)}\right\}} \times f_n$, which from (1) should be f_1, is also given in Table 1. As can be seen, these values are close to the fundamental frequency but tend systematically to increase with n. This is just the behaviour to be expected, since Q is also increasing with n and the values f_n are therefore decreased proportionately less at the higher frequencies.

It is of interest to recall a marginal observation made in the earlier work[5] but rejected because of insufficient supporting evidence. There seemed to be some indication there of modes at frequencies of about 63, 69, 75, 81 and 87 c./s. with $Q \approx 10$. These values extrapolated back to a fundamental frequency of about 8·5 c./s. In the light of the present (stronger) evidence, it seems quite probable that the earlier result did in fact constitute an observation of the continuation of the series of modes reported here.

An incidental result may be noted in connexion with the remarks on the nature of radio noise below 20 c./s. From the depth of the valley below the lowest mode on some of the records, for example, Fig. 5 (full line), it seems likely that, at least under the conditions of these measurements, the noise due to local charge fluctuations in the air does not become dominant until below 5 c./s.

In conclusion, it should be mentioned that while these observations seem to confirm the stable, round-the-clock structure of the Earth-ionosphere cavity modes, they were, after all, made all in one day at one place. Since the properties of the modes (peak frequency and Q) depend on the nature of the lower ionosphere, it is easily conceivable that there are effects that were missed in these observations. There is certainly room for further work, both experimental and theoretical, to obtain a better understanding of this phenomenon.

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THEORETICAL LIMITING THICKNESSES FOR SINGLE SCATTERING IN ELECTRON MICROSCOPY

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THE quantitative aspects of electron microscopy have been examined recently by a number of authors[1-7] and it is generally agreed that accurate measurements of mass-thickness, that is, the product of thickness and density of the specimen, can be made only on specimens for which the contrast in the electron-microscope image is proportional to the mass-thickness (w). (Contrast is here defined as $\ln(I_0/I)$, where I_0 and I are respectively the intensities of the electron beam incident on the specimen and that received at the image plane.) The maximum limit ($w_{\text{lim.}}$) of the range within which $\ln(I_0/I)$ is proportional to w is therefore of importance, since its value for given operating conditions of the electron microscope governs the choice of specimens suitable for quantitative work.

Values of $w_{\text{lim.}}$ have been deduced on theoretical grounds, based essentially on the point of transition from single to multiple electron scattering as the mass-thickness of a specimen increases. Experimental results[1,8-11] produced by measurements on the variation of image-contrast with w show that for a variety of operating conditions values of $\ln(I_0/I)$ up to 3 and values of w in the range 0–100 μgm. cm.$^{-2}$ are within the range where the contrast is directly proportional to the mass-thickness of the specimen.

Theoretically the situation is rather confused. At the present time, two theories of electron scattering are in current use, due to Leisegang[12] and Lenz[13] respectively. Leisegang's theory is restricted to a consideration of elastic scattering only, while Lenz treats both elastic and inelastic processes. The two elastic scattering theories are fundamentally the same, since they are based on the same quantum-mechanical treatment (for example, Bohm[14]). Using these two theories of scattering, essentially three different theoretical definitions of $w_{\text{lim.}}$ have been proposed, giving values of the limiting thickness which differ considerably from one another both in magnitude and in physical implication.

It is the purpose of this article to point out the discrepancy in magnitude between the experimental results and the theoretical estimates of $w_{\text{lim.}}$, to review the definitions of $w_{\text{lim.}}$ and to discuss which of them is physically the most satisfactory, to correct errors which have arisen in the literature in the calculation of some of the theoretical values, and to suggest a system of symbols for the theoretical parameters, since there is no accepted notation in this field of study.

The relation between contrast and mass-thickness under single-scattering conditions is simply expressed by the equation:

$$\ln(I_0/I) = Sw \tag{1}$$

where S is the effective scattering cross-section per gram of the material. For scattering by a single (amorphous) element, S is related to the corresponding atomic cross-section, σ, by the equation:

$$S = \frac{\sigma N_0}{A} \tag{2}$$

where N_0 is Avogadro's number and A is the atomic weight of the material. The theoretical value of $w_{\text{lim.}}$, above which S in equation (1) is no longer independent of w, is given by the value of w beyond which the theoretical basis of equation (2) (that is, single-scattering conditions) is no longer valid.

In this article elastic scattering cross-sections will be denoted by the subscript E or e, inelastic by I or i and the sum of the two by T or t. Capital letters indicate the results of integrating the differential cross-sections over all possible scattering angles ($0 \leqslant \theta \leqslant \pi$), and small letters indicate integration from a lower limit of the objective-aperture semi-angle, α.

For example:

$$\sigma_T = \sigma_E + \sigma_I \tag{3}$$

$$\sigma_e = \int_\alpha^\pi \frac{d\sigma_E}{d\Omega} 2\pi \sin\theta \, d\theta \tag{4}$$

$$\sigma_I = \int_0^\pi \frac{d\sigma_I}{d\Omega} 2\pi \sin\theta \, d\theta \tag{5}$$

$$S_t = S_e + S_i \tag{6}$$

The values of $w_{\text{lim.}}$ based on the definitions given by various authors and evaluated for carbon and an accelerating potential of 50 kV. on the basis of either the Leisegang or Lenz theory are given in Table 1. The definitions are considered separately below.

The first three values of $w_{\text{lim.}}$ in Table 1 are based essentially on the same definition of the *Aufhellungsdicke* or 'transparency thickness' due to von Borries[15] and represent (apart from the factor 0·53 in the third value) the values of w in which the mean number of elastic scattering acts per electron is unity (that is, for material of unit density the mean free path for acts of elastic scattering). The factor 0·53 has recently been introduced by Zeitler and Bahr[2] to produce a value of $w_{\text{lim.}}$ within which not more than 10 per cent of the incident electrons are scattered elastically more than once. The values of $w_{\text{lim.}}$ in Table 1 obviously differ considerably according to the definition adopted, and show only an order-of-magnitude agreement with the experimental values already quoted.

The von Borries definition can only be valid when elastic scattering is much more important than inelastic and predicts a value of $w_{\text{lim.}}$ which is independent of the objective aperture. Since the elastic-scattering theories predict that $S_E \simeq S_e$ for the usual apertures in electron microscopy ($10^{-3} \leqslant \alpha \leqslant 10^{-2}$ radian), the dependence on aperture can be neglected on this definition. Lenz's theory, which deals with inelastic as well as elastic scattering, predicts that for high Z, $S_e \gg S_i$, but that for low Z, for example, organic specimens, $S_e \simeq S_i$. This means that, in general, the restriction of a definition of $w_{\text{lim.}}$ to the value of $1/S_E$ cannot be maintained. However, it is important to examine the values of $1/S_E$ given on the basis of the Leisegang and Lenz theories in order to explain the apparent discrepancy between the values. The discrepancy is at first sight disturbing, since both theories have a common basis in quantum mechanics.

The difference between the values of $1/S_E$ arises partly from a different choice of approximation to the electronic charge distribution of the scattering atom. The value of σ_E is proportional to the mean squared radius of the distribution, denoted by Θ/Z (ref. 13) or $6R^2$ (ref. 12). Lenz, using Hartree wave functions, gives $\Theta = 9{\cdot}10\ (a_H)^2 Z^{1/3}$ for carbon, whereas Leisegang uses the expression $R = a_H Z^{-1/3}$ (that is, $\Theta = 6\ (a_H)^2 Z^{1/3}$). The values of Θ thus differ by a factor of 1·52, while the remaining discrepancy can be accounted for as follows.

Differential scattering cross-sections are often expressed in terms of a characteristic scattering angle, χ_0 (refs. 17, 12) or θ_0 (refs. 13, 2, 6), and σ_E is proportional to $\frac{1}{\chi_0^2}$. If λ is the wave-length of the scattered electron, then:

$$\chi_0 = \lambda/2\pi R \tag{7}$$

which reduces, using the Leisegang approximation for R, to:

$$\chi_0 = Z^{1/3} \frac{e^2}{c\hbar} \frac{\sqrt{1-\beta^2}}{\beta} \tag{8}$$

where β is the ratio of the velocity of the electron to the speed of light. The expression which appears in Leisegang's paper[12] is:

$$\chi_0 = 0{\cdot}48 Z^{1/3} \sqrt{1-\beta^2}/\beta \text{ (degrees)} \tag{9}$$

whereas on re-calculation we find that the numerical constant has the value 0·418. Leisegang (personal communication) agrees with us, and finds he had carried over a numerical error from the earlier paper of Molière[17]. The result is that theoretical cross-sections calculated on the basis of equation (8) (see, for example, Bahr[1], Zeitler and Bahr[2,6], De and Sadhukhan[18]) are about 30 per cent too small. Combined with the factor 1·52 mentioned above, this explains the difference between values of S_E derived from Leisegang's paper[12] and those derived from Lenz's work[13].

Another error has been the occasion of differences between Lenz's published values and those calculated by others (refs. 3, 19, 5, 20) from his expressions. In his equation for σ_E, there appears the term Θ/a_H^2, where $a_H = \hbar^2/me^2$ is subject to relativistic variation through the mass, m, of the incident electron. The value of Θ is also expressed in terms of a_H^2, but in this case a_H is merely a convenient length (the Bohr radius of the hydrogen atom) and is invariant. By cancelling out a_H in the Lenz expres-

sion, one thus loses a factor (> 1) which becomes increasingly important at higher accelerating voltages. Leisegang's theory has not been liable to this error, because the relativistic variations always appear explicitly in the equations.

The two possibilities of including both elastic and inelastic scattering in a definition of the limiting value of w for single scattering, namely, $1/S_T$ and $1/S_t$, have both been used[16,3]. While $1/S_T$ is a logical and rigorous extension of von Borries's definition for elastic scattering and gives a valid limit for the accurate measurement of differential cross-sections (the subject of Haine and Agar's paper), it can bear little relation to the effect of scattering on the image-contrast, since most electrons, if inelastically scattered, still reach the image plane under normal conditions. This raises the question whether, in considering the effect of plural scattering, deflexions through all angles should be given equal weight; an electron which is inelastically scattered through an angle much smaller than α and is then scattered through (probably) a larger angle is effectively singly scattered so far as the image contrast is concerned.

The above kind of argument explains why inelastic scattering is ignored in defining a critical thickness for conditions in which $S_i \ll S_e$, although inelastic scattering, and multiple scattering in the rigorous sense, are still undoubtedly taking place. If this procedure (that is, the neglect of scattering processes with deflexions smaller than α) can be justified, a similar case must exist for neglecting the total inelastic cross-section (calculated for $\alpha \rightarrow 0$) when finite apertures are used. Thus when inelastic scattering has to be taken into account, a reasonable course would be to use S_i in estimating its effect, and to use $1/S_t$, rather than $1/S_T$, as a measure of critical thickness. This course appears to have been followed by Cosslett[3], since he mentions a critical mass-thickness, x_c, given by $x_c = 1/\mu$, where μ corresponds to our S_t. The value of $1/S_t$ is the theoretical mass-thickness, in which the mean number of scattering acts per electron with a deflexion greater than α is unity.

Table 1. DEFINITIONS AND VALUES OF THEORETICAL LIMITING THICKNESSES FOR C AT 50 KV.

Author	Definition $w_{lim.}$	Scattering theory	$w_{lim.}$ (μgm.cm.$^{-2}$)
von Borries (ref. 15)	$1/S_B$	Leisegang	21 7
von Borries (ref. 15)	$1/S_E$	Lenz	11 2
Zeitler and Bahr (ref. 2)	$0{\cdot}53/S_E$	Leisegang	11 5
Haine and Agar (ref 16)	$1/S_T$	Lenz	1·8
Cosslett (ref. 3)	$1/S_t$	Lenz*	8 3

* Using values of $R = 0\ 529\ Z^{-1/3}$ Å., $\alpha = 5 \times 10^{-3}$ radian

It appears to us that the logical theoretical definition of the critical thickness for single-scattering in electron microscopy is $1/S_t$, which takes both elastic and inelastic scattering into account, converts into the von Borries definition at high Z or large-aperture angles where $S_t \simeq S_e \simeq S_B$, and includes the effect of variation of aperture on the number of electrons which reach the final image plane.

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PROTEIN CATABOLISM

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SIGNIFICANT progress has been made in recent years in determining the mechanism involved in protein biosynthesis[1-3]. This process has been shown to depend on the enzymatic formation of activated amino-acids (as amino-acyl adenylates) and on their transfer to soluble ribonucleic acids. A highly efficient (although incompletely understood) incorporation of these amino-acids bound to soluble ribonucleic acids into protein in the microsomes then takes place. On the other hand, relatively little attention has been given to protein catabolism. It is still not established whether protein catabolism involves a reversal of the steps known to occur in protein biosynthesis or proceeds by an entirely different mechanism. It is the purpose of this article to show how the results of several investigations bearing on protein catabolism in higher organisms which have been variously interpreted actually support the thesis that an amino-acid derivative is an intermediate degradation product of protein. Such a mechanism not only explains the experimental data cited but is also particularly attractive because of its energy-conserving nature, and because, as mentioned above, amino-acid derivatives have been demonstrated as intermediates in protein biosynthesis[4].

The experimental results of Whipple and co-workers[5] were interpreted by postulating an intermediate in the breakdown of one protein and the biosynthesis of another. These investigations showed that when serum proteins containing carbon-14 lysine were injected intravenously into dogs, 30–40 per cent of the radioactivity, still in the form of lysine, was incorporated into the tissue and organ proteins without appreciable loss of activity as carbon-14 dioxide in the expired air. When similarly labelled proteins were fed to dogs, a high content of

carbon-14 dioxide was expired. Whipple concluded that the mechanism of transfer of carbon-14 from labelled plasma protein to organ protein did not involve breakdown to free amino-acids, but rather proceeded by protein cleavage only to the polypeptide stage. The organ proteins were formed by the subsequent re-assembly of these peptides.

In pursuing the problem of the mechanism involved in the transfer of labelled amino-acids from one protein to another, Francis and Winnick[6] and Friedberg and Walter[7] attempted to inhibit the transfer of amino-acids from one protein to another by flooding the system under study with large amounts of unlabelled amino-acids. It was found that the formation of newly labelled protein from labelled administered protein could not be decreased or inhibited by this method. Loftfield and Harris[8] have interpreted the above results[6,7] on the basis that exogenous (injected or fed) and endogenous (derived from protein degradation) amino-acids do not readily reach equilibration. The formation of intermediates other than free amino-acids in the breakdown of one protein and the synthesis of another would, however, be in harmony with the observations[6,7] and with the interpretation of Loftfield and Harris already mentioned. Such degradation products, far from readily reaching equilibration with free amino-acids, would also be preferred precursors in the synthesis of new protein. It is of interest to note in this connexion that it has been demonstrated that a considerable part of newly synthesized protein is derived from the breakdown products of endogenous protein[8].

More direct experimental evidence for intermediates in protein degradation comes from the work of Simpson[9] and from that of Steinberg and Vaughan[10], They demonstrated that the release of radioactivity from labelled proteins in rat liver slices was depressed by anaerobic conditions, by cyanide, by 2,4-dinitrophenol, and by certain amino-acid analogues. This work implies that protein catabolism is tied to a supply of energy. It has been suggested[10] that a linkage between protein catabolism and protein biosynthesis might also be involved. Korner and Tarver[11] investigated, under cell-free conditions, protein catabolism in the sub-cellular fractions of labelled rat liver and found that release of amino-acid from nuclei and mitochondria is inhibited by anaerobiosis and by uncoupling oxidative phosphorylation. More recently, Penn[12] reported that the degradation of serum albumin by rat liver mitochondria is also dependent on an energy supply and that some amino-acid derivatives, detectable by spectrophotometry, appear to be involved as intermediates. Although these experiments cannot be unequivocally interpreted at present (see Korner and Tarver[11]), the results of Simpson, Steinberg and Vaughan and Penn certainly suggest that protein degradation is not simple proteolysis, and that intermediates are involved in protein catabolism.

There is further evidence which indicates that intermediates other than free amino-acids might be involved in protein degradation. When radioactively labelled proteins, peptides, and amino-acids were injected into yolks of embryonated chicken eggs[13], the rate and extent of uptake of label into the chick embryonic protein were found to be identical for the three types of precursors. Considering that there are no free amino-acids in the yolk, but large amounts of diluting protein, it was concluded that protein is the preferred embryonic protein precursor. The uptake of homologous and heterologous proteins by the embryo was identical. Furthermore, the site of protein breakdown appears to be in the yolk, whereas protein synthesis occurs in the embryo proper. Since there is no equilibration between added free amino-acids and those derived from yolk protein, I was led to the conclusion that an intermediate, other than free amino-acids but one directly derivable from protein, is involved.

Chin, Tannenberg and Moldave[14], in experiments with Ehrlich ascites cells, recently found that incubation with isotopic free amino-acids led to the accumulation of considerable amounts of free amino-acids within the cell during incorporation into proteins. Incubations with isotopic proteins led to labelling of proteins without significant accumulation of intracellular free amino-acids. These results are interpreted by Moldave as indicating intermediates other than free amino-acids in the degradation of one protein and the subsequent synthesis of another.

Conceivable intermediates in the process of protein breakdown and new protein synthesis are: free amino-acids, peptides and amino-acid derivatives (that is, some forms of activated amino-acids). I have shown that the experimental evidence cited points to intermediates other than free amino-acids. Of the two remaining possibilities, the amino-acid derivative is the more probable choice, since a large number of experiments conducted in the past ten years have made peptide intermediates in protein metabolism most unlikely. Walter *et al.*[15] found that amino-acids and peptides derived from homologous serum proteins were incorporated into serum proteins (as well as organ proteins) at essentially the same rate and to the same extent. This cast doubt on the role of peptides derived from proteins as intermediates in protein synthesis. Other experiments[16–17] dealing with the breakdown of serum proteins, transfused from donor to recipient at various times after injection of labelled amino-acids, also have led to the conclusion that peptides are not involved. Such residues of individual amino-acids incorporated into serum proteins at different times are lost from these proteins at the same rate.

In a series of *in vivo* experiments, Simpson and Velick[18], Askonas *et al.*[20] and Muir *et al.*[21] investigated the problem of protein synthesis by administering labelled amino-acids to animals and determining the specific radioactivities of these amino-acids in various parts of the peptide chain of isolated, specific proteins. They found identical specific radioactivities in the injected amino-acids derived from different parts of a protein. This indicates that the entire protein molecule was formed at the same time and from the same amino-acid pool. In this connexion an apparent contradiction to the argument must be mentioned. Anfinsen and co-workers[22,23], in their investigations *in vitro*, found differing specific activities of incorporated labelled amino-acids derived from various parts of ovalbumin, insulin and ribonuclease. These authors concluded that peptides were intermediates in protein synthesis. However, Loftfield and Harris[8] showed, in subsequent experiments, in which rats were continuously infused with labelled valine, *iso*leucine and leucine, that the specific activities of the intracellular free valine, *iso*leucine and leucine of liver and the specific activities of these amino-acids in a protein (ferritin) formed by the liver were identical. It thus appeared that if peptide intermediates are involved, they must be derived only from amino-acids and not from preformed protein. Whether labile amino-acid derivatives are the intermediates involved in

protein breakdown and synthesis of new protein could not be experimentally decided by these investigations. Such amino-acid derivatives could also give rise to free amino-acids during the isolation of 'free' amino-acids from tissue.

I have shown how a variety of experimental results dealing with aspects of protein catabolism can all be interpreted uniformly by postulating amino-acid derivatives as intermediates in the re-utilization of amino-acids derived from one protein for the synthesis of another. In the transfer of labelled residues from one protein to another, the amino-acids did not exchange with large pools of added amino-acids[5-7], a fact which suggests the presence of an intermediate. Peptides were excluded as intermediates on the basis of the rate of incorporation of amino-acid into various parts of the same protein[19-21], and on the basis of identical specific activities of intracellular amino-acids and of these amino-acids in a protein in rats continuously infused with labelled amino-acids[8].

The experiments of Simpson[9], Steinberg and Vaughan[10] and Penn[12] have shown that protein degradation is not simple proteolysis. Specific energy requirements for protein catabolism were indicated. Intermediates were shown to be involved in protein degradation, and it has been suggested that these might be similar to some of the intermediates known to participate in protein biosynthesis[10,12].

The preferred utilization of precursor protein (rather than peptides or amino-acids) in a system[13] in which protein breakdown and protein synthesis are apparently spatially removed led to the conclusion that an amino-acid derivative, not in equilibrium with added free amino-acids, is involved as an intermediate. In other experiments it was shown[8] that the breakdown products of endogenous protein are highly efficient precursors of newly formed protein. Furthermore, the demonstration[14] at a time of active protein synthesis of the accumulation of labelled free amino-acids in certain cells when labelled free amino-acids are supplied but not when labelled protein is supplied is again indicative of the participation of amino-acid derivatives as intermediates.

The possible analogy between the cleavage of peptide bonds and the enzymatic cleavage of other macromolecules has been pointed out[10]. For example, in the cases of glycogen and ribonucleic acid, which also can be split hydrolytically, the enzymatic cleavage need not be hydrolytic[24,25]. The cleavage of peptide bonds may similarly require an acceptor substance. Amino-acid derivatives have been shown to be intermediates in protein synthesis. The re-utilization of amino-acids from one protein for the synthesis of another involving amino-acid derivatives as intermediates would therefore conserve energy. A large number of the experiments cited have implicated an intermediate other than free amino-acids in the breakdown of proteins. Since peptides have been excluded by a number of investigations as the intermediates involved, the most likely intermediate is an amino-acid derivative. It is possible that this amino-acid derivative is similar to, or identical with, one of the intermediates known to participate in the anabolic process.

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FORMS OF TOBACCO MOSAIC VIRUS

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THE study of strains or variants of tobacco mosaic virus may be simplified by considering the natural association between host species and the forms of the virus infecting them in the field. The forms of the virus occurring naturally in different host species have distinctive biological properties which divide them into categories similar to those delimited by biophysical properties. Data on the constitution of the tobacco mosaic virus proteins show similarities and differences between strains that appear congruent with the same grouping. Forms of virus may be distinguished partly by physical and chemical properties, partly by biological criteria.

Siegel and Wildman[1] and Ginoza and Atkinson[2] studied differences in biophysical properties among 8 tobacco mosaic virus strains. Four of the 8 were single-lesion selections characteristic of virus populations in 3 host species. They were *U*1 and *U*2, representing majority and minority components in a sample of tobacco mosaic virus[3,4]; *U*5, from *Nicotiana glauca* Grah.[5]; and *U*8, Holmes's strain from the ribwort plantain, *Plantago lanceolata* L.[6]. These 4 strains were placed according to biophysical differen-

ces in 3 groups. Two strains, *U*2 and *U*5, were placed in the same group. Though they were from different hosts and gave different mosaic symptoms, they had similar biophysical properties. Included in the *U*1 group were 2 mutants from *U*1 type isolates, one, *U*4, the heat-induced masked strain[7], the second, *U*7 from ultra-violet irradiated *U*1 virus. Also in the group was *U*3, possibly a derivative or minor component of the ribgrass isolate. A fourth group was reserved for *U*6, a yellow mutant of *U*1 with changed biophysical properties.

Knight *et al.*[6–10] found the amino-acid content in the protein fraction of an ordinary severe tobacco mosaic virus isolate, like *U*1, similar to that of the masked strain, *U*4. There were differences in the amino-acids of this pair, the ribgrass strain (*U*8) and a yellow mutant similar to *U*6. The chemical and biophysical data agree in distinguishing some strains and grouping others. In a general sense, these data bear out the expectation that similarities or differences in the constitution of the protein shells of virus strains should be reflected as similarities or differences in biophysical properties.

The main biological criterion for a form may be defined by the presence and persistence, as a natural infection in one or more host species, of a type of tobacco mosaic virus with uniform biophysical properties. A form need not, and in practice does not, consist of one symptom variant. It is subject to mutation and selection that may change the level of systemic symptom expression in whole populations[11]. The masked strain is an example showing that the constitution and properties of the virus protein shell may remain unaffected by such changes[8]. Commonly also mutation may produce variants of the virus, like *U*6, with properties beyond the limits of the original form, but these are soon eliminated in the field by competition with better adapted strains. They fail to pass the test of persistence under natural conditions. It is possible that a strain like *U*6 might infect a new host in which it could persist, or changes like that reported for the cowpea strain of the virus[12] might occur in Nature. Such events would be evidence for the production of new forms by mutation, but they would not eliminate the essential discontinuity between forms.

The dominant tobacco form of the virus, corresponding to strain-group 1 of Siegel and Wildman[1], has special biological effects marking it off from other forms of tobacco mosaic virus. It causes systemic symptoms in some *Nicotiana* spp., including *N. sylvestris*, which react to many tobacco mosaic virus isolates with necrotic local lesions. These host reactions are heritable[13,14]. The dominant tobacco form also produces characteristic yellow mutants in systemically infected host plants[15]. Cytologically, it causes typical reactions in invaded cells (unpublished). Such biological characters, as well as biophysical and chemical data, may be used to distinguish between the tobacco form and others.

Johnson and Valleau[16] tested many samples of tobacco mosaic virus, some from stored tobacco leaf up to 50 years old, some collected directly from field crops. They kindly sent a portion of their collection of isolates for further testing in this laboratory. The majority of symptom variants were similar to *U*1 in their reactions, but among them were mild isolates similar to *U*2. The forms of virus most common in tobacco seem to have remained almost the same for 50–80 years.

In southern California, isolates of tobacco mosaic virus from naturally infected *Nicotiana glauca* have produced necrotic local lesions on *N. sylvestris*[5], though single lesion isolates varied greatly in symptom expression. A detailed study of one variant, *U*5, has shown its biophysical properties to be almost indistinguishable from those of *U*2[1,2]. Variants giving host reactions similar to those of *U*5 have been found in *N. glauca* elsewhere[17,18].

*U*5 was isolated from *N. glauca* in disturbed natural vegetation on the campus of the University of California at Los Angeles. Another species in the same plant community, *Solanum xantii* Gray, was also found infected with tobacco mosaic virus. The dominant form in *S. xantii* gave small white local lesions on first transfer to *N. glutinosa*, instead of the characteristic necrotic local lesions of *U*1 and *U*2; and on *N. sylvestris* it produced mosaic symptoms. It was thus distinguished from both the *U*1 and *U*2 forms of tobacco mosaic virus. The *S. xantii* virus included 2 minor components: one appeared to be of the *U*1 form, the other caused necrotic local lesions even in Turkish tobacco, variety Samsun. Two species of Solanaceae, *N. glauca* and *S. xantii*, growing in the same plant community for a number of years, were infected with different forms of the virus.

There is evidence from southern California[18] and numerous references in the literature[19–22] that tomato normally carries a form of tobacco mosaic virus differing from that in tobacco. It includes many symptom variants giving necrotic local lesions on *N. sylvestris*. Still other forms of the virus appear regularly in host species from families unrelated to Solanaceae[6,13,23]. Though some of these forms of the virus are insufficiently differentiated, the general pattern is becoming clear. Natural infections in a single plant species seem to consist mainly of one or a small number of forms. Generally one form of the virus is dominant. Symptom variants of a form that is dominant in one host species may be present as minor constituents of the virus infecting other species. The occurrence, in widely separated regions, of the same or similar forms of the virus in a particular host, for example, in tobacco, *N. glauca*, or tomato, minimizes the chance that these associations are merely of regional origin.

The mutual acceptance between a host species and a well-adapted form of the virus seems to be associated with the constitution of the virus protein (see above). To assume that a causal relationship exists between the nature of the protein and initial acceptance of the virus particle may be premature, but it accords well with the view that infection is a 2-step process[24–26]. The shedding of the protein shell and release of the nucleic acid depend on the acceptance of a virus particle at an appropriate site in the host tissue. The protein surrounding the core of nucleic acid is more likely to influence the first stage of association with structural elements of the invaded cell than is the nucleic acid itself[25]. Re-infection and further multiplication of newly formed virus particles, after local or systemic transport to non-infected cells, again demands acceptance at appropriate sites. At each re-infection, if it occurs from whole virus particles, initial acceptance would be influenced by the constitution of the virus protein, and in turn would influence the chances of the nucleic acid being freed to reach appropriate sites for multiplication. The degree of adaptation of the protein shell to the cells of a particular host may thus introduce a correspond-

ing degree of specificity into the initial reactions of a plant species to the form of virus infecting it. In the final act of infection the nucleic acid would presumably be decisive.

At a different level there is evidence on the nature of selectivity between host species and forms of tobacco mosaic virus. First, a process of exclusion may exist. The tobacco varieties responding to a form of virus with necrotic local lesions are essentially immune to it in the field[27]. The *U*1 form alone is likely under natural conditions to infect tobacco varieties reacting with necrotic local lesions to *U*2. In a more positive sense, variants of the *U*1 form are adapted to tobacco because they multiply rapidly to high concentrations, and are invasive but not crippling to the host plant. The reason for the dominance of the *U*2–*U*5 form in *N. glauca* appears to be of this sort (R. A. Solberg, unpublished). The distribution of *U*5 in the younger tissues of infected *N. glauca* is somewhat less patchy than that of *U*1, and the *U*5 virus approaches closer to the stem apex of infected plants. During a long period under natural conditions of serial transmission this difference should be enough to allow symptom variants of the *U*5 form to appear as the sole or the dominant type of tobacco mosaic virus in *N. glauca*—as they do.

The persistence in tobacco of low concentrations of *U*2 mixed with the dominant *U*1 form indicates that the 2 forms may have slightly different requirements for multiplication or re-infection, giving *U*2 a competitive advantage at a limited proportion of multiplication sites. In general this may explain why minor forms of tobacco mosaic virus are found mixed with dominant forms in a number of host species.

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A NEW INTERPRETATION OF *JAMOYTIUS KERWOODI* WHITE

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JAMOYTIUS KERWOODI White is based on two specimens from the Upper Silurian sediments of Logan Water, near Lesmahagow, Lanarkshire, about half a mile upstream from Logan House. The specimens are *B.M.*11284 (holotype) and *B.M.*11285. White[1] described the animal as an agnathan with the following characteristics: "No armour or endoskeletal calcification; notochord persistent; simple lateral fin-folds present; median fin-fold represented by elongated dorsal and anal fins. Eyes probably simple, very large and anteriorly placed. Muscle segments simple and numerous with single flexure and undivided by horizontal septum. Mouth ? terminal; intestine short and straight".

The order Euphanerida and family Jamoytiidae were erected on the basis of the above characters. This interpretation placed *Jamoytius* in an important position in relation to early vertebrate evolution, and various authors[2–6] have commented on the original interpretation and on the phylogenetic position of *Jamoytius*.

White regarded *Jamoytius* as a primitive naked fish-like chordate, probably "a conservative element of the main stock from which the various groups of craniate chordates arose". He considered *Jamoytius* as a possible ancestor of the living Acrania, for example, *Amphioxus*. Berrill[2] commented on the absence of branchial apparatus and suggested that *Jamoytius* had a pharynx and atrium comparable with that in *Amphioxus*. He also speculated on the nature of the eye. Stensiö[6] re-interpreted the "carbonized muscle remains" as scale rows and noted the resemblance to the scales of some of the Anaspida. He assigned the family Jamoytiidae to the super order Anaspida. Tarlo[7] confirmed Stensiö's conclusions, and re-interpreted other parts of the holotype, for example, dorsal fin rays as ridge scales.

The importance of any new material of this animal is thus obvious, and this work concerns the discovery of two further specimens at the original locality. The first (in counterpart *F.R.*1393 *a* and *b*), collected by Prof. F. H. Stewart, is a large individual, lacking head and tail. The second (*A.R.*59.103), an almost complete specimen discovered by me, has been prepared to expose the ventral (?) surface (Fig. 1*b*). Examination of material in the Scottish Geological Survey, collected by Macconochie and Tait, yielded one fragment (in counterpart *G.S.E.*, 11882, 11883), and a poorly preserved specimen was found in the Slimon Collection, Kelvingrove Museum, Glasgow. A small individual bringing the total to seven has also been discovered in material purchased by the Department of Geology, Princeton, from Tait in 1923 (*P.U.* 12865 in counterpart).

Examination of the new material reveals that the original interpretation must be modified, although the basic concept of body-shape, lateral and median fin-folds appears sound. The new evidence concerns the scales, eyes, mouth, branchial apparatus and caudal fin. The segmental structures in the holotype,

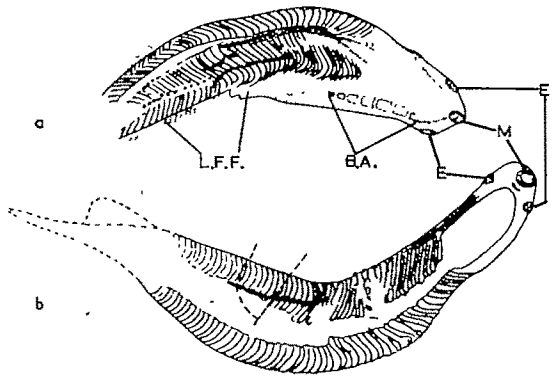

Fig 1. *Jamoytius kerwoodi* White. *a*, The holotype, *B M* 11284, simplified drawing after White (ref. 1, text Fig. 1) re-interpreted with additions; *b*, the new complete specimen, *A.R.* 59.103, with a portion of the body restored from the counterpart
E, eye, *M*, mouth; *B.A.*, branchial apparatus (or apertures); *L.F.F.*, lateral fin-fold
Both specimens from the Logan Water, Lanarkshire. (× ½)

*B.M.*11284 (ref. 1, text Fig. 1) were interpreted as carbonized remains of body muscles (myomeres) separated by clear infillings representing the vanished septa (myocommata). Evidence against such an interpretation is as follows: of the seven known specimens, six have the segmental structures preserved, and several of the specimens show varying degrees of relief in these structures. The poorly preserved *B.M.*11285 is thus unrepresentative and misleading. It now seems certain that the preserved structures were originally more substantial than myomeres and myocommata and are remains of exoskeletal ossification or scales, as suggested by Smith[5] and Stensiö[6]. The structures interpreted by White as muscle fibres are a cross-striation ornamentation on the scale surface, or tubercle rows such as are present in the Anaspida. The ridges representing "the vanished septa" may be interpreted as the thickened basal ridges of the scales, running dorso-ventrally, but I feel that the evidence for this is not conclusive.

*A.R.*59.103 was embedded in a laminated grey siltstone, and extensive preparation was required to expose the complete fossil, which is little more than a carbon film. The surface exposed appears to be the ventral side of the animal. (The holotype, *B.M.*11284, is probably the dorsal side with some of the ventral structures showing through.) The animal as preserved is 21–22 cm. in length and dorso-ventrally flattened (Fig. 1*b*). The body axis has been twisted after death through almost 90°. Three well-defined structures in the unarmoured head region are interpreted as lateral eyes and a mouth The mouth (*M*) is median sub-terminal and roughly circular (5·0–5·5 mm. in diam.) with a distinct dark rim (1 mm. wide). It thus resembles somewhat the mouth in the living cyclostomes. Very small denticle-like structures were observed on part of the rim. The two stains interpreted as eyes (*E*) are moderately large (3–4 mm. in diam.), lateral and situated about 1 cm. posterior to the mouth. The structures in the head region of *B.M.*11284 (ref. 1, text Fig. 1) can be re-interpreted in view of this discovery. The lateral stain (*E*) interpreted as an eye is indeed such, but the well-defined, oval object in a terminal position (*E*) is the mouth. The other eye is situated on the blunt protuberance to the right of the mouth, where a dark stain can be seen, both in the specimen and in White's figure, although it is less distinct than the left eye.

The well-developed (and ossified) branchial structures which are so characteristic of the known Anaspida are not present in *Jamoytius*, and their absence has led several authors to suggest the existence of a pharynx and an atrium. One of the most surprising of the new discoveries was that the holotype *B.M.*11284 does have traces of the branchial apparatus preserved. While examining *B.M.*11284, using optical equipment of a higher quality than that available at the time of the original description, I was able to distinguish a series of exceedingly faint structures extending backwards from just behind the right eye to a point opposite the eighth preserved scale row. These structures (Fig. 1*a*, *B.A.*), apparently seven in number, may be the branchial apertures or even the outline of the gill sacs themselves, in which case the external openings could be quite small, as in the lamprey. The presence of 'advanced' branchial apparatus disproves Berrill's suggestion[2] of a pharynx and atrium, and settles the argument as to whether *Jamoytius* could have given rise to the modern Acrania.

The scale rows in *A.R.*59.103 first appear some 4 cm. from the anterior margin of the head and are well preserved along most of the length of the body, but become very faint near the tail. The scales show no indication of having been arranged in rows like those of the Anaspida and seem rather to have been continuous from the mid-dorsal line to the ventral surface, where they fall short of the mid-line, leaving a scale-free ventral strip (1·0–1·5 cm. wide) which extends for most of the length of the body and widens underneath the head.

The structures in *B.M.*11284 which White (ref. 1, text Fig. 1, *L.F.F.*) interpreted as the lateral fin-folds tucked underneath the body, and which Westoll[3] suggested were the remains of the dorsal and anal fins, are interpreted here as the ventral termination of the body scales, mentioned above. It seems more likely that the ragged patches interpreted by White as displaced skin (*D.S.*) are, in fact, the lateral fin-folds with faint traces of the fin rays preserved. In *A.R.*59.103 the scales are only occasionally strongly disrupted, a cross-striation ornament is present and the scale surface has been irregularly fractured on a minute scale. The scales almost certainly reflect the underlying myomeres, with single forward flexure which is more acute anteriorly than posteriorly.

Only a faint outline of the caudal region remains; the axis of the tail appears to be twisted and it seems likely that *Jamoytius* possessed a reversed heterocercal (hypocercal) tail such as is found in the Anaspida.

The second of the new specimens (*F.R.*1393 *a* and *b*) lacks both head and tail but shows clearly the scales and other structures of a portion of the body 13 cm. long. The ventral termination of the scale rows is well preserved, and some longitudinal striation is seen in the scale-free strip. Scale relief is strong and the size of the scales indicates that this individual was the largest of the seven specimens.

The fragment with counterpart (*G.S.E.*, 11882, 11883) from the Scottish Geological Survey has the best-preserved section of the lateral fin-fold yet seen. The fin is broad with a well-defined outer margin and at one end shows faint but definite fin rays running almost to the margin. Scale relief is strong. The Princeton specimen (*P.U.*12865 in counterpart) and that found in the Kelvingrove Museum, Glasgow, are both small individuals and not particularly well preserved.

Several of these specimens possess structures comparable with those which White interpreted in the holotype as notochord and intestine; but more and better preserved material is required before this and other aspects of *Jamoytius* can be satisfactorily explained. In brief, the new evidence concerns the presence of exoskeletal ossification (scales); lateral eyes; a terminal, subcircular mouth; a branchial apparatus not unlike that in the Anaspida and the living cyclostomes; fin rays in the lateral fin-folds; a hypocercal (?) tail. *Jamoytius* is too far advanced to be an ancestor of the living Acrania and shows a close relationship with the Anaspida. Whether it is itself an anaspid[6,7] is a matter for speculation; but of all the known fossil Agnatha, *Jamoytius* would seem to be the closest to the living Cyclostomata. The age of the enclosing sediments is not yet accurately known, but marine invertebrate faunas from both above and below the *Jamoytius* horizon are indicative of the Wenlockian (or even earlier) rather than the Ludlovian as was previously thought. The "Ludlow fish-bed" of Peach and Horne[8] from which the specimens come is actually much lower in the succession than the "Ceratiocaris Beds" with which they were originally correlated. *Jamoytius* and the two coelolepids found in the same bed are the earliest complete chordates yet found in Britain, and their relatively high degree of organization indicates a long pre-Wenlockian history. It is hoped that more material will be discovered during my work in the area and the results will be published in detail at a later date.

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HOPLONEMERTINES, MYXINOIDS AND DEUTEROSTOME ORIGINS

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THE metazoa are generally dichotomized into the Protostomia, in which the embryonic blastopore becomes or is associated with the mouth, and the Deuterostomia, in which the embryonic blastopore becomes or is associated with the anus[1]. The hoplonemertines (an order of the phylum of proboscis worms, Rhynchocoela or Nemertina)[2] develop in a way which is not typical of either group, the blastopore being quite separate from both mouth and anus invaginations[3], which suggests that this proterostome group might be transitional to the deuterostomes. If this is the case, organ homologies between hoplonemertines and deuterostomes are to be expected and the deuterostome group with which most homologies are shared would be identified as the most primitive of the deuterostomes. A surprising number of homologies, some of which were early suggested by Hubrecht[4], appear to be shared by the hoplonemertines with the myxinoid cyclostomes[5], the most primitive vertebrate group.

These homologies are presented in the following two paragraphs. Like-numbered structures are those which resemble each other and are presumed to be homologous.

In myxinoids the *nasopharyngeal duct* (1), *mouth* (2) and *gill slits* (3) develop from a series of lateral expansions of an ectodermal foregut which perforate to form slit-like openings to the exterior[6]. On the dorsal roof of the nasopharyngeal duct is the *glandular hypophysis* (4), which is intimately connected in the development of vertebrates with the *anterior somites* (5)[7] and the notochord. The notochord is composed of a tubular multi-layered fibrous *sheath* (6) surrounding vacuolated gelatinous *notochord contents* (7) in which lies a flat, fibrous band, the *notochord strand* (8), extending along the notochord axis. *Skeletal cartilage* (9) first appears between and comes to surround the hypophysis and the anterior end of the notochord. Cartilage also is found superficially, associated with *horny teeth* (10). Associated with, and just ventral to, the notochord sheath is the *dorsal aorta* (11), a major vessel of the *closed circulatory system* (12). The digestive tract has a prominent ventral *liver* (13) and terminates in a definite *anus* (14). Sense organs include a pair of inverse retina *lateral eyes* (15), a vestige of the direct retina *pineal eye* (16) found in other vertebrates, a pair of *labyrinth organs* (17), *neuromast organs* (18) of taste and the lateral line system, and *olfactory organs* (19). The olfactory organs, which lie in the nasopharyngeal duct, are closely associated with the *dorsal neural tube* (20). Both types of structures develop from the ciliated neural plate, which invaginates as a groove and closes over at the neuropore to form the neural tube and an anterior external lip, the primordium of the olfactory organs. The eyes and olfactory organs are connected directly to the dorsal neural tube, but other sense organs and all muscles are connected to it by *solid nerves* (21) which connect to the dorsal sensory *alar plates* (22) and the ventral motor *basal plates* (23) of the dorsal neural tube.

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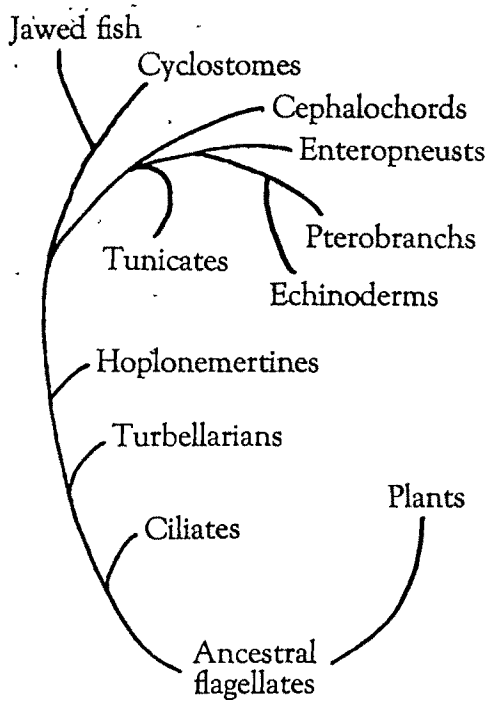

Fig 1. Revised deuterostome phylogeny

In *Malocobdella*, a form usually classed separately but closely related to the hoplonemertines, the *secondary mouth* (1, 2, 3) develops as a lateral expansion of an ectodermal foregut which perforates to form a slit-like opening to the exterior. On the dorsal wall of the secondary mouth of hoplonemertines lies the proboscis, an organ for capturing food with prominent *glandular components* (4), and *muscular components* (5), which develops as an invagination toward and comes to lie inside the proboscis sheath-rhynchocoel complex. This complex is composed of a tubular multilayered muscular *proboscis sheath* (6) surrounding a closed cavity filled with *rhynchocoel-fluid* (7) in which lies the flat muscular band, the *retractor* (8), extending from the posterior end of the sheath to the end of the proboscis. The proboscis develops armament composed of a *stylet base* (9) and a sharp *stylet* (10). Lying sometimes in, and sometimes ventral to, the proboscis sheath is the *dorsal vessel* (11), a major vessel of the *closed circulatory system* (12). The digestive tract may have a large ventral *gastric diverticulum* (13) and terminates in a definite *anus* (14). Sense organs may include inverse retina *lateral eyes* (15), *direct retina eyes* (16)[8], *cerebral organs* (17), *onion-shaped organs* (18)[9], and a medial *frontal organ* (19, 20) which lies on the dorsal anterior margin of the secondary mouth and may develop from a flat plate of ciliated ectodermal cells which invaginates as a groove. These sense organs and all muscles are connected by *solid nerves* (21) to a solid brain, composed of a pair of sensory *dorsal ganglia* (22) and a pair of motor *ventral ganglia* (23).

Each of the homologies suggested involves a number of specific positional, histological, and embryological similarities. In addition, the relations among structures of hoplonemertines are usually the same as those among the homologous structures of myxinoid cyclostomes. While a few resemblances between organisms can reasonably be explained by convergent evolution, the large number of resemblances observed, the existence in an order of nemertines of homologues for major myxinoid structures, and similar relations among homologous organs can only be reasonably explained by phylogenetic affinity.

Accordingly, it is suggested that early myxinoids evolved from an early hoplonemertine by means of the following transformations. The secondary mouth was repeated serially to produce the three types of foregut apertures of myxinoids. The glandular proboscis failed to invaginate into the proboscis sheath-rhynchocoel complex and remained at the anterior end of that complex as the glandular pituitary. The muscular proboscis invaginated laterally along the proboscis sheath-rhynchocoel complex and was subdivided to form the enterocoelous somites. The rhynchocoel fluid became gelatinous and the proboscis sheath and retractor became non-contractile in forming the notochord. Only a single pair of lateral eyes was retained while these and other sense organs enlarged and differentiated. The frontal organ closed over at the neuropore and lengthened back over the notochord as a closed tube. This tube fused with the solid brain of nemertines to form the vertebrate tubular brain with alar and basal plates. This fused structure then lengthened back with replication of dorsal mixed and ventral proboscis motor nerves to form the spinal cord with dorsal mixed and ventral somatic motor nerves. The vestige of the original proboscis nerves remained as the neural hypophysis or infundibulum.

The phylogeny of the deuterostomes can be revised to be consistent with this hypothesis by considering primitive jawless fish to be the primitive deuterostome stock, from which other deuterostomes are derived by loss of sensory organs, specialization, and in some cases neotony[10]. Deriving the jawless fish from the hoplonemertines then connects the deuterostomes to a phylogenetic sequence beginning in the primitive protista ancestral to both plants and animals[11], and thereby delineates the early evolutionary history of man's own line (Fig. 1).

A paper detailing similarities between suggested homologues, discussing more fully the embryological similarities of nemertines and deuterostomes, outlining transitional stages, and comparing the present hypothesis with other current views of vertebrate origins is in preparation.

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LETTERS TO THE EDITORS

PHYSICS

Impossible Magnetic-Field Self-Patterning

THE 'self-sustaining' Corbino disk recently proposed[1] is suspect. It was suggested that an axial magnetic field could Hall-deflect from an impressed radial current the azimuthal current just necessary for its existence. Inside, or axis side (outside, respectively), of an elemental current ring, its field contribution has indeed the sense of the field responsible for the ring, for inward (outward) motion of the dominant carriers. Outside (inside) the ring, however, its contribution is counter-sense to the field at the ring. This crucial embarrassment makes it difficult to imagine any finite, that is, physical, possibility for field self-patterning.

Certainly Midgley's solution, $B_z = Ar^{-k}$, $J_\theta = (k/\mu\eta_0)\, Ar^{-k-1}$, with neither changing sign, is trivial in the finite. In a disk with non-vanishing inner radius (finite radial current density) and finite outer radius, the fields at radii just within the inner and outer boundaries, lying inside and outside, respectively, all but an arbitrarily small circulating current, must differ in sign or both vanish. Thus A, the constant of integration, is zero. In an alternative view, the azimuthal current density, J_θ, must go the 'wrong' way just within the outer (inner) boundary, for inward (outward) motion of dominant carriers, unless J_θ vanishes identically.

Perhaps the one-dimensional formulation is insufficient. Specifically, the tacit neglect of the term $\partial B_r/\partial z$ in the θ-component of curl $\mathbf{B}$ is puzzling and possibly unjustified. One might have thought that, in the presence of azimuthal current, the radial component of the field would change considerably, and monotonically, along an axially directed path through a thin, but finite, current slab; and that at a true current sheet Maxwell's equation would not be applicable.

It should be stressed that only the theory of magnetic-field self-patterning in a finite, unencumbered Corbino disk has been considered here. No disparagement of the magnetic power amplifier or bi-stable trigger circuit suggested by Midgley is intended. Suitable biasing at the outer boundary, for example, might replace 'infinity'.

Self-patterning, or self-determining, fields (the terms 'self-sustaining' and 'self-maintaining' have unfortunate energetic connotations) are sustained (*a*) by exogenous current or (*b*) by current from motional induction within the system considered. In the light of impossibility theorems[2,3] for certain simple classes of steady-state, magnetofluid-dynamic dynamos (type *b*), one might hypothesize that type-*a* self-patterning fields in cases of material homogeneity, high symmetry, and topological simplicity are unlikely to exist. For its own sake as a fundamental problem, and also for its possible relation to the important fluid dynamo problem under type *b*, the question of the possibility of type-*a* self-patterning fields deserves closer attention.

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IT is true that Cowling's impossibility theorem would apply to a finite and unencumbered disk. To achieve a non-zero solution, it is essential that a finite disk be encumbered to the extent of an input coil, or a magnetic feedback path as proposed in Fig. 2 of my communication. If such configurations of the magnetic field with more than one interlinkage of the electric circuit were admissible in the astronomical context, the difficulties of dynamo maintenance would be reduced.

The essentially one-dimensional solution is valid for a disk of finite thickness and permeability μ, bounded either by a medium of infinite permeability or by an axial stack of similar disks, such that $\partial/\partial z \equiv 0$. A finite disk not so bounded demands a more elaborate solution, in which B_r varies with z.

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Short-Period Time Variations of Extensive Cosmic Ray Showers

AN exploratory experiment has been conducted to determine whether or not short-period fluctuations in the arrival of extensive showers are sufficiently systematic to warrant detailed study.

Two Geiger–Müller tubes 4 cm. in diameter and 40 cm. in length were connected in a coincidence circuit, and the output was recorded on an oscillograph with a paper speed of 5 mm./sec. The two tubes were placed parallel and were horizontally separated by 1 metre. The equipment was placed on the roof of a building free from obstructions. Two such equipments were operated independently. Approximately one count per minute was obtained.

A total of 60 records, 5 hr. in length, were studied. There were 30 such records for each equipment, The two equipments were separated by 12 and 330 m.. so that the results obtained are regarded as independent samples.

The time-interval between successive counts, τ_i, was listed as a function of the serial number of the count, i. This provides about 300 data pieces per record. The auto-correlation function was computed for each record, and was afterwards used to obtain the spectral curve. If the time-interval between successive counts is independent of any preceding or succeeding such time-interval, the auto-correlation function should be identically zero for lags of one or

more. The corresponding spectral curve should be flat, analogous to white noise.

Twelve spectral estimates were obtained for each curve. The flat spectral curve analogous to that of white noise was subtracted from the observed spectral curve. It was assumed that each spectral estimate was independent of other spectral estimates in the same curve, and that positive and negative departures from the flat curve are equally likely. The twelve spectral estimates were divided into three groups corresponding to long, middle, and short periods. The number of records showing 0, 1, 2, 3, or 4 positive departures within a group was noted and compared with the expected number (see Table 1). The differences between the observed and expected results are statistically significant.

Table 1. Number of Positive Departures from Flat Spectral Curve

No. of +	I	II	III	Expected
0	13	5	18	4
1	12	13	9	15
2	14	18	19	22
3	11	14	9	15
4	10	10	5	4

Table 1 shows a tendency for all negative or all positive departures in group I, all positives in group II, and all negatives in group III. This suggests a maximum in the spectral curve near the boundary of group I and group II. The maximum corresponds to a periodicity in the range of 4–9 counts.

The experiment thus suggests that long time-intervals between successive counts tend to be followed by long intervals approximately 4–9 counts later. The average time-interval between counts was 74 sec., so that a systematic variation in the arrival of extensive showers is indicated in the range of 5–11 min.

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Separation Factor of Tritiated Water Fractional in Distillation

A. H. Price has published[1] a table of values of vapour pressure of tritiated water. As these values differed greatly from our previous results, based on enrichment experiments of tritiated water in fractionating columns[2,3], it was decided to re-evaluate these results, taking into account our latest data of column operation[4].

The unit process separation factor for tritiated water (THO) from ordinary water (H_2O), defined as the ratio of the concentration of tritiated water in the liquid phase to that in the vapour phase at equilibrium (at low concentrations), may be found from known concentrations at the top of a separation column and at the bottom of it or in the boiler. The general theory and detailed calculations were given by Dostrovsky *et al.*[5,6].

α_T is found from the relation :

$$N_B/N_R = \alpha_T \exp[(KZ/L)\ (\alpha_T - 1)] \qquad (1)$$

where α_T is the separation factor for tritiated water ; N_B and N_R are boiler and reservoir concentrations of a batch-operated column ; K is transfer coefficient for vapour-liquid interface ; Z is length of column ; L is flow of liquid down the column.

The value of α_T reported by us previously was $1{\cdot}055 \pm 0{\cdot}002$ at 260 mm. mercury[2]. The values found from later experiments are given in Table 1.

Table 1

Column	I	II	III
Pressure (mm. mercury)	260	260	760
Unit separation factor α_T	$1{\cdot}053 \pm 0{\cdot}002$	$1{\cdot}051 \pm 0{\cdot}002$	$1{\cdot}036 \pm 0{\cdot}001$

These values are considerably smaller than the value of $1{\cdot}13$ found by Price[1].

It should be pointed out that for both pressures the ratio $(\alpha_T - 1)/(\alpha_D - 1)$ is $1{\cdot}37 \pm 0{\cdot}02$.

The main source of error in our results is ascribed to the error in estimate of the values of KZ. These could not be measured directly and were calculated, using the enrichment values of tritiated oxygen in the same system. Inserting the known values of α_D into equation (1), the KZ values were calculated for each fractionating column.

The pressure in columns I and II was regulated by a manostat connected to a vacuum tank. The columns were tested for vacuum before each run. There was a pressure differential of 15 mm. between the boiler and the condenser and the average value was used. In column III the pressure differential was negligible.

The error resulting from pressure fluctuations was estimated to be small compared with other factors mentioned.

The tritium activity was determined in a Geiger–Muller counter measuring the activity of hydrogen obtained from reduction of water samples by zinc. This method has been found accurate to within $\pm$ 1 per cent for the measurement of relative activity. Deuterium concentrations were measured in a mass spectrometer.

The error quoted for α_T includes the above-mentioned errors, on the assumption, however, that values of KZ obtained from measurements on deuterium are valid for the determination of tritium enrichment.

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Effect of Specular Reflexions on the Radiation Flux from a Heated Tube

In my communication under the above title[1] there appears an error in expression (7) for F_L''. The expression should read :

$$F_L'' = \sigma T^4 \sum_{r=0}^{\infty} \varepsilon^2(1-\varepsilon)^r \int_L^{\infty} \mu\left(\frac{h}{r+1}\right) dh$$

$$= \sigma T^4 \sum_{r=0}^{\infty} \varepsilon^2(1-\varepsilon)^r\,(1+r)\ \xi\left(\frac{L}{r+1}\right)$$

Taking the radiation from a black surface as reference, one can then show that the deficit from it of the flux of radiation from the mouth of a uniformly heated cylinder of length L, closed at the other end, is $(1-\varepsilon)$ times the corresponding deficit for the flux from the mouth of a cylinder of same diameter and of length $2L$, but open at both ends.

For the cylinder considered in the communication, which is closed at one end, and the length of which is five times its diameter, and the inner walls of which have an emissivity $\varepsilon = 0\ 75$, the fraction $(1-\varepsilon)$ of the incident radiation that is not absorbed by the surface being specularly reflected by it, the flux of radiation across the mouth is found to be short of that from a black-body by only 0·23 per cent. As emphasized in the communication, the approach to black-body radiation holds over the whole of the 2π solid angle, unlike in the corresponding case when the walls of the cylinder have a matt surface.

Thus for a given emissivity the cylinder with specularly reflecting walls has a distinct advantage, as a source of black-body radiation, over one with a matt surface. For a given material, however, the effective emissivity will be markedly greater when the surface is matt than when it is polished.

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GEOCHEMISTRY

Trace Element Relationships and Terrestrial Origin of Tektites

RECENTLY, Cherry, Taylor, and Sachs[1] reported from an examination of australite data "that silica concentration is significantly negatively correlated with the concentrations of aluminium oxide, ferrous oxide, magnesium oxide, potassium monoxide, and calcium oxide". Further, they suggest that tektite composition can be explained as the result of a mixing process between silica and some other material such as shale.

It would appear that the possibility of partial volatilization of several of the component oxides during formation of the tektite glass has not been considered by many workers in this field. If tektites were produced suddenly at temperatures near the boiling point of some of the components, then heavy losses of oxides more volatile than silica should follow. The silica content would also decrease somewhat from loss of SiO. Oxides of higher boiling point than silica, namely, aluminium oxide, ferrous oxide, magnesium oxide, and calcium oxide, would be enhanced in the resulting glass. This would account for the negative correlation of these oxides with silica without invoking a mixing of two materials such as shale and quartz. Recent work of Friedman, Thorpe, and Senftle[2] tends to confirm this point of view.

Table 1 compares three tektites of different ages but similar silica content with a quartz-porphyry of comparable silica content. It is seen that the tektites in general are higher in alumina, ferrous oxide, calcium oxide, and magnesium oxide and lower in sodium oxide and potassium oxide than the igneous quartz-porphyry.

Table 1. COMPARISON OF COMPOSITION OF THREE TEKTITES FROM DIFFERENT FALLS WITH A QUARTZ-PORPHYRY

	1	2	3	4
SiO_2	76 56	80 52	79·51	79·75
Al_2O_3	11 54	9 44	10 56	10·47
Fe_2O_3	0·17	—	0 60	0 64
FeO	3·99	1 98	3·11	0·92
CaO	1·62	1·84	1·48	0·15
MgO	3·60	1·73	1·35	0·13
MnO	0·08	0 09	0·06	Trace
Na_2O	1 32	0·52	0 91	1·36
K_2O	0·82	3 15	1 25	6·01
TiO_2	0·60	0 72	0 63	0 15

Col. 1, Composition of an Ivory Coast tektite, analysis quoted by Barnes (ref. 3); col. 2, composition of a moldavite, analysis quoted by Barnes (ref. 3); col. 3, composition of an australite, analysis quoted by Barnes (ref. 3); col. 4, composition of a quartz-porphyry, analysis quoted by Iddings (ref. 4).

In order to test the proposition that tektites are produced at high temperatures and volatilization had taken place, the gallium/germanium ratios of a series of tektites and related terrestrial materials have been determined; the gallium oxide (Ga_2O_3) being less volatile and germania (as GeO) more volatile than silica (as SiO). Table 2 gives the results of some of these analyses. It is clearly seen that tektites have higher gallium/germanium ratios than terrestrial impactite glasses (Aouelloul glass, Darwin glass, and pumice glass, Cañon Diablo, Arizona), sand (Něchov, Czechoslovakia), and sandstones (Aouelloul sandstone, Cañon Diablo sandstone). That there is volatilization taking place in tektites is clearly brought out in the australite example where the second melting producing the flange has caused an increase in the gallium content over that found in the core. The Aouelloul impact glass shows an increase in gallium and decrease in germanium over the sandstone at the crater. Here the temperature was so intense that crystallites are absent in the glass. Darwin glass shows a higher germanium content than has been found in any tektite. In contrast to Aouelloul impact glass the pumice glass from Cañon Diablo crater did not reach a high enough temperature to form a compact glass and melt the coesite present (in the sample examined) and shows little change in Ga/Ge ratio. In confirmation of the work of Chao, Shoemaker, and Madsen[5], the main crystalline constituent in this glass was found to be coesite (by X-ray diffraction). The tektites in general have gallium contents of 0·9–9·8 p.p.m. and germanium contents of 0 06–0·40 p.p.m. Analyses for a given tektite fall are consistent for cores.

The high temperature of formation of tektite glasses, the quenching of the melt before thorough mixing can take place, and the shapes (before secondary melting), all indicate that the formation of these glasses is from impact. As Urey has suggested[6], a thorough search should be continued for explosion

Table 2. GALLIUM/GERMANIUM RATIOS OF TEKTITES, IMPACTITES AND RELATED MATERIALS

	Ga (p.p.m.)	Ge (p.p.m.)	Ga/Ge
Moldavite, Něchov, Czechoslovakia	3 1	0·15	21
Sand, Něchov, Czechoslovakia	9·6	1 64	6
Australite (core)	0 9	0 06	15
Australite (flange), same specimen	1 5	0·04	37
Aouelloul glass	4 7	0 67	7
Aouelloul sandstone	3 0	1·38	2
Darwin glass, Tasmania	2 5	0 58	4
Pumice glass, Cañon Diablo, Arizona	1 5	0·44	3
Sandstone, Cañon Diablo, Arizona	1 5	0·40	4
Tektite, Thailand	9·0	0·20	45
Indochinite, Dalat, S. Annam	8 2	0 21	39
Tektite, Ivory Coast	9·8	0·35	28
Billitonite	8 2	0 40	20
Tektite, Anda, Philippine Islands	7 1	0·40	18
Javanite	4 6	0 34	14

craters large enough to account for tektite formation as a terrestrial event.

Mr. J. Anania and Mrs. S. A. Todd performed the analyses, and Dr. S. Pollack made the X-ray determination of coesite. Detailed publication of gallium/germanium ratios of additional tektites, meteorites, and related materials will be made elsewhere.

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CHEMISTRY

Crystallinity of Calcium Chondroitin Sulphate

WELL-DEFINED macroscopic shapes containing symmetry elements are generally regarded as a sign of crystalline arrangement of molecules. Recently, Kargin[1] demonstrated that polymer molecules might have a regular geometrical aggregate as viewed in the electron microscope without being crystalline so far as X-ray diffraction measurement is concerned and vice versa. In our work with calcium chondroitin sulphate *A* we encountered apparently a similar phenomenon. Einbinder and Schubert[2] reported that calcium chondroitin sulphate (their so-called mid and tail fraction) showed crystalline shapes under the microscope when precipitated with ethanol from aqueous solution. These same fractions, however, proved to be amorphous in our X-ray diffraction experiments. Further investigation also revealed that the 'head' fraction of calcium chondroitin sulphate which Einbinder and Schubert[2] reported as amorphous under the microscope was highly crystalline in X-ray diffraction studies. Detailed analysis of these results will be reported elsewhere.

All three fractions of calcium chondroitin sulphate *A* were isolated from acetone-dried bovine trachea according to the method A_2 of Einbinder and Schubert[2] (extraction with aqueous potassium chloride and potassium carbonate, repeated purification with kaolin, dialysis, precipitation of the potassium salt and finally conversion to calcium salt). The yield was comparable to that reported previously. However, the crystalline 'head' fraction had a high ash content, and further purification was necessary. This was achieved by redissolving this fraction in distilled water, centrifuging at 6,000 r.p.m. for 20 min. and precipitating the supernatant with 3 vol. of absolute ethanol. Only about 10 per cent of the original head fraction was recovered this way. This new isolated head fraction was highly crystalline and had the following micro-analysis: C = 33·34 per cent, H = 6·08 per cent, N = 2·96 per cent, S = 2·05 per cent, Ca = 2·70 per cent. The theoretical value for a new type of calcium chondroitin sulphate which is sulphated only at every third chondroitin unit with 5 moles of water of hydration per chondroitin ($C_{41}O_{23}H_{33}N_3SO_3Ca.15H_2O$) would be C = 33·02 per cent, H = 6·03 per cent, N = 2·75 per cent, S = 2·09 per cent, and C = 2·62 per cent.

The middle and tail fractions of calcium chondroitin sulphate *A* had the following microanalysis:

	C	H	N	S	Ca
Mid	27·95	5·49	2·31	4·90	5·99
Tail	28·09	5·50	2·31	4·46	6·00
Theoretical of repeating unit of calcium chondroitin sulphate *A* ($C_{14}H_{18}NSO_{14}Ca.5H_2O$)	28·61	4·98	2·39	5·45	6·81

All three fractions indicated the same two spots on paper chromatography of their acid hydrolysate: glucuronic acid and galactosamine. Infra-red absorption spectra of the fractions were taken by a double-beam Beckman *IR*-7 spectrophotometer on films of 0·02 mm. thickness. The infra-red spectra of the middle and tail fractions were identical, and, therefore, only one is reproduced in Fig. 1. On the other hand, the head fractions showed distinct differences. The most important among these are the absence of the sulphate band at 725 cm.$^{-1}$ and the shift of the band from 928 to 955 cm.$^{-1}$. Similarly the sulphate band[3,4] at 1,240 cm.$^{-1}$ has greater intensity in the tail fraction than in the crystalline head fraction. The band between 1,000 and 1,150 cm.$^{-1}$ is broader in the case of the crystalline fraction, possibly indicating hydrogen bonding of primary and secondary alcohols with other polar groups which is lessened if the polymer chain is more highly sulphated (tail fraction).

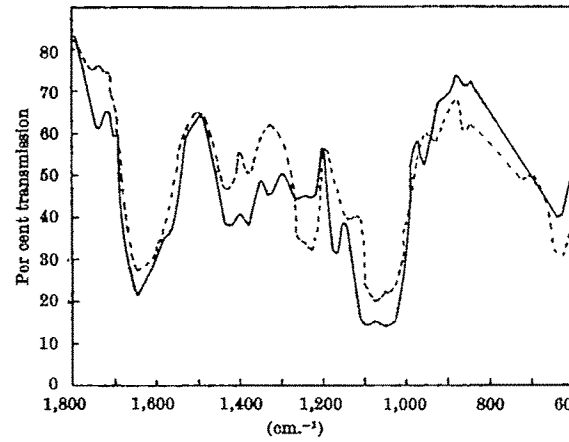

Fig. 1. Infra-red absorption spectra of the head fraction (——) and the tail fraction (- - - - -) of calcium chondroitin sulphate from bovine trachea

One might come to the general conclusion with respect to structure and crystallinity among the chondroitin sulphate isomers as follows: the crystalline 'head' fraction is a calcium chondroitin sulphate polymer sulphated only at every third chondroitin moiety, as both infra-red and microanalysis indicate. Due to the fact that this fraction went through only the mildest additional treatment (centrifuging and reprecipitating) it is unlikely that this is an artefact of the preparation. The intrinsic viscosity in 0·1 *M* sodium chloride solution of this fraction was the lowest, 0·22 dl./g., compared with 3·09 dl./g. of the middle fraction and 0·9 dl./g. of the tail fraction. Its precipitation with the smallest concentration ethanol also indicates that the head fraction is less polar than the other two fractions which are actually precipitated according to their molecular weights.

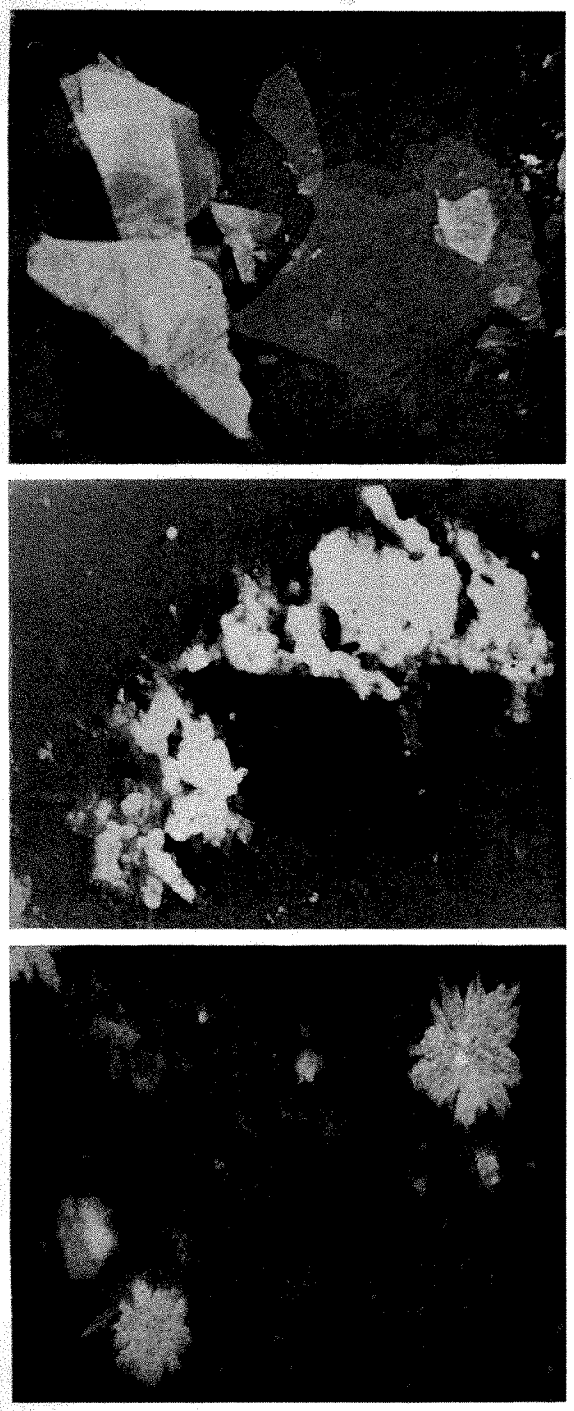

Fig. 2. Electron micrographs of calcium chondroitin sulphate precipitated with ethanol from aqueous solution. Platinum shadow casting. Black lines indicate 1μ. Top, head fraction; middle, mid fraction; bottom, tail fraction

Thus it seems plausible that the frequent and bulky side groups of sulphate prevent crystalline alignment of the chains, and one gets ordered polymer regions only when the degree of sulphation is reduced together with shorter polymer chains.

In the light of the above conclusion we wanted to investigate whether Kargin's observation can apply to chondroitin sulphate, that is, whether the microscopic structure has anything to do with the molecular organization. Electron micrographs were taken with an RCA *EMU 2B* electron microscope under conditions described previously[5]. The three fractions isolated were dissolved in distilled water and reprecipitated in ethanol, and a loopful of the colloidal suspension was placed on a screen 15 min. after the addition of ethanol and shadowed with platinum. The electron micrographs are shown in Fig. 2.

The head fraction, which showed high crystallinity in X-ray diffraction, formed sheet-like aggregates sometimes with well-defined edges. This is not unlike those electron microscopic structures one observes in polycrystalline synthetic high polymers such as polyethylene.

The higher-molecular weight calcium chondroitin sulphate *A* (mid fraction), which was completely amorphous in X-ray diffraction, showed also completely amorphous aggregation in the electron microscope.

The tail fractions aggregated in shapes similar to those observed by Einbinder and Schubert[2]. These aggregates had orderly regions comparable to liquids only as viewed by X-ray diffraction. Still, there was a certain amount of symmetry although they lacked the higher symmetry elements of crystals. Probably this was a fraction with low enough molecular weight to provide anisotropic chains for orientation, but still having enough bulky side-groups to prevent orderly alignment. This, therefore, may represent Kargin's transition group between geometrical crystallinity and the completely amorphous state.

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Preparation of Silver Iodide Sol by Ion-exchange Resin

WHEN preparing a silver iodide sol by mixing solutions of silver nitrate and potassium iodide:

$$AgNO_3 + 2KI \rightarrow AgI\ I^-/K^+ + KNO_3$$

the electrolyte potassium nitrate has to be removed.

The use of electrodialysis is a very elaborate process, so the obvious thing is to replace it by ion-exchange resins.

This method has two drawbacks:

(1) a strongly basic anion-exchange resin adsorbs part of the sol particles;

(2) a weakly basic resin gives organic impurities to the sol.

My experiments showed that extracting the resin with water in a Soxhlet for 24 hr. is sufficient to remove these impurities completely.

This effect is clearly demonstrated by the conductivity of the effluent water of the ion-exchange columns of extracted and non-extracted resin respectively.

Table 1

$\sigma \times 10^{-6}\ \Omega^{-1}$ cm.$^{-1}$ effluent water	Before	After
Strongly acid resin	20	2–4
Weakly basic resin	20–200	2–4

Solutions of 200 m.mol. silver nitrate/l. and 220 m.mol. potassium iodide/l. (10 per cent excess) were used. The strongly acid exchange resin was 'Amberlite *IR* 120 *H*', the weakly basic 'Amberlite *IR* 45'.

The sol mixture was first sent over the strongly acid resin, the weakly basic reacting only in the *p*H interval 0–7.

By this method an 80 per cent yield of sol was obtained, with a conductivity of $\sigma = 2$ to 3×10^{-5} Ω^{-1} cm.$^{-1}$.

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Oscillographic Polarography of Highly Polymerized Deoxyribonucleic Acid

Proceeding from my finding[1,2] that nucleotides, nucleosides and the bases of nucleic acids can be analysed by alternating current oscillographic polarography[3–5], I have also tried to study polymerized deoxyribonucleic acid by this method.

The apparatus used was a Polaroskop *P* 524 (Křižík, Praha). With this apparatus it is posssible to plot dE/dt against E (Fig. 1). The analysis was carried out by means of the dropping mercury electrode in the same electrolytes as were used in my previous work[1,2]. All measurements were carried out with specimens of deoxyribonucleic acid from calf thymus.

I have established that in a medium of molar ammonium formate, deoxyribonucleic acid shows an anodic indentation at the same potential as deoxyguanylic acid (Fig. 2). Other characteristics of both indentations are also analogous (dependence on direct voltage, temperature, concentration of the electrolyte), which appears to indicate that that due to deoxyribonucleic acid is brought about by deoxyguanylic acid bound in the molecule of deoxyribonucleic acid. In order to verify this observation, I removed the adenine and guanine from the deoxyribonucleic acid molecule by treating it with dilute hydrochloric acid (*p*H 1·6, 37° C.)[6], and analysed the apurinic acid obtained in this way by oscillographic polarography in ammonium formate as medium. No characteristic anodic indentation was observed on the oscillogram; but, on the contrary, a new cathodic indentation was formed approximately in the same region where an indentation is produced by deoxycytidilic acid under similar conditions (Fig. 3). This indentation is shown even after drastic denaturation of deoxyribonucleic acid and, in fact, becomes deeper.

Thus in non-denaturated deoxyribonucleic acid, deoxyguanylic acid reacts oscillo-polarographically,

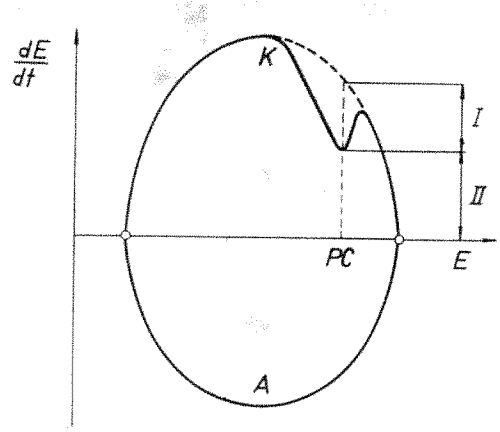

Fig. 1. Graph of dE/dt against E. The nature of the material analysed is characterized by the potential of the indentation (*PC*), which is somewhat similar to the polarographic half-wave potential. The quantity of the material is characterized by the depth of the indentation. For qualitative analysis, the height II, which can be measured much more easily, is generally measured. *K*, Cathodic part; *A*, anodic part

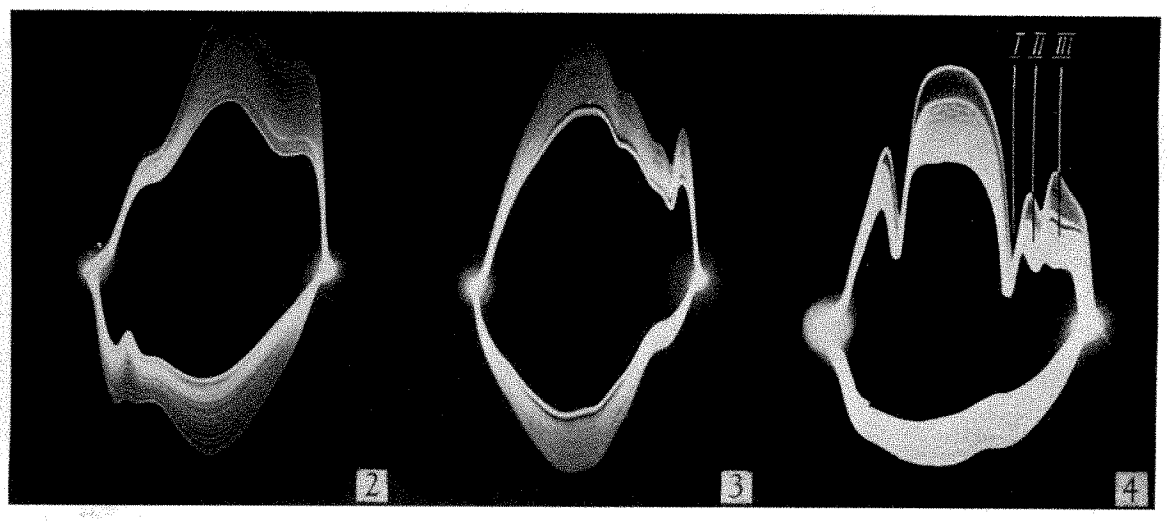

Fig. 2. 100 μgm. deoxyribonucleic acid/ml. 1 *M* ammonium formate
Fig. 3. Apurinic acid in 2 *M* ammonium formate (concentration corresponding to 2 mgm. of deoxyribonucleic acid)
Fig. 4. 900 μgm. deoxyribonucleic acid + 5 μgm. plasma albumin/1 ml. 10^{-3} *M* hexamine cobaltic trichloride in 0·1 *M* ammonium chloride-ammonium hydroxide. Indentations due to cobalt, I; deoxyribonucleic acid, II; protein, III

whereas deoxycytidylic acid bound in its molecule is inactive. This phenomenon may be perhaps interpreted in the following manner: one part of the guanine purine ring, which is of great importance for the formation of the anodic indentation (apparently an amino-group in position 2 is involved[2]), is found in the molecule near the surface, whereas the analogous part of the pyrimidine ring of cytosine (apparently the 6-amino-group[2]) is hidden inside the molecule where it participates in the formation of the hydrogen bond. In apurinic acid, where the double-helical structure is completely destroyed, deoxycytidylic acid is not blocked sterically in any way so that its oscillo-polarographic activity may manifest itself. Free deoxyadenylic acid and deoxythymidylic acid do not show the characteristic indentation in ammonium formate as medium, and consequently no indentations due to these nucleotides can be expected if they are bound in the molecule of deoxyribonucleic acid.

I have also studied deoxyribonucleic acid and apurinic acid in 2 *M* sodium chloride as medium; both substances yield oscillograms that differ only slightly. In 1 *M* sodium hydroxide, the oscillograms of deoxyribonucleic acid differ considerably from those of apurinic acid.

In cobalt and nickel solutions[7], proteins give an indentation even at a very low concentration[8]. Since the deoxyribonucleic acid indentation is produced in this medium at a different potential, I was able to use the oscillopolarographic reaction for detecting deoxyribonucleic acid and proteins in the presence of each other. In this manner, proteins can be detected even in the presence of an abundance of deoxyribonucleic acid (Fig. 4).

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Fluorescence of Organic Traces in Inorganic Substances

IN previous publications[1] I have directed attention to the fluorescence due to traces of organic substances in commercial inorganic chemicals and in minerals. What was not clear was the relation of my experiments to the somewhat similar ones of Ewles[2]. Recent investigations have now convinced me that we were observing two quite different phenomena. This is best shown by the following experiments:

(1) Exciting alumina (Merck, for chromatography) with 254 mμ, I obtain fluorescence that is not enhanced by weak annealing and not destroyed by 1 min. at red heat, and also phosphorescence, in perfect agreement with Ewles, who had to heat his samples for hours at high temperatures to get rid of the fluorescence. I find, however, that the phosphorescence no longer appears after 1 min at red heat and is not regenerated by adding traces of organic substances.

(2) On the other hand, on exciting alumina which has been exposed to atmospheric dust with 365 mμ, there is no noticeable phosphorescence, and the fluorescence is enhanced by weak annealing, destroyed by 1 min. at red heat and regenerated by weak annealing after adding traces of organic substances.

Under condition (1) we have the Ewles effect: luminescence of adsorbed water or other substances containing the OH-group; under condition (2) fluorescence of organic traces occurs.

The latter, frequent in minerals, has now also been found in certain meteorites: Hvittis (Finland), Stannern (Moravia); it remains to be seen if these have acquired traces of organic substances after their arrival on the Earth or already in outer space.

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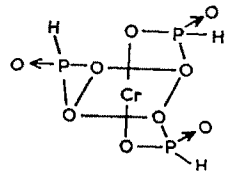
Triphosphitochromic Acid

TRIVALENT chromium forms, with dibasic anions of oxygen-containing acids, complex ions of the type $[Cr(AA)_3]^{3-}$, in which the ligands are bound to the central atom through oxygen atoms. The best-known representatives of this group of compounds are trisulphatochromates(III)[1,2] and complex anions with organic acids[3], for example, with oxalic[4,5] and lactic[6] acid. The complex with lactic acid is the stable and relatively strong trilactatochromic acid $H_3[Crlact_3]$. The phosphite anion, which may also act as a bidentate oxoligand[7], forms a similar triphosphitochromic acid $H_3[Cr(HPO_3)_3]$.

Free triphosphitochromic acid can be prepared in crystalline form by dissolving freshly precipitated chromic hydroxide (precipitated by ammonia at *p*H ~ 8) in a boiling aqueous solution of phosphorous acid, followed by crystallization. The decahydrate of triphosphitochromic acid is obtained, forming green crystals soluble in water and methyl alcohol, practically insoluble in ethyl alcohol and ether, of density 2·03 at 20° C. The complex is paramagnetic, having a molar magnetic susceptibility of $7 \cdot 8 \times 10^{-3}$ at 20° C. The compound liberates its ten water molecules at 40° C. The conductometric and *p*H metric titration of triphosphitochromic acid solutions by sodium hydroxide show that the compound prepared is a tri-basic acid ($K_1 \sim 2 \times 10^{-3}$, $K_2 \sim 4 \times 10^{-6}$, $K_3 \sim 4 \times 10^{-7}$) and forms sodium and ammonium salts easily soluble in water, and salts of alkaline earths, transition and heavy metals which are only slightly soluble. The ammonium salt $(NH_4)_3[Cr(HPO_3)_3].6H_2O$, sodium salt $Na_3[Cr(HPO_3)_3].4H_2O$ and barium salt $Ba_3[Cr(HPO_3)_3]_2.8H_2O$, have been prepared in the crystalline state. Aqueous solutions of the acid and its salts show, as may have been expected, reducing properties, and reduce, for example, after standing for some time, silver salts to metallic silver. The reduction, however, takes place much more slowly than with the free, non-complex phosphite anion.



Similarly to the trioxalatochromic anion[5], the triphosphitochromic anion must also, because of its proposed structure, have optical isomerism. This has been proved experimentally by transforming triphosphitochromic acid via the tri-*d*-strychnine salt to optically active sodium *d*-triphosphitochromate(III). Compounds containing the triphosphitochromic anion in one of its stereoisomeric forms, however, are rapidly autoracemized in aqueous solution, so that it has been impossible to determine the value of molecular rotation, or to separate the other stereoisomer. The triphosphitochromic anion is, however, interesting by the fact that it is a further representative of the, as yet very rare, type of purely inorganic (that is, carbon-free) optically active compound.

The determination of the instability constant of the triphosphitochromic anion, which has been carried out by *p*H-measurements and by spectrophotometric methods, has shown that the anion is highly complex ($K \sim 2 \times 10^{-11}$); this is surprising because of the presence of three four-membered rings in the molecule. In some analytical reactions, masking of chromium is, in fact, observed. It is, for example, impossible to precipitate either chromic hydroxide or phosphate from solutions of the triphosphitochromic anion.

In comparison with the other anionic oxo-complexes of trivalent chromium, the free acids of which are known either only in dilute solutions (trilactatochromic acid or other complexes with organic acids), or are not defined in the crystalline state (trisulphatochromic acid), or lastly are totally unknown in the free state (trioxalatochromic acid), the triphosphitochromic anion is remarkable for the fact that free triphosphitochromic acid is stable and well defined even in the crystalline state.

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BIOCHEMISTRY

Effects of α-Lipoic Acid on the Respiratory Chain of Plant Mitochondria

THIS communication describes the effects of oxidized α-lipoate (6:8-dithio-*n*-octanoate) on the respiration and oxidative phosphorylation of mitochondria isolated from red beetroot (*Beta vulgaris* L.)[1]. Both spectrophotometric (Table 1) and manometric (Table 2) results showed that added lipoate (0·1 m*M*) caused substantial inhibition of the oxidation of reduced coenzyme I and of coenzyme I-linked substrates with oxygen, ferricytochrome *c* and 2:6-dichlorophenol indophenol as oxidants. However, the oxidation of succinate was not inhibited by lipoate at 0·1 m*M* concentration (Table 1). Lipoate caused a marked stimulation (about 100 per cent) of the succinate–cytochrome *c* reductase activity of mitochondria modified by freezing and thawing or by exposure to hypotonic conditions.

Table 1. EFFECTS OF OXIDIZED LIPOATE ON ENZYMIC ACTIVITIES OF MITOCHONDRIA FROM BEETROOT

Substrate	Oxidant	Enzymic activities*	
		Control	With lipoate (0·1 m*M*)
Reduced coenzyme I (0·13 m*M*)	oxygen†	0·67	0·17
	ferricytochrome *c* (60 μ*M*)	3·77	1·18
	dye ‡ (65 μ*M*)	6·73	4·53
Malate (50 m*M*)	ferricytochrome *c* (60 μ*M*)	0·29	0·08
Malate (50 m*M*) plus coenzyme I (0·13 m*M*)	ferricytochrome *c* (60 μ*M*)	0·87	0·14
Succinate (50 m*M*)	ferricytochrome *c* (60 μ*M*)	0·34	0·31
	dye‡ (65 μ*M*)	1·25	1·26
Ferrocytochrome *c* (60 μ*M*)	oxygen†	5·44	9·73

* Changes in extinction were determined spectrophotometrically at 340 mμ for coenzyme I, at 550 mμ for cytochrome *c*, and at 600 mμ for 2,6-dichlorophenol indophenol. Results are expressed as ΔE/min./mgm. of mitochondrial nitrogen at room temperature (about 25° C.), for 3 ml. of reactants in 1-cm. cells.

† Solutions were equilibrated with air.

‡ 2:6-dichlorophenol indophenol.

As shown in Table 2, esterification of inorganic phosphate was more strongly inhibited by added lipoate than was substrate oxidation. Other results with α-ketoglutarate and with pyruvate as substrates suggest that the substrate-level phosphorylation may not be inhibited. Lipoate had little effect on the adenosine-triphosphatase activity of beetroot mitochondria with or without added magnesium chloride.

Sodium arsenite (1 m*M*) did not affect the inhibition of the oxidation of reduced coenzyme I caused by oxidized lipoate, whereas it prevented a small progressive inhibition caused by reduced α-lipoate (6:8-dimercapto-*n*-octanoate). The action of the dimercaptan is attributed to progressive formation of oxidized lipoate. The effects shown in Tables 1 and 2 do not appear to involve dimercaptan formed enzymically in the mitochondria.

The effects shown in Tables 1 and 2 could not be duplicated with short-chain fatty acids (*n*-valerate, *n*-caprate, *n*-caprylate, *n*-caproate), nor with cysteine, cystine, oxidized glutathione or 2:3-dimercaptopropanol (BAL). Although the oxidation of reduced coenzyme I was inhibited (56 per cent) by BAL (10 m*M*), the presence of BAL did not interfere with the inhibitory effect of oxidized lipoate. Bovine serum albumin (0·17 per cent), but not ethylenediamine tetraacetate or ascorbate, prevented the inhibitory effect of lipoate on the oxidation of reduced coenzyme I; presumably albumin binds lipoate. Cystine (0·1 m*M*) caused an inhibition (60 per cent) of cytochrome *c* oxidase activity in contrast to the stimulation caused by lipoate (Table 1).

Table 2. EFFECT OF OXIDIZED LIPOATE ON OXIDATIVE PHOSPHORYLATION CATALYSED BY MITOCHONDRIA FROM RED BEETROOT*

Expt.	Substrate	Control			With lipoate			
		$Q^N_{O_2}$	P/N	P/O	Lipoate concentration	$Q^N_{O_2}$	P/N	P/O
1	α-ketoglutarate (50 m*M*) + malonate (50 m*M*)	225	43 6	2·95	0 5 m*M*	26 0	1 1	1·03
2	Malate (50 m*M*)	149	24 9	1 87	0 1 m*M*	50	5 8	1 34
					0 5 m*M*	16	0 8	0·56
	Malate (50 m*M*) plus coenzyme I (0·48 m*M*)	195	31·4	1 80	0·1 m*M*	54	5·5	1·14
					0 5 m*M*	34	0 7	0·24
3	Succinate (50 m*M*)	441	41·3	1 05	0·1 m*M*	455	23·5	0 58
					0·5 m*M*	177	0	0
4	Malate (50 m*M*)	241	23 6	1 64	0 1 m*M*	91	5 4	1 00
	Malate (50 m*M*) plus 2:4-dinitrophenol (0 1 m*M*)	224	—	—	0·1 m*M*	74	—	—

* Measurements were carried out manometrically at 25° C.; the esterified phosphate was estimated as glucose-6-phosphate as previously described (ref. 1).

$Q^N_{O_2}$ is μlitres of oxygen/hr./mgm. of mitochondrial nitrogen.

P/N is μmoles of orthophosphate esterified/hr /mgm. of nitrogen, and P/O is ratio of moles of orthophosphate esterified to atoms of oxygen consumed.

The effects of lipoate were quite different from those obtained with other respiratory chain inhibitors[1,2] such as amytal, antimycin *A* and 2-hydroxy-3-(2-methyloctyl)-4-hydroxyquinoline-N-oxide and no competitive or synergistic effects were observed when each of these compounds was added with lipoate. Whereas oxidized lipoate had little effect on succinate–cytochrome *c* reductase activity of fresh mitochondrial preparations (Table 1), antimycin *A* and 2-hydroxy-3-(2-methyloctyl)-4-hydroxyquinoline-N-oxide were strongly inhibitory[1,2]. However, prolonged incubation with oxidized α-lipoate particularly at 0·5 m*M* concentration, caused inhibition of the succinate–cytochrome *c* reductase and of succinate oxidase (see Table 2). Oxidized lipoate also differed from amytal in causing a somewhat similar inhibition of oxidation of reduced coenzyme I with either ferricytochrome *c* or 2:6-dichlorophenol indophenol as oxidant (Tables 1 and 3).

Extinction changes measured at 520 mμ showed that lipoate at 0·1 m*M* had little effect on the swelling of freshly isolated mitochondria. However, a pronounced effect was obtained at 0·5 m*M* lipoate. The swelling was enhanced by the addition of substrates and was reversed with adenosine triphosphate (5 m*M*) plus magnesium chloride (3 m*M*) and prevented with bovine serum albumin (0·17 per cent). However, the effects of lipoate on the enzymic systems of both beetroot mitochondria damaged by hypotonicity or by freezing, and optically clear suspensions obtained by treatment of mitochondria with sodium deoxycholate, were similar to the effects observed with intact mitochondria. Thus the lipoate-induced swelling does not account fully for the effects shown in Tables 1–3.

Table 3. COMPARATIVE EFFECTS OF OXIDIZED α-LIPOATE AND AMYTAL ON THE ENZYMIC REDUCTION OF 2:6-DICHLOROPHENOL INDOPHENOL CATALYSED BY THE BEETROOT MITOCHONDRIA

Substrate	Enzymic activities*			
	Control	with α-lipoate (0 1 m*M*)	with amytal (3·6 m*M*)	with lipoate (0 1 m*M*) plus amytal (3 6 m*M*)
Reduced coenzyme 1 (0 26 m*M*)	8·55	5·86	8 42	5 71
Malate (50 m*M*)	2 64	0 82	2 19	0 98
Malate (50 m*M*) plus coenzyme 1 (0·48 m*M*)	5 32	1·50	5·20	1·78

* ΔE/min./mgm. of mitochondrial nitrogen; see Table 1

Similar effects to those shown in Tables 1 and 2 have been obtained with mitochondria isolated from wheat roots, silver-beet petioles, cauliflower buds and pea cotyledons. The aerobic oxidation of reduced coenzyme I by rat-liver mitochondria was inhibited (50 per cent) by lipoate (0·1 m*M*). The effects on other enzymic systems of animal mitochondria are being further studied.

The effects of lipoate described here do not appear to involve the coenzyme function of lipoate in the oxidative decarboxylation of α-keto acids. The stimulation of cytochrome *c* oxidase, the induced swelling and the activation of succinate–cytochrome *c* reductase may all reflect the ability of lipoate to form a complex with lipoproteins. The inhibition of coenzyme I oxidation (Table 1) and the uncoupling of phosphorylation (Table 2) are more clearly associated with the disulphide bond of oxidized lipoate. Lipoate appears to act on, or very close to, the dehydrogenase which activates coenzyme I (Tables 1 and 3). Reduced coenzyme I–cytochrome *c* reductase as extracted from heart muscle mitochondria is a flavoprotein which requires intact sulphydryl groups for activity[3,4]. Recently, Green and co-workers[5] found that this enzyme is inhibited by 1 m*M* concentrations of dimercaptans (BAL, lipoate and lipoamide) which would have been rapidly oxidized. Dixon *et al.*[6] have recently found that the enzyme is inactivated by oxygen with concomitant displacement of the flavin prosthetic group, possibly due to oxidation of —SH groups of the enzyme (see ref. 7).

It is suggested that the inhibition of the respiratory chain oxidation of reduced coenzyme I (Tables 1–3) is due to inhibition of the primary dehydrogenase by oxidized lipoate which may enter into

—SH . . . . —S—S—

exchange reactions[8], with sulphydryl groups essential for the dehydrogenase activity. The uncoupling of oxidative phosphorylation by lipoate may be due to a

similar type of exchange reaction with sulphydryl groups essential for phosphorylation[9].

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A Factor in Agar which reverses the Antibacterial Activity of 1-Methyl-3-nitro-1-nitrosoguanidine

WHILE working with 1-methyl-3-nitro-1-nitrosoguanidine, an anticancer agent in mice[1,2] and an antibacterial agent *in vitro*, we observed that Difco agar contained a factor which inhibited the activity of 1-methyl-3-nitro-1-nitrosoguanidine against *Escherichia coli* strain S. The activity of this compound was tested by the filter paper disk-assay method on minimal[3] medium *p*H 6·8, containing 2 per cent agar. The zones of inhibition were smaller when the medium was sterilized by steaming for 20 min. than when sterilized by autoclaving (15 lb./sq. in.) for the same length of time (Table 1). Several lots of Difco agar had the same property, but other commercially available agars did not. These latters agars are: *BBL* (Baltimore Biological Laboratory), *NBC* (Nutritional Biochemical Co.), 'Ion Agar No. 2' (Oxo, Ltd., London), and Difco 'Noble Agar'.

Difco agar was freed of the factor by extraction with water or methyl alcohol, but not with ethyl alcohol, acetone, or butanol. The aqueous or methanol extracts (vacuum dried and reconstituted in water) reversed the effect of 1-methyl-3-nitro-1-nitrosoguanidine when added to liquid cultures and assayed turbidimetrically. Aqueous extracts lost all activity within 24 hr. at room temperature, but were stable for at least four weeks at −10° C.

Table 1. EFFECT OF AGAR ON THE ACTIVITY OF 1-METHYL-3-NITRO-1-NITROSOGUANIDINE AGAINST *Escherichia coli*

Agar	Preparation	Diameter of zone of inhibition (mm.)*		
		40 μgm./disk	100 μgm./disk	200 μgm./disk
NBC†	Steamed	27	33	36
NBC†	Autoclaved	28	34	39
BBL‡	Steamed	25	31	35
BBL	Autoclaved	26	33	35
'Difco' Lot No. 616	Steamed	12	15	16
'Difco' Lot No. 616	Autoclaved	26	30	38
'Difco' Lot No. 188	Steamed	12	14	16
'Difco' Lot No. 188	Autoclaved	26	33	36

* 12-mm. filter paper disk. Incubation, 18 hr.; 37° C.
† Nutritional Biochemical Co., Cleveland, Ohio.
‡ Baltimore Biological Laboratory, Baltimore, Maryland.

The activity of 1-methyl-3-nitro-1-nitrosoguanidine is reversed by amino-acids, —SH compounds, methylamine and ascorbic acid (personal observation). The active extracts were ninhydrin-negative. Polarographic analysis revealed no —SH or S—S compounds. There was no detectable amount of ascorbic acid. The factor did not absorb ultra-violet light.

Compounds with biological properties similar to 1-methyl-3-nitro-1-nitrosoguanidine were tested for their response to the agar factor. The antibacterial activity of 11 nitrosoguanidines, differing only in the alkyl substituent on N–1, was reversed. Only 1-chloroethyl-3-nitro-1-nitrosoguanidine was not reversed even though the analogous compounds, 1-ethyl and 1-chloropropyl-3-nitro-1-nitrosoguanidines, were reversed. The activity of 1-nitroso-2-nitramino-2-imidazoline, a condensed nitrosoguanidine, and of 5-diazouracil was reversed, but that of nitrogen mustard, azaserine, 'Mitomycin *C*', β-propiolactone, 4-nitroquinoline-N-oxide was not. The agar factor had no effect on the antibacterial activity of penicillin, streptomycin, or aureomycin.

There is in Difco agar a water- and methanol-soluble, heat-unstable substance which reverses the antibacterial activity of the anticancer agents, 1-alkyl-3-nitro-1-nitrosoguanidines and 5-diazouracil. The isolation and identification of this factor might be helpful in elucidating the mechanism of action of these compounds.

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A New Approach to the Study of Thiamine Deficiency

IT is well known that dietary deficiency of thiamine impairs normal carbohydrate metabolism because of the role of cocarboxylase as coenzyme in the oxidative decarboxylation of pyruvate and α-ketoglutarate[1], and the transaldolation and transketolation[2] of aldoses and ketoses, which inhibit the liberation of the energy necessary to maintain tissue in its living state. Also, it has been shown that fat has a sparing action on the thiamine[3]; but little is known concerning protein metabolism in this form of avitaminosis.

Re-investigation[4] of this problem has shown that glyoxylic acid, a metabolic intermediate, arises from excessive breakdown of tissue protein; by radioactive isotopic tracer study, the origin of this acid was proved to be glycine. The presence of glyoxylic acid in normal animals is transient, since it can be reconverted into glycine or further metabolized into formate and then into carbon dioxide and water, or it can be excreted in the urine.

However, in animals deficient in thiamine, difficulties arise in the disposal of the glyoxylic acid. A block occurs in its enzymatic oxidative decarboxylation to formate, due to the absence of co-carboxylase[5]; as a result, various tissues may be affected by its cumulative toxic effect. The kidneys gradually lose their capacity to eliminate this acid, and thus aggravate its detrimental effect on all tissue metabolism. The syndrome seen in experimental animals is similar to the clinical findings in cases of thiamine deficiency.

It has been shown not only that fat spares thiamine, but also that a possibility exists that fat may provide ample amounts of acetyl–coenzyme *A* to condense with glyoxylic acid to form malate, thus annulling the detrimental effects of the glyoxylic acid. It has been suggested also that the glyoxylic acid condenses with a 4-carbon Krebs cycle intermediate to compete for the aconitase dehydrogenase system[6].

The present work also indicates that it cannot be assumed that an animal deficient in thiamine follows the same metabolic patterns as a normal animal, except for its inability to utilize carbohydrate properly. The whole metabolic pattern is altered, and it changes and shifts continually in order to fulfil the necessary energy requirements under this abnormal condition. The results indicate that the interdependency of the metabolism of carbohydrate, fat and protein is responsible for the underlying causes of this phenomenon.

A detailed account of this work will be published in due course.

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Re-assessment of the Stoichiometry of Photophosphorylation

THE light-induced phosphorylation of adenosine diphosphate to adenosine triphosphate by chloroplasts is associated with, and presumably coupled to, a transfer of electrons. In most of the systems investigated water has been the electron (or hydrogen) donor, and flavin mononucleotide, vitamin K_3, ferricyanide or triphosphopyridine nucleotide has been the electron (or hydrogen) acceptor. The early work was carried out on systems involving flavin mononucleotide or vitamin K_3 or both. Unfortunately the reduced forms of these substances are readily re-oxidized by molecular oxygen, and this re-oxidation of the electron acceptor by the oxidized electron donor resulted in a cyclic process in which the electron flux could not be measured. Consequently the stoichiometry of the reaction or reactions forming adenosine triphosphate could not be established. However, with the discovery that phosphorylation also accompanied the reduction of substances the reduced forms of which were not re-oxidized, this difficulty disappeared. Both Arnon and his associates[1] and Avron and Jagendorf[2] reported that one mole of adenosine triphosphate was formed for every two moles of electrons transferred in the reduction of ferricyanide or triphosphopyridine nucleotide. This stoichiometry has been widely quoted.

I have confirmed the observations of these workers. Indeed in 36 determinations involving ferricyanide reduction, it was found the ratio of adenosine triphosphate to electron pairs transferred was 1·00, with a standard error of the mean of only $\pm$ 0·017. Moreover, a similar stoichiometry for flavin reduction and adenosine triphosphate formation has been observed when precautions were taken to trap the hydrogen peroxide formed by the reaction of oxygen with reduced flavin mononucleotide[3]. Nevertheless, there are the following reasons for believing that this rather precise ratio of 1·00 is fortuitous and without biological significance.

(1) Unless the mechanisms coupling oxido-reductions to phosphorylation are exceedingly complex, the ratio of adenosine triphosphate to the electron pairs must be represented by a whole number. An experimental average of precisely unity suggests that the theoretical maximum is probably higher, since to establish the validity of a larger ratio, such as 2, it need only be established that any one experimental value is truly in excess of unity. On occasion, values of the ratio consistently greater than unity have been obtained, in spite of the fact that there are certain to be some biological and assay losses of adenosine triphosphate.

(2) The reduction of ferricyanide, triphosphopyridine nucleotide or flavin mononucleotide by illuminated chloroplasts can proceed in the absence of phosphorylation. The presence of optimal amounts of adenosine diphosphate, orthophosphate and magnesium ions increase this 'basic' rate two- to threefold. Therefore chloroplasts isolated by the methods currently employed must be equipped with a mechanism for electron transfer which is not coupled to phosphorylation. Obviously any electrons carried by this mechanism must be subtracted from the total flux before the stoichiometry of the reaction, which does involve phosphorylation, can be computed. Unfortunately, we only know with certainty the extent of this basic, non-phosphorylating process in the absence of phosphorylation; the simultaneous activity of the phosphorylating system might alter or almost abolish the 'uncoupled' reaction. Krogmann, Jagendorf and Avron[4] recognized the need to evaluate the competition between the systems, but were unable to come to any conclusion on the basis of the evidence then available. The new evidence presented below can be best interpreted by assuming the continuing existence of most of the basic, non-phosphorylating electron transport at all degrees of activation of the phosphorylating system. Consequently a revision of current estimates of the stoichiometry of the phosphorylating reaction is indicated.

Chloroplasts from the leaves of young pea plants were isolated, washed once and re-suspended in an ice-cold buffer consisting of 135 gm. sucrose, 3·0 gm. *tris*(hydroxymethyl)aminomethane and 1·0 gm. sodium chloride per litre, adjusted to *p*H 7·95 with sulphuric acid. An amount of this suspension containing about 50 μgm. chlorophyll was placed in a 1-cm.^{2} cuvette with buffer, adenosine triphosphate (5×10^{-4} *M*), magnesium sulphate (3×10^{-3} *M*), hexokinase (1·3 mgm.), glucose ($1{\cdot}5 \times 10^{-2}$ *M*) and 1·0 μmole potassium ferricyanide. Dipotassium hydrogen phosphate labelled with phosphorus-32 was added in

various amounts giving final concentrations from 5×10^{-4} M to 2×10^{-3} M. Total volume of the reaction mixture was 2·0 ml. Ferricyanide reduction was followed spectrophotometrically in an apparatus described elsewhere[5]. The formation of adenosine triphosphate was measured by the method of Nielsen and Leninger[6]. The chloroplasts were illuminated by red light at intensities well above saturation.

The levels of phosphate employed stimulated the rate of ferricyanide reduction from about 10 per cent to approximately 250 per cent. The rate in the absence of phosphate was re-determined every few minutes. By subtracting this rate from the rates observed with the various phosphate concentrations, rates were obtained which were attributed to the phosphorylating process. A proportion of the total ferricyanide reduction was thereby somewhat arbitrarily assigned in each case to the phosphorylating process. Obviously, if this procedure is valid, a linear relationship between the amount of adenosine triphosphate formed and the amount of ferricyanide reduction assigned to the phosphorylating process should be observed, the linearity being a measure of the validity of the assumption and the slope of the line giving a measure of the stoichiometry of the phosphorylating reaction.

Fig. 1 shows that the experimentally determined points do indeed lie reasonably close to a line which represents the ratio of adenosine triphosphate to electron pairs as 2. (The points nearest the origin are, of course, those least precisely located since they represent values obtained by the subtraction of two very similar rates. However, their position consistently above the line may well mean that the assumed complete independence of the phosphorylating and uncoupled processes is actually only an approximation of the truth.) This value of 2 agrees with the value obtained by Krogmann and Vennesland[7] for their 'oxidative' photophosphorylation, a phenomenon which is probably fundamentally related in some manner not yet elucidated to the 'reductive' photophosphorylation described here. It would appear, therefore, that chloroplast phosphorylations occur either at two oxido-reduction levels, each stage involving a two-electron shift, or alternatively, at a single level with the transfer of a single electron. In any event the implied formation of two molecules of adenosine triphosphate for each triphosphopyridine nucleotide ion reduced would furnish more than enough adenosine triphosphate for the operation of the photosynthetic cycle proposed by Calvin and his associates[8], whereas one molecule of adenosine triphosphate per reduced triphosphopyridine nucleotide molecule would be insufficient.

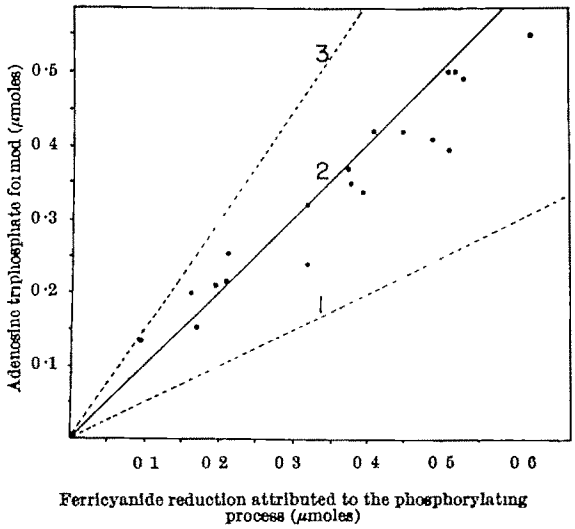

Fig. 1. Relationship between the amount of adenosine triphosphate formed and the amount of ferricyanide reduction which may be attributed to the phosphorylation-coupled electron-transfer system. In each event one micromole of potassium ferricyanide was reduced by illuminated pea chloroplasts in the presence of optimal concentrations of adenosine diphosphate, magnesium ions, hexokinase and glucose. The rates of reduction of ferricyanide and formation of adenosine triphosphate were varied by changing the phosphate concentration of the medium. The reduction to be attributed to the phosphorylating system (X) was calculated on the basis of the arbitrary assumption that the phosphorylating and non-phosphorylating systems were independent at high light intensities. Thus $X = A - B/A \times 1.0$ μmole, where A is the rate in the presence of phosphate and B is the rate in the absence of phosphate. Lines 1, 2 and 3 are the theoretical lines based on the above assumption with ratios of adenosine triphosphate to electron pairs equal to 1, 2 and 3 respectively

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Ramulosin, a $C_{10}H_{14}O_3$ Compound produced by the Fungus *Pestalotia ramulosa*

EARLY in 1959 we obtained through the courtesy of Dr. D. Brewer of the Atlantic Regional Laboratory a non-sporulating strain of *Pestalotia ramulosa* v. Beyma, an imperfect fungus belonging to the order Melanconiales. This strain was received as *Truncatella ramulosa* (v. Beyma) Steyaert, and is present in the Agricultural Research Service Culture Collection as *NRRL* 2826. When originally isolated by Brewer[1] from the tailing trough slime of a paper mill in New Brunswick, Canada, the organism formed spores typical of the species, but became asporogenous during subsequent transfers.

In the course of our culture work with this strain, we noticed copious formation of white crystals when the fungus was grown for 4–5 weeks at room temperature on malt extract agar (malt extract, 20 gm.; peptone, 1 gm.; *d*-glucose, 20 gm.; agar, 20 gm.; distilled water, 1,000 ml.). With the view of obtaining material for chemical investigation, we made a study of cultural conditions and found that in still culture as much as 370 mgm. of crystalline product accumulated on the surface of a nutrient solution (100 ml.) contained in an Erlenmeyer flask (300 ml.). A pure product (m.p. 121–122° C.), tentatively designated as ramulosin, was easily obtained by filtration, ether-acetone extraction of the dried mat, and recrystallization of the crude product from dilute alcohol. Elementary analyses and a Signer molecular weight determination showed the molecular formula to be $C_{10}H_{14}O_3$.

Optimum temperatures for growth and crystal formation have been determined to be about 20° C. and

15° C., respectively. Above 27° C., there is very little growth and no crystal formation. Still cultures in flasks at 15° C. showed visual evidence of crystal formation in about 26 days; the 370 mgm. yield we report was obtained in 93 days. *D*-glucose and *d*-glutamic acid appear to be the best carbon and nitrogen sources for crystal formation. No sporulation by *NRRL* 2826 has yet been observed by us. Two other strains of *Pestalotia ramulosa* which do sporulate did not produce crystals.

Chemical studies are in progress.

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Effect of Tetracycline Antibiotics on the Proteolysis of Fish Muscle

DURING recent experiments on the storage of herring over a 21-day period in normal ice and in ices containing chlortetracycline and oxytetracycline, an attempt was made to correlate changes in the bacterial flora with some of the changes which occur in the muscle.

Observations on the lower volatile fatty acids have already been reported[1], when it was found that the antibiotics did not affect their rate of production. This work has now been extended to the free amino-acids, estimated by the method of Moore, Spackman and Stein[2].

The results obtained showed that the changes occurring in the amino-acids followed a regular pattern. Proline, methionine, threonine, alanine, glutamic acid, lysine, valine, *iso*leucine and leucine showed a gradual increase up to around the fourteenth day, followed by a decrease. Phenylalanine, tyrosine and serine showed little change, while histidine, arginine and possibly glycine decreased steadily throughout the period.

In the cases where the amino-acid content changed over the period, there was always a larger residue in the treated, compared with the untreated, fish, this difference being greater at 14 days than at 7 days. Bacterial counts were lower on the skins of treated compared to untreated fish.

There are three possible explanations for these observations: (1) the activity of the selected bacterial flora may be greater than that of the flora on the untreated fish; (2) the selected flora are primarily proteolytic (*Pseudomonas* spp. and *Achromobacter* spp.), and even if their overall activity is not increased relative to the untreated fish, accumulation of amino-acids may occur due to the reduction of other groups which utilize them; (3) autolysis in the muscle may continue independently of the bacterial flora, amino-acids thus formed being utilized by bacteria. Reduction in the number of bacteria due to the presence of the antibiotics then leads to an accumulation of the acids in the treated fish.

There is reason to believe that the flora selected during antibiotic treatment is less active biochemically, particularly in the presence of the antibiotics[3-5]. Many enzyme systems are also depressed by antibiotics[6]. Thus it is unlikely that increased proteolysis occurs during antibiotic treatment, and it is therefore possible that the increased accumulation of the amino-acids in the treated fish was due to reason (3), the acids being produced autolytically, and their rate of accumulation governed by their assimilation rather than their production by bacteria. Furthermore, the observation that the increase in the amino-acids occurred during the first fourteen days of storage—before the stabilization of the dominant bacterial flora—again indicates that during the critical early stages of spoilage, proteolysis proceeds independently of the bacterial enzymes.

These results will be reported in greater detail elsewhere.

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Determination of Acid Phosphatase Activity in Cells of Prostatic Tumours

A SIMPLE technique by which cell material can be easily secured from prostatic tumours with the aid of transrectal aspiration biopsy has recently been described[1]. The material thus obtained was shown to consist largely of plugs of epithelial cells with occasional admixture of blood. In the present work these tissue fragments were isolated for determination of their acid phosphatase activity.

The aspirate from the prostatic gland was suspended in 10 c.c. citrate buffer of *p*H 4·9 (ref. 2), containing 0·015 per cent 'Triton *X*-100' (ref. 3) and rendered hypertonic by addition of 2 per cent sodium chloride in order to minimize diffusion of the enzyme from the cells[4]. The large tissue fragments consisting of epithelial cells were sedimented by horizontal centrifugation for about 20 sec. at 500 r.p.m. In this series of experiments the sediment was washed twice more by re-suspension and centrifugation in the above-described medium. The isolated and washed cell material was finally suspended in 2 c.c. citrate buffer of *p*H 4·9 and stored in a refrigerator at 4° C. for 24 hr. The acid phosphatase activity of the cell-containing buffer solution was then estimated roughly by dropping 0·01 c.c. of the supernatant on to test paper specific for acid phosphatase, as previously described[5]. Taking as a guide the intensity of the coloured spot on the test paper, it was possible to select an appropriate incubation time (15–180 min.) for obtaining extinction for the final solution within the limits of the spectrophotometer used. In order to evaluate the enzymic activity quantitatively, the centrifuge tube containing the cell material in 2 c.c. citrate buffer of *p*H 4·9 was placed in a water-bath at 37° C. for 5 min. Substrate (0·2 c.c. of 1 per cent solution of disodium phenyl phosphate) was added to the tube. After a given time based on

Table 1. ACID PHOSPHATASE ACTIVITY OF CELLS FROM PROSTATIC TUMOURS

Case No.	Diagnosis	Acid phosphatase activity* of isolated cell material	Protein content in micrograms	Acid phosphatase activity* per μgm. protein
1	Benign hypertrophy	457 527	45 37	10·2 14·2
2	Benign hypertrophy	1,134	294	3 9
3	Benign hypertrophy	2,267 831	96 52	26 6 16 0
4	Cancer	13·2 19 2	25 23	0·5 0·8
5	Cancer	14 0 6 9	49 52	0·3 0 1

* Enzymic activity expressed in μgm. phenol liberated during 1 hr.

the activity estimated by the test paper method, the reaction was arrested by addition of 2 c.c. saturated sodium fluoride solution. The tube was centrifuged for 5 min. at 5,000 r.p.m.; the supernatant was then decanted into a test-tube and the amount of phenol therein determined according to the method of Stolbach *et al.*[2], using a diazo reagent. The sedimented material was preserved for subsequent protein assay by the method of Lowry *et al.*[6].

The acid phosphatase activity of cell material isolated from prostatic tumours—in most cases two parallel determinations were performed—is shown in Table 1. Also shown is the total protein content of the sedimented material following incubation, as well as the acid phosphatase activity per μgm. of protein. It will be seen that the enzymic activity in cells isolated from prostatic carcinoma was lower than that in cells isolated from benign hyperplasia.

A more detailed report of the present work, including correlation of the acid phosphatase activity found in cells from prostatic tumours with the enzymic activity in circulating blood, will be published at a later date.

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Diurnal Variation in Aldolase and Phosphatase Activity in the Cactus Plant

WHEREAS considerable information is available regarding the enzymatic mechanism of carbon dioxide fixation during acidification in succulents[1-3], very little seems to be known about the role of enzymes in the diurnal variation in acids and carbohydrate. If the 3-carbon atom acceptor of carbon dioxide is derived from starch or sugar by the Embden–Meyerhof–Parnas series of reactions, aldolase may be expected to play an important part in the processes of acidification and de-acidification. We have studied the activity of aldolase in cactus tissue at different hours of the day and night, and have found a marked diurnal variation. Phosphatase activity was also found to undergo rhythmic alteration.

Nopalea dejecta used in the experiments was grown in the open, in garden soil. Aldolase activity was assayed by the method of Sibley and Lehninger[4]. The activity of the enzyme was expressed in mm.^{3} of fructose-1 : 6-diphosphate split in 30 min. at *p*H 8·6. Phosphatase activity, using pre-adjusted sodium pyrophosphate as substrate, was assayed by the method reported earlier[5]. A unit of this enzyme liberated 1 μgm. orthophosphorus at 30° C. in 15 min. at *p*H 6·0. The specific activity of the enzymes was calculated in terms of mgm. dry weight.

The analytical data for aldolase, phosphatase, total acidity, total nitrogen (by the micro-Kjeldahl method) and protein (by the biuret reaction) obtained in a typical experiment are shown in Table 1.

Table 1. DIURNAL VARIATION IN *Nopalea dejecta*

Hours of collection of samples	Specific activity/mgm. dry weight		Acidity/gm. dry weight of tissue (ml. *N*/10 sodium hydroxide)	Total nitrogen/gm. dry weight of tissue (mgm.)	Protein/gm. dry weight of tissue (mgm.)
	Aldolase	Phosphatase			
8 a.m.	4·07	7 2	47 6	18 8	86
12 a.m.	3·32	10·3	11·7	19·6	101
4 p.m.	2·31	11·8	8·0	19 7	102
8 p.m.	3 00	10·5	12·6	18·4	82
12 p.m.	3·62	9 5	20·0	18·4	72
4 a.m.	4 96	9 5	28·8	17·9	68

The results show that aldolase specific activity was high at 8 a.m., and that there was a drop during the next 8 hr., the activity at 4 p.m., being the minimum. There was a subsequent progressive increase in the enzyme activity, the specific activity at 4 a.m. being the maximum during the 24-hr. period of observation. Phosphatase activity also showed a diurnal variation, but in the reverse direction and of a lower magnitude. The activity in the samples at 12 a.m. and 4 p.m. was higher than in the samples collected earlier in the morning and late at night. The titratable acidity was high in the morning and at night and was a minimum in the day-time, as was to be expected. Total nitrogen per mgm. dry weight did not alter significantly over the 24-hr. period. However, the protein content was found to alter, being distinctly higher in the samples collected at 12 a.m. and 4 p.m. It may also be pointed out that the diurnal alteration in the aldolase activity becomes even more prominent when the activity is expressed in terms of mgm. protein instead of mgm. dry weight. Assays carried out on mixed homogenates established that the diurnal variations in aldolase and phosphatase activity were real and not apparent.

The increased aldolase activity observed in the dark may be thought of as an adaptive response leading to increase in phosphoenolpyruvic acid, the acceptor of carbon dioxide during the acidification phase of crassulacean metabolism. As already reported[5], the phosphatase of cactus homogenate is unspecific and acts also on fructose-1 : 6-diphosphate. It is likely that the increase in phosphatase activity in the day-time is related to increased synthesis of carbohydrate from organic acid, one step of which

series of reactions requires the hydrolytic split of a phosphate group of fructose-1 : 6-diphosphate.

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Biochemical Chlorination in *Streptomyces aureofaciens*

THIS communication is concerned with the effect of chlorinated fatty acids on the formation of chlortetracycline. Experiments were carried out with shake cultures of *Streptomyces aureofaciens*, strain *B*-28 (ref. 1).

It has already been shown[1-3] that some strains of *Streptomyces aureofaciens* are able to utilize exhaustively the chloride content of an available medium for the synthesis of chlortetracycline. We have found that replacing the inorganic chloride of the medium by the organically bound chlorine of some chloro-fatty acids, the micro-organism was capable of using this different source of chlorine also for the synthesis of chlortetracycline. Quantitative differences could be detected in the rate of utilization of chlorine, depending on the structural position of the chlorine atom (Table 1). This type of chlorination was also substantially inhibited by bromide as well as 2,5-dimercapto-1,3,4-thiadiazole.

Table 1. UTILIZATION OF THE CHLORINE OF CHLORO-FATTY ACIDS FOR THE BIOSYNTHESIS OF CHLORTETRACYCLINE

		Per cent
Sodium chloride	($1 \cdot 5 \times 10^{-3}$ *M*)	100·0
Chloroacetic acid	,,	84·5
Dichloroacetic acid	,,	10·1
Trichloroacetic acid	,,	4·9
α-Chloropropionic acid	,,	4·7
β-Chloropropionic acid	,,	67·3
α,β-Dichloropropionic acid	,,	21·7
α-Chlorobutyric acid	,,	8·3
β-Chlorobutyric acid	,,	53·9
γ-Chlorobutyric acid	,,	70·3
α,β-Dichlorobutyric acid	,,	12·3

Considering the possibilities of chlorine utilization from chloro-fatty acids, three pathways may be suggested as shown in Fig. 1.

The first step in reaction 1 supposes a dechlorination of the chloro-fatty acid (enzymic or spontaneous) yielding inorganic chloride which would be utilized further in the usual way. The second reaction may be regarded as a 'transchlorination' process, that is, a transfer of chlorine from one substrate to another without mixing with inorganic chloride. In the case of the third reaction incorporation proceeds

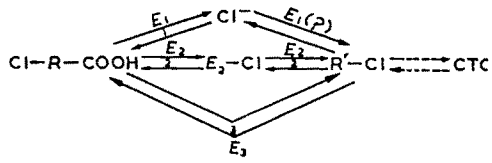

Fig. 1. E_1, E_2 and E_3 represent the enzymes or enzyme systems catalysing the different reaction patterns. *R* is substituted for a single or longer hydrocarbon chain, while *R'* has to be interpreted as a common hypothetical intermediate of the biosynthetic process leading to tetracyclines, which can be chlorinated to form chlortetracycline (CTC), otherwise in the absence of utilizable chlorine it participates in tetracycline production

without the cleavage of the original carbon–chlorine bond of the chloro-fatty acid.

Since our experimental results (to be published elsewhere) precluded the possibility of spontaneous chlorine decomposition, only an active enzymic dechlorination can be assumed for the first case. On the basis of our early investigations, occurrence of the third reaction type seems to be less probable. This conclusion is supported by the incorporation results obtained with the isomeric chloro-butyric acids, too; namely, in the case of an incorporation reaction proceeding without the cleavage of the carbon–chlorine linkage—particularly fragmentation of the fatty acid molecule is reasonably assumed by this process—the significant differences yielded with the chloro-butyric acids (Table 1) are scarcely interpretable. Considering the intramolecular structural arrangements of the variously substituted acids and the possibility of steric inhibition, results summarized in Table 1 can be well explained on the basis of reaction 1 or 2. More detailed results and discussion will be published shortly, elsewhere.

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Hydroxyproline in Primary Cell Walls of Higher Plants

VARIOUS investigators have given evidence for the presence of protein in the cell walls of higher plants[1-6]. We give evidence here for the occurrence of protein in the walls of sycamore (*Acer pseudoplatanus* L.), and bean (*Phaseolus vulgaris*). This protein contained hydroxyproline, and differed in this respect from the protein of the cell contents. Hydroxyproline has been found by Steward and Thompson[7] to occur in the protein of tissue cultures of carrot and potato, and Pollard and Steward[8] showed that the protein containing this imino-acid was stable in the growing cells and was not metabolized.

The plant tissues used in this work are listed in Table 1. The rotary shaker technique described by Nickell[9] was used for growing the sycamore cell suspensions which were derived from callus tissue originating from explants of secondary cambial tissues taken from the tree in November 1958. Bean cell suspensions were derived from hypocotyl or seeds. Growth was measured by withdrawing samples from the cultures and determining the dry weight of cells per ml. of suspension over a period of 21 days.

Sycamore and bean cells were broken by shaking a thick suspension in water with glass beads (2 mm. in diameter) at approximately 50 c./sec. for 2 min. at 2° C. in a cell mill[10]. Microscopic examination showed

Table 1. ANHYDRO HYDROXYPROLINE CONTENT OF CELLS AND CELL FRACTIONS (PERCENTAGE DRY WEIGHT)

	Whole cells	Cell walls	Cell contents
Sycamore cell suspensions	0·51	1·28	< 0·1
Phaseolus vulgaris callus	0·425	2·7	—
Hypocotyl	0·36	0·88	—

that no intact cells were present after the procedure. The walls were isolated and washed 15 times with water by centrifugation (800*g* for 30 sec.). The cell contents were isolated by freezing and drying the supernatant from the cell-wall preparations.

The preparations were hydrolysed with 6 *N* hydrochloric acid in a sealed tube at 105° C. for 18 hr., and after evaporation under reduced pressure, the hydroxyproline was estimated by the method of Neumann and Logan[11]. A quantitative amino-acid analysis was made by the method of Moore, Spackman and Stein[12]. The results are shown in Tables 1 and 2.

Table 2. AMINO-ACID ANALYSIS OF SYCAMORE CELL WALL PREPARATIONS

	Gm. anhydro residues/100 gm protein	Residues/10^5 gm. protein
Hydroxyproline	12 9	114
Aspartic	8 5	74
Threonine	3·8	38
Serine	9 4	108
Glutamic	8 2	64
Proline	4 5	46
Glycine	3 2	56
Alanine	3·6	50
Valine	6 2	63
Methionine	1 5	12
*iso*Leucine	3 8	33
Leucine	5 7	51
Tyrosine	5 1	31
Phenylalanine	4·4	30
Lysine	13 0	102
Histidine	3 4	25
Arginine	3·3	22
Hydroxylysine	0 0	0

Of the total hydroxyproline of the cells, nearly all was found in wall hydrolysates, while only traces (< 0·1 per cent) appeared in hydrolysates of the cell contents. The percentage of hydroxyproline in the wall protein is similar to that of mammalian collagens[13] but the amino-acid analysis shows no other similarities (Table 2). No amino-sugars have been detected.

Although the hydroxyproline content of the sycamore wall preparation varies slightly with different growth conditions, it remains the same when cells from the same culture are broken under various conditions. We have used cells suspended in 0·1 *M* triethylamine, in buffers at *p*H 2 (0 1 *M* glycine/hydrochloric acid and 0·1 *M* acetate), *p*H 10 (0·1 *M* borate), and in 40 per cent sucrose in which the cells were plasmolysed. These extreme conditions were chosen to neutralize acidic and basic groups respectively and to prevent adsorption of protein during cell breakage.

The percentage of wall in the cell may be calculated from the hydroxyproline content estimated for the whole cells and cell walls. For sycamore in the stationary phase of growth the figure obtained was high (40 per cent), but this agreed very well with that obtained by quantitative recovery of walls from a known weight of cells.

The primary nature of these walls is inferred not only because of their origin from rapidly dividing cells (the mean generation time during exponential growth was 48 hr.) but is also suggested by other work still in progress. This has shown (*a*) that the wall is about 1200-Å. thick when sectioned and examined with the electron microscope; (*b*) that parallel or fasciated microfibrils are not present; (*c*) that the walls contain pectin, hemicellulose and α-cellulose in proportions typical of cambial tissue.

The evidence suggests that protein containing hydroxyproline is an integral part of the wall of actively growing cells.

We wish to thank Miss B. Worboys for carrying out amino-acid analysis. One of us (D. T. A. L.) gratefully acknowledges the receipt of a grant from the Agricultural Research Council.

Note added in proof: We are pleased to note that D. K. Dougall and K. Shimbayashi (*Plant Physiol.*, 35, 396; 1960) detail essentially similar findings to our own.

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PHYSIOLOGY

Kinetics of Muscular Contraction: the Approach to the Steady State

A DISTINCTIVE feature of muscular contraction is the dependence of the contractile force on the contraction velocity. For steady contractions, at a given length of the muscle, the interaction between force and motion is characterized by the well-known 'force–velocity' relation[1]. In the present experiments this interaction has been characterized further by measuring the kinetics with which a steady contraction velocity is established following a step change in force.

The experiments were made with an apparatus which simultaneously measured both the motion of, and the force developed by, the sartorius muscle of the frog. The tibial end of the muscle was attached to a lever. Displacement of the muscle was measured by coupling the lever to an RCA 5734 transducer tube through a compliant spring. Force was recorded by measuring, with a second 5734 tube, the strain of the structure supporting the pelvic end of the muscle.

To minimize distortion of the displacement record by the inertia of the recording system, the lever was made as light as possible without sacrificing rigidity: the equivalent mass at the point of attachment of the muscle turned out to be approximately 170 mgm. The lever was loaded with a nearly inertia-less force, a compliant spring attached near the fulcrum and stretched by a weight. To dampen unavoidable high-frequency mechanical oscillation, viscous loading was also added: the lever was constrained to pull a length of wire (41 mgm.) through heavy oil. The loaded lever was prevented from stretching the muscle by a

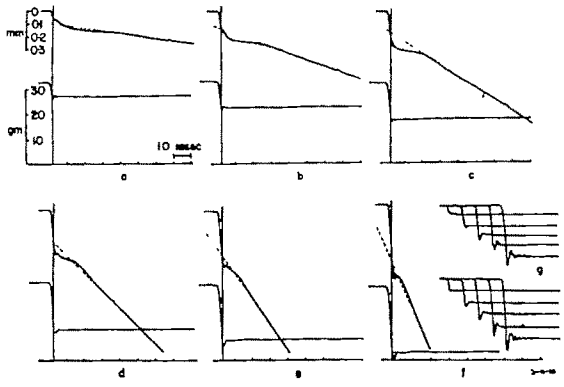

Fig. 1. Response of frog sartorius muscle to a sudden change in force. Upper trace, displacement; lower trace, force; time marks, 10 msec.; standard length, 35 mm.; weight, 66 mgm.; temperature, 0° C. The muscle is initially at the standard length and the record is started after full tetanic force, P_0, has developed. The vertical line defines t_0. Afterload: (*a*) 0·84 P_0, (*b*) 0·69 P_0, (*c*) 0·55 P_0, (*d*) 0·40 P_0, (*e*) 0·26 P_0, (*f*) 0·10 P_0. In (*g*) the muscle is replaced by a spring of compliance 0·017 mm./gm. The afterloads in consecutive releases are the same as (*a*), (*b*), (*c*), (*d*) and (*e*), respectively

stop; a second stop, which could be suddenly withdrawn, controlled release of the lever.

The muscle, in Ringer solution at a controlled temperature, was stimulated (0·1 msec. pulses, 30 c.p.s.) with a multielectrode assembly. After tetanic force (P_0) was fully developed, the stop on the lever was suddenly withdrawn. Recording started just prior to release of the lever: displacement and force were simultaneously displayed on the upper and lower traces of a double-beam oscilloscope.

A typical experiment showing the motion of the muscle when the load on the lever was suddenly reduced from P_0 to $P < P_0$, at 0° C., is shown in Fig. 1. The motion divides naturally into two phases, separated by the vertical line (which defines t_0). In the first phase, contraction is accompanied by a rapid fall in force. (This is the classical 'quick-release' experiment[2]. The stress–strain relation in this phase characterizes the 'series elastic' element[3].) After the force of the muscle falls to the value of the load on the lever, there follows a second phase in which the displacement takes place at essentially constant force (isotonic). However, the contraction velocity does not reach the steady value $V(P)$ until at least 15 msec. after t_0. For the force steps in *a*, *b* and *c*, the velocity is first greater than, and then less than, the final steady value. With greater force steps, *d*, *e* and *f*, the approach to the steady state is more discursive.

Is the delay in reaching a steady contraction velocity in the second phase attributable to the contractile element of the muscle or to the mass of the recording system? The latter possibility arises because the effective elasticity of the muscle and the mass of the lever interact to form an oscillating system. However, this inertial contribution to the displacement record can be evaluated because it is reflected as a corresponding transient in the force record. This is shown in *g*, where the muscle was replaced by a simple spring the elasticity of which approximates that of the 'series elastic' element. When the spring is stretched to a force of P_0 and the lever, with different afterloads, is released, oscillation in the displacement trace is exactly mirrored in the tension trace. The amplitude of this inertial transient increases with the magnitude of the tension step; the period is less than 4 msec.

In the experiments with muscle, since the force beyond t_0 is substantially constant in *a*, *b* and *c*, the velocity transients in these cases can be attributed entirely to the contractile element. The fact that the duration of these transients (> 15 msec.) is considerably greater than the period of the inertial transient (see *g*, and also the force traces of *d*, *e* and *f*) is in agreement with this conclusion. Of course, since P is constant there can be no change in the length of passive elastic elements in series with the muscle.

The same criterion applied to *d* indicates that the velocity transient in this case includes a just measurable inertial contribution. In *e*, and even more so in *f* (where the inertial contribution is just visible), the velocity transient is distorted by the inertia of the recording system.

The influence of temperature on the kinetics of the isotonic velocity transient is shown in Fig. 2. Releases from tetanic tension to the same afterload (one for which the transient is prominent) were made at 0°, 3·5°, 7·0° and then again at 0°. The duration of the velocity transient, Δ, estimated graphically, is obviously a function of temperature, which makes it extremely unlikely that the transient could have originated in the recording system. In fact, the temperature coefficient of Δ is nearly the same as that of V/P_0, suggesting that both the duration of the transient and the characteristic speed are controlled by the same process.

It has often been supposed that the force–velocity relation for steady contractions, $V = V(P)$, can be applied to contractions in which P and V are not constant. Thus the motion of the contractile element has been calculated from the instantaneous tension, $P(t)$, by integration of the force–velocity relation[1]:

$$\int V\mathrm{d}t = \int V(P(t))\mathrm{d}t \qquad (1)$$

This equation neglects the time required for the velocity of the contractile element to adjust itself to a change in force. Since the present experiments show that a measurable time, the magnitude of which depends on the change in force, is required for the steady velocity to become established, equation (1) cannot be expected to yield quantitative results. Careful analysis of the isometric myogram has led to the same conclusion[4].

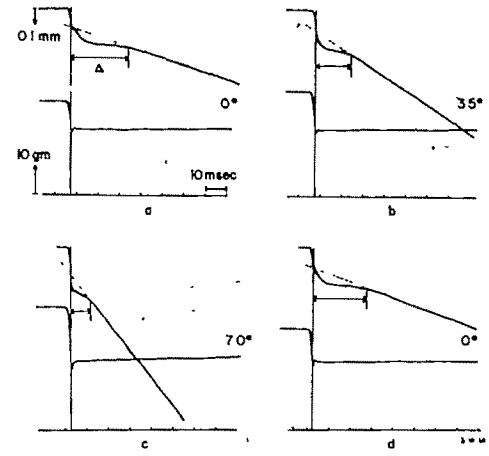

Fig. 2. Influence of temperature on the isotonic velocity transient. Upper trace, displacement; lower trace, force; time marks, 10 msec. Same muscle as Fig. 1. (*a*) 0°, (*b*) 3·5°, (*c*) 7·0° and then (*d*) 0°. Δ is a graphical estimate of the duration of the isotonic velocity transient

The line defined by backward extrapolation of the steady contraction intersects the displacement trace very nearly at t_0, which means that the time average of the velocity transient is approximately equal to the steady-state velocity. It is for this reason that the isotonic quick-release method of measuring series elasticity gives results similar to those found with the controlled-release method[4].

The observed velocity of the muscle is the average of the velocities of the individual parallel fibres, weighted according to the fibre elasticity. If there were dispersion in either the force–velocity relation of the contractile elements or the stress–strain relation of the elastic elements, at t_0 the individual muscle fibres would begin to shorten at somewhat different velocities. However, the velocity differences would not persist because the difference between the displacement of the muscle and that of each fibre would be taken up in the fibre elastic element, changing the force therein, until the velocity of each fibre became the same. Since the change in muscle velocity resulting from this process will be considerably less than the range of fibre velocities at t_0, it is unlikely that equilibration of fibre velocities could contribute appreciably to the very wide range of velocities in each of the isotonic transients described above. Also, the fact that the velocity transients were reproducible in more than 30 different preparations suggests that dispersion of fibre properties can be neglected. Apparently, the transients reflect directly the working of the contractile element; in this case, the kinetics provide a quantitative basis for evaluating models of the contractile process.

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Disuse of a Central Synapse and Spontaneous Activity in the Optic Nerve

CURRENT theories of learning assume that transmission through a synapse is facilitated by repeated use of that synapse[1]. Some support for this theory is provided by the occurrence of 'post-tetanic potentiation' at many synapses, although the duration of this effect, a few minutes at most, can scarcely reflect the long-lasting changes responsible for learning and similar phenomena. It has been argued that disuse of a synapse should produce the reverse effect, a decreased synaptic efficacy. The experiments of Eccles *et al.*[2] showed that after a few weeks disuse of the synapse between 1*a* afferents and motoneurones in the spinal cord there was almost complete absence of the post-synaptic response, but post-tetanic potentiation lasted for a much longer time than normally. In these experiments, disuse was obtained by severance of the afferent fibres, necessarily causing damage to the surviving parts of the neurones. These authors stressed the desirability of avoiding such damage in the study of disused synapses.

We have attempted to produce disuse in the dorsal nucleus of the lateral geniculate ganglion of cats, in the synapse between optic nerve fibres and lateral geniculate cells. In one series of experiments light was excluded from the eyes of adult cats either by keeping them in a darkroom (4 cats kept for approximately 3, 10, 16, 17 months respectively) or by covering one eye with a special light-tight mask (1 cat, 2 months). In another series the visual receptor cells were selectively destroyed by oral administration of a drug, 1 : 5 - di - (*p* - aminophenoxy)pentane dihydrochloride (M. and B. 968*A*)[3]; 5 cats have been examined at approximately 11 days, one month, 7 months, 7 months and 13 months respectively ('treated' cats).

The synapse has been studied by stimulating the optic nerve electrically and recording with a steel microelectrode the electrical field response in the lateral geniculate ganglion; the anæsthetic was allobarbitone ('Dial', Ciba). Briefly, we find the optic nerve normal in both groups by all our criteria—threshold, conduction velocity, excitability (both after single and repetitive stimulation). The post-synaptic response is also normal in the cats kept in darkness. It is only in the treated cats that there is any difference. Even here the response to a single stimulus is quite normal with regard to latency, amplitude and wave form; there is certainly no depression. However, during and following repetitive stimulation there is much less depression of the synapse than in normal cats.

Excitability of geniculate cells to orthodromic stimuli was measured in 2 of the treated cats using conditioning and test pulses in the usual way. In the normal cat there is a depression of the post-synaptic response maximal at about 20 msec. after a single response; at this time the response is reduced to about 32 per cent of normal (range 20–44 per cent)[4]. In the treated cats, apart from changes occurring within about 3 msec. (which were not examined in detail in these experiments) the excitability of the synapse did not fall below 70 and 80 per cent respectively.

Excitability was also tested in all cats by applying trains of stimuli. In the normal cat (Fig. 1*a*) geniculate cells will discharge only 3 or 4 times in response to volleys in the optic nerve at frequencies of about 250/sec.; cats kept in darkness behave similarly (Fig. 1*b*). On the other hand, in treated cats some geniculate cells can fire almost indefinitely at this rate and in general the postsynaptic response shows much less depression with successive afferent volleys (Fig. 1*c* and *d*).

There are also changes in the post-tetanic responsiveness of geniculate synapses. In the normal cat tetanic stimulation of the optic nerve at about 500/sec. for about 15 sec. is followed by a brief period of potentiation and then a period of depression, usually profound, lasting for hours[5,6]. This depression, a very striking feature in the normal cat, is also obtained in cats kept in darkness but not at all in the treated cats, even after only 11 days blindness.

The retinas and lateral geniculate nuclei of several cats have been examined histologically. In cats kept in darkness both structures appear normal with Nissl staining. In the treated cats there was considerable destruction of visual receptor cells, but the bipolar and ganglion cells of the retina and the geniculate cells appear normal. We assume, therefore, that the drug has no direct action on any part of the visual system except the receptor cells. Now, although there is a spontaneous discharge in the retinal ganglion cells, this is dependent on the integrity of the visual receptor cells[7]. Hence in our treated cats the optic nerve must be relatively silent

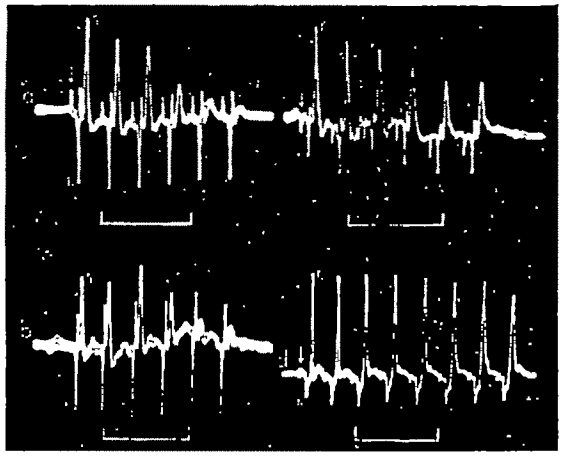

Fig. 1. Recording from the lateral geniculate ganglion. Responses to a train of 6 or 8 stimuli applied to optic nerve. Stimulus strength about twice threshold in each case. Response to a single stimulus consists of a positive/negative wave (t_1) due to the large optic tract fibres, followed by a negative wave (r_1) due to the geniculate neurones. (↓) Stimulus artefacts. Note that t_1 is only slightly affected during the train, whereas r_1 is greatly depressed in (*a*) (normal cat) and (*b*) (cat kept in darkness) and much less depressed in (*c*) and (*d*) (2 treated cats). Horizontal bars 10 msec. Negativity upwards

and the electrophysiological changes we observe must be due to disuse of many of the lateral geniculate ganglion synapses.

Two important inferences can be made from these results. The first is that disuse in this synapse does not reduce synaptic efficacy; in fact the synapse shows an improved ability to transmit impulses. This observation is in agreement with those on the peripheral nervous system in which disuse causes hypersensitivity of the post-synaptic element, both to drugs and to nervous impulses[6]. This hypersensitivity can be produced not merely by denervation but also by section or inactivation of penultimate or even antepenultimate neurones. There is also evidence that similar effects can be obtained within the central nervous system[8].

Because geniculate cells do not normally require much convergent activity to discharge them[9] the single response might not appear very different even if the cells were hypersensitive. Furthermore, there is only a small 'subliminal fringe' of cells in the lateral geniculate ganglion[6]. Hence a hypersensitivity would show itself only when the synapse was otherwise depressed, for example, during a tetanus and during the prolonged depression that follows a brief tetanus. Under such conditions the post-synaptic response remains large in the treated cats.

Although the disuse produced by Eccles and his colleagues may be a disuse complicated by damage, their finding that there is a parallel improvement in adjacent synapses which probably received increased use is free of this criticism and supports the assumption mentioned in the first sentence of this report. Experiments involving disuse of a synapse may not be helpful for theories of learning if the synapse involved has already been used. It might be more profitable to study synapses before they come into use, for example, in fœtal material or very young animals.

The second inference is that since the geniculate synapses in cats kept in darkness do not show this change they cannot be disused and must therefore be receiving a continuous discharge from the retina. It is known that there is such a spontaneous discharge in optic nerve fibres even after dark-adaptation for 1 hr. (apparently the longest period of observation)[10]. Our results suggest that this discharge continues indefinitely in the dark. The spontaneous discharge of sensory receptors in the absence of obvious stimuli is well known, of course, and may be a necessary condition for a high degree of sensitivity.

Full details of these experiments will be published elsewhere. This work was aided by grants from the National Health and Medical Research Council of Australia, from the Ophthalmic Research Institute of Australia and from the Consolidated Medical Research Funds of the University of Sydney. The M. and B. 968*A* was kindly supplied by Dr. R. Wien of May and Baker, Ltd., Dagenham, Essex.

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Prophylactic Treatment of Post-traumatic Audiogenic Epilepsy

Reactivity of rats to a strong acoustic stimulus may be increased by the formation of artificial epileptogenic foci by local application of aluminium hydroxide (alumina-cream[1]) in various regions of the brain, especially the cortical motor and acoustic area.

Foci treated with alumina-cream correspond morphologically and functionally to post-traumatic epileptogenic foci[1].

The possibility of preventing the onset of post-traumatic epilepsy by prophylactic administration of anti-epileptic drugs during the latency period, that is, between trauma and the appearance of the first seizure, has, as yet, neither been studied experimentally on animals nor statistically evaluated in clinical material.

In the present experiments an attempt has been made to influence the onset and the course of post-traumatic audiogenic epilepsy by prophylactic administration of phenyl-ethyl-barbiturates ('Dormiral', Spofa).

Experiments were performed on rats two months old, non-susceptible to an acoustic epileptogenic stimulus at 6–8 weeks of age. Since the non-susceptibility at this age does not exclude, according to our experience (at least in some of the genetic strains), the possibility of onset of audiogenic epilepsy at a

Table 1. Number of Epileptic Rats, Number of Rats with Convulsive Seizures and Average Number of Convulsive Seizures in Individual Groups

Group	n	Epileptic rats		Rats with convulsive seizures		Average % of convulsive seizures
		number	%	number	%	
T	29	21	72 5	14	48·3	37 73
C	31	14	45 2	11	35 5	31 10
P	18	7	38 9	3	16 7	12·40
		1		2		3

Significance: $T\,1 \times C\,1 - \chi^2 = 3\,526$, $P = 0\,05$
$T\,1 \times P\,1 - \chi^2 = 3\,880$, $P = 0\,05$
$T\,2 \times P\,2 - \chi^2 = 3\,540$, $P = 0\,05$
$T\,3 \times P\,3 - t = 2\,152$, $P = 0{\cdot}05$

later age, a control group of rats was formed without trauma, the susceptibility of which to an acoustic epileptogenic stimulus was determined throughout the experiment and with which the experimental groups were compared.

The motor and acoustic area of the ipsilateral hemisphere was traumatized in 63 animals by micro-injection of 16 mm.^{3} alumina-cream with the aid of a stereotaxic apparatus. In 30 of these rats thus traumatized phenyl-ethyl-barbituric acid was administered for eight weeks in a dose 1·180 gm./kgm. body-weight *per os*. During the following six weeks this dose was gradually reduced to zero. Both groups of rats, traumatized and control, were then tested twice a week with a strong acoustic stimulus. The occurrence and symptomatology of the seizures was observed for a period of 150–160 days after trauma, or fifty–sixty days after termination of prophylactic treatment (that is, up to the age of 210–220 days). Twenty-nine traumatized rats, 18 traumatized rats with prophylactic anti-epileptic treatment and 31 control rats survived the experiment and were included in the final statistical evaluation.

Survey of results is given in Table 1 and Fig. 1.

From these it can be concluded that the number of epileptic rats in the group with prophylactic treatment did not differ fundamentally from the control group. Prophylactic treatment thus reduces the occurrence of post-traumatic audiogenic epilepsy to the level of the control group and also reduced the occurrence of post-traumatic epilepsy with convulsive fits.

Rats in which audiogenic epilepsy occurred in spite of prophylactic treatment exhibited a significantly smaller number of convulsive seizures (see lower half of figure), that is, lighter forms of audiogenic epilepsy.

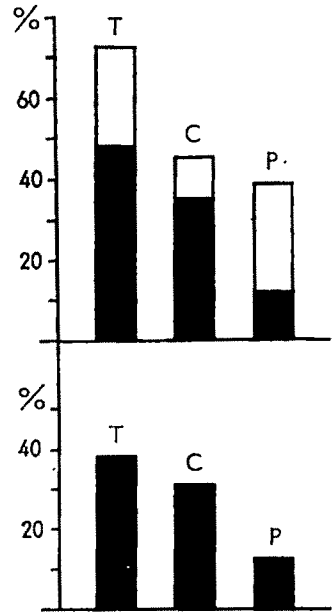

Fig. 1. Above, white columns, percentage of epileptic rats in individual groups; black columns, percentage of rats with convulsive seizures; below, average percentage of convulsive seizures in relation to the total number of seizures in epileptic rats of individual groups.

T, group of rats with traumatic foci without prophylactic treatment; P, group of traumatized rats with prophylactic treatment; C, control group

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Rate of Passage of Inert Particles through the Alimentary Tract of the Cow

In studying the effect of physical factors on the rate of passage of food residues through the alimentary tract of animals, inert particles of known physical characteristics have been used (see, for example, refs. 1 and 2).

We have obtained new evidence on the effect of the specific gravity of an inert particle on its rate of passage through the alimentary tract of the cow. For this purpose rubber particles ranging in specific gravity from 1·02 to 1·21 and weighing 15 mgm. were used. Particles of each specific gravity and of different colours were placed (via a rumen fistula) in the reticulo-rumen and abomasum simultaneously and then recovered from the fæces. Particles from the reticulo-rumen gave a measure of the time particles were retained in the total gut, and those from the abomasum showed the retention in the hind gut; the difference between these two values represented the time of retention in the reticulo-rumen.

The time of retention of a particle in the reticulo-rumen was inversely proportional to its specific gravity, whereas the time of retention in the hind gut was directly proportional to the specific gravity of the particle. An example is shown in Table 1, giving the results of an experiment with four cows receiving approximately equal intakes of roughages. Mean times of retention for the four cows have been calculated by the method of Castle[3].

Table 1

Specific gravity of particle	Mean time of retention (h) of particles in: total alimentary tract (a)	hind gut (b)	reticulo-rumen (a–b)
1 02	102 2	29 0	73 2
1 06	81 6	30 5	51·1
1·12	73 4	37·6	35·8
1 21	70 5	51 7	27 8

King and Moore[2] suggested that there is an optimum specific gravity of approximately 1·2 for the rate of passage of inert particles through the alimentary tract of the cow. Our results are similar, and show in addition that the time particles of equal weight are retained in the whole tract is a resultant of two complementary components each independently related to specific gravity. The relevance of this concept to the differential rates of passage of roughages and concentrate foods is being studied.

One of us (M. F.) wishes to thank the University of Melbourne and the Australian Dairy Produce Board for financial help.

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Renal Oxygen Tension

Urine oxygen tension is regularly lower than the oxygen tension of renal venous blood. When urine does not contain large amounts of reducing substances, for example, ascorbic acid, the urinary oxygen consumption is very low and cannot account for the low oxygen tension of fresh pelvic urine[1]. It has been calculated that only insignificant oxygen tension gradient may exist across the tubule wall[2]. The low urine oxygen tension therefore indicates that some segment of the tubule system has a lower oxygen tension then renal venous blood. Reeves *et al.*[3] have suggested a low oxygen tension in the peritubular capillaries due to 'plasma skimming'[3], and that urine oxygen tension is determined in the convoluted tubules. As the collecting ducts have been shown to be freely permeable to water and urea, however, an equilibration of the urine oxygen tension with medullary oxygen tension as well seems highly probable. Determination of the availability of oxygen to a platinum electrode introduced into the various zones of the dog kidney was therefore undertaken.

Healthy dogs, weighing 15–28 kgm., were anæsthetized by 'Nembutal', 25 mgm./kgm. body-weight, and one kidney exposed by a flank incision. No water was given on the day of experiment, and the dogs were accordingly in the antidiuretic state. Available oxygen was determined by a 0·4-mm. thick uncovered platinum electrode of 8-mm. length. A silver plate coated with silver chloride was used for anode. A constant potential of 0·6 V. was applied between the cathode and anode[4]. The platinum electrode was inserted vertically into the exposed kidney, generally causing negligible amounts of hæmorrhage. The electrode was then moved stepwise into the renal parenchyma, 2–7 mm. each time, allowing time for stabilization at each point. After withdrawal of the electrode, indian ink was injected into the channel left by the electrode. The kidney was then removed and examined for exact localization of the electrode positions. Experiments were performed both during air and oxygen breathing. The fall-off of available oxygen produced by clamping the renal artery was examined with the electrode in various positions.

Available oxygen was regularly lower in the renal medulla than in the cortex. A stepwise decrease of

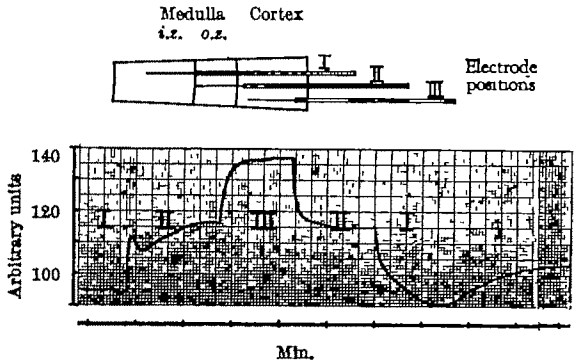

Fig. 1. Available oxygen in the various zones of the kidney. Electrode positions shown in schematic drawing (above). *i.z.*, inner zone; *o.z.*, outer zone

the electrode current was obtained in most experiments during stepwise introduction of the electrode from cortex to medulla. By pulling out the electrode in the same manner, the reverse picture was obtained (Fig. 1). Unfortunately no absolute values for oxygen tension are provided by the present technique. Clamping of the renal artery during oxygen breathing caused a very fast initial reduction of cortical available oxygen, describing an upward concave curve, while medullary available oxygen initially showed slow decrease and then fell off very rapidly, giving an upward convex curve. The difference is most readily explained from the oxyhæmoglobin dissociation curve by assuming an oxygen tension of the renal cortex of at least 80 mm. mercury and a medullary oxygen tension less than 60 mm. mercury during oxygen breathing.

The oxygen consumption is probably not higher in the medulla than in the cortex. The low medullary oxygen tension must therefore result from a relatively low medullary blood-flow, or from perfusion of the renal medulla by blood of low hæmatocrit. A decreasing oxygen tension towards the papilla might also result from counter-current diffusion of oxygen from the descending to the ascending limbs of vasa rectæ and the loops of Henle, as proposed by Levy[5].

From the present findings the low urinary oxygen tension is readily explained by equilibration between the renal medulla and urine passing through the collecting ducts. It should be admitted, however, that the high oxygen tension of the renal cortex as determined polarographically does not necessarily imply a high oxygen tension in the peritubular capillaries. Blood of high hæmatocrit passing through hypothetical shunts in the cortex would presumably influence the polarographic reading to the same degree as would the cell-poor moiety passing through the peritubular capillaries.

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Tissue Respiration and Transamination in Cold Stress

IN the phylogenetic evolution of thermoregulation, under cold stress, liver and kidney tissues of poikilothermal toads show a marked increase in succinate and ascorbate oxidation to 105–150 per cent of that at 30° C.; in stenothermal birds, there is an increase of only 22–35 per cent, while in the homoiothermal rat there is a depression of 21–27 per cent. This indicates that in the rat the depression of respiration is greater in flavoprotein or preflavoprotein systems than in the cytochromes, while in the toad and bird the augmentation of respiration by cytochrome system is 1·2–1·3 times greater than in the flavoprotein or preflavoprotein systems[1]. An attempt has been made in the present work to locate the nature of the evolution of oxidative enzymes in the preflavoprotein systems and also to indicate the nature of changes in oxygen consumption with amino-acid substrates and transamination in these systems.

Experiments were carried out on albino rats of either sex weighing 150–200 gm. and on pigeons and toads, thirty-two animals of each species being used. These animals were divided into two groups, one group being kept at 25° C. (control) and the other at 0° C. in a refrigerator for 2½ hr. (cold). The animals were killed, their liver and kidney collected, weighed and homogenized in isotonic cold potassium chloride solution. 0·4 ml. of 10 per cent homogenate was used in two Warburg flasks with pyruvate substrates for Krebs cycle oxidation[2], and in the other two with 0·5 ml. of 0·5 *M* sodium aspartate and 0·2 ml. of 0·5 *M* sodium α-ketoglutarate for the study of oxygen consumption[3] and transamination reaction[3]. The gas phase was air and the oxygen measurement was made for 30 min. after an equilibrium period of 10 min. and, immediately after, transamination reaction was studied quantitatively by oxaloacetate measurement after decarboxylation to pyruvate[3].

The results are shown in Table 1. The Krebs cycle oxidation system in the rat shows a depression of 15–19 per cent only at the lower temperature, and the depression is definitely in the preflavoprotein system rather than in the flavoprotein or in the postflavoprotein systems. A very slight augmentation of 11 per cent in toad and of 40 per cent in bird tissue indicates that the augmentation in cold stress lies at the flavoprotein and the postflavoprotein systems rather than in the preflavoprotein systems. This shows that in the phylogenetic evolution of thermoregulation, flavoprotein and cytochrome systems were evolved earlier in the poikilotherms and in the stenothermal birds and the preflavoprotein systems were evolved much later in the homoiothermal mammals. The oxygen consumption with amino-acid substrate under cold stress increases in rat tissues and only in the liver of toad and bird, but the kidney tissues of the two latter species show a very marked depression in oxygen consumption. In cold stress, the transamination reaction is, however, increased in both liver and kidney of all three species examined. Cold stress is known to stimulate the secretion of thyroid hormone, and the possible role of this hormone on the preferential oxidation of amino-acid in the liver in contrast to kidney of toad and pigeon or the role of pyridoxine on amino-acid oxidation[4] has not been determined in the present investigation. These results suggest that although transamination reactions have evolved quite early in the phylogenetic scale, amino-acid oxidation in the kidney has evolved only to a small extent in the mammals.

Table 1. The Q_{O_2N} (oxygen consumption in μl./mgm. nitrogen per hr.) of liver and kidney homogenates of rats, pigeons and toads at 25° C. (control) and those exposed to 0° C. for 2½ hr. (cold) with Krebs's cycle oxidation pyruvate substrate (I), with 0·2 *M* sodium aspartate substrate (II) and transamination capacity expressed as μgm. pyruvate formed by decarboxylation of oxaloacetate (ref. 3) after 30-min. reaction per hr. per mgm. tissue nitrogen (III). μ Value is calculated on the basis of ambient temperature difference of 0–25° C. Average of 16 animals in each group

Subject	Reaction	Liver				Kidney			
		Control	Cold	Change (per cent)	μ value	Control	Cold	Change (per cent)	μ value
Rat	I	24·6 ± 2·8	20·9 ± 1·8	− 15·1	32 ± 7	36·0 ± 2·4	29·3 ± 1·7	− 18 6	180 ± 13
	II	27·4 ± 2·5	45·9 ± 2 1	+ 67 6	268 ± 15	44·7 ± 2·9	74·0 ± 2·5	+ 65·5	259 ± 12
	III	377·1 ± 3·6	578·4 ± 3·7	+ 53·4	221 ± 5	387·8 ± 3·1	501·0 ± 3·1	+ 29·2	132 ± 6
Toad	I	29 4 ± 2·6	32·7 ± 1·2	+ 11·3	58 ± 12	57·7 ± 2·8	64·1 ± 2·3	+ 10·9	54 ± 10
	II	33·1 ± 2·4	59·5 ± 2·6	+ 79·7	303 ± 12	117·4 ± 4·3	59·7 ± 3·2	− 49·1	347 ± 14
	III	415·6 ± 5 6	557 9 ± 8·4	+ 34·3	151 ± 7	510·4 ± 5·4	668·9 ± 2·1	+ 31·1	140 ± 2·5
Pigeon	I	89 0 ± 2·4	124·3 ± 2·9	+ 39·6	172 ± 13	82 3 ± 2·3	117·9 ± 3·4	+ 43·3	186 ± 13
	II	62·4 ± 2 6	76·0 ± 2·7	+ 21·7	102 ± 12	82·7 ± 1·8	66 1 ± 2·3	− 20·1	116 ± 12
	III	183·7 ± 2 9	205 5 ± 4 2	+ 11·9	58 ± 6	231 3 ± 1·7	269·5 ± 3·6	+ 16 5	79 ± 6

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Vitamin A Acid and Hypervitaminosis A

ALTHOUGH vitamin A acid plays no part in the visual cycle[1], it is active in the systemic functions of vitamin A in that it maintains normal growth and skin appearance[1,2]. With Prof. R. A. Morton, we have found (unpublished work) that vitamin A acid also prevents the rise of ubiquinone concentration in rat liver, a characteristic effect of vitamin A deficiency[3].

We have now compared the effectiveness of vitamin A acid with that of vitamin A (fed in the form of a high-potency fish oil) in producing hypervitaminosis A. Thus, two male rats weighing 95 and 105 gm. were fed daily 4 mgm. vitamin A acid (as the sodium salt).

Growth stopped and bleeding appeared around the eyes and nose after 4 days. One animal was killed after 10 days when apparently on the point of death; the other was killed in a similar condition after 17 days. The bones were very rarefied, and all long bones showed fractures.

Two other male rats weighing 63 gm. were fed 25,000 I.U. vitamin A (≡ 7·5 mgm. alcohol) a day in the form of a high-potency fish oil (0·5 ml.). They grew slowly; the first fracture and signs of bleeding were noticed after 18 days. One of the animals died on the twenty-second day; the other was killed when on the point of death after 28 days. The bones showed signs of rarefaction which did not approach the severity of the resorption and rarefaction seen in the animals fed vitamin A acid. Only one fracture was found in each of the animals.

Vitamin A acid therefore produced the typical signs of hypervitaminosis A [4] at a much lower dosage and in a much shorter time than did vitamin A itself (as the ester). These findings support the hypothesis[5] that vitamin A acid is formed from vitamin A alcohol and is closer to the systemically active form of the vitamin. We suggest that feeding vitamin A acid is more effective in producing hypervitaminosis A because it by-passes the normal control on the supply of 'active vitamin A' to the tissues.

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HÆMATOLOGY

β-Globulin Variants in Two Species of Monkeys

VARIOUS β-globulin types have been demonstrated, using starch-gel electrophoresis, in several species of mammals, namely, man[1], cattle[2], sheep[3], goat[4] and horse[5]. The present communication reports the discovery of similar variations in two species of monkey, *Macaca mulatta* and *M. irus*. Variations in the monkey β-globulins were initially detected by paper electrophoresis using barbital buffer at *p*H 8·6. However, the β-globulins were much better resolved when starch-gel was used instead of paper.

Serum samples were obtained from 46 rhesus (*M. mulatta*) and 49 cynomologus (*M. irus*) monkeys. Electrophoresis was carried out using the vertical starch-gel technique of Smithies[6]. The starch gels were prepared in borate buffer, *p*H 8·3, with hydrolysed starch (Connaught Medical Research Laboratories), and the serum samples subjected to electrophoresis at 20° C. for 16–18 hr. using a voltage gradient of 5–6 V./cm. After electrophoresis, the gel was sliced horizontally into two halves and stained with concentrated naphthalene black for ½ min.

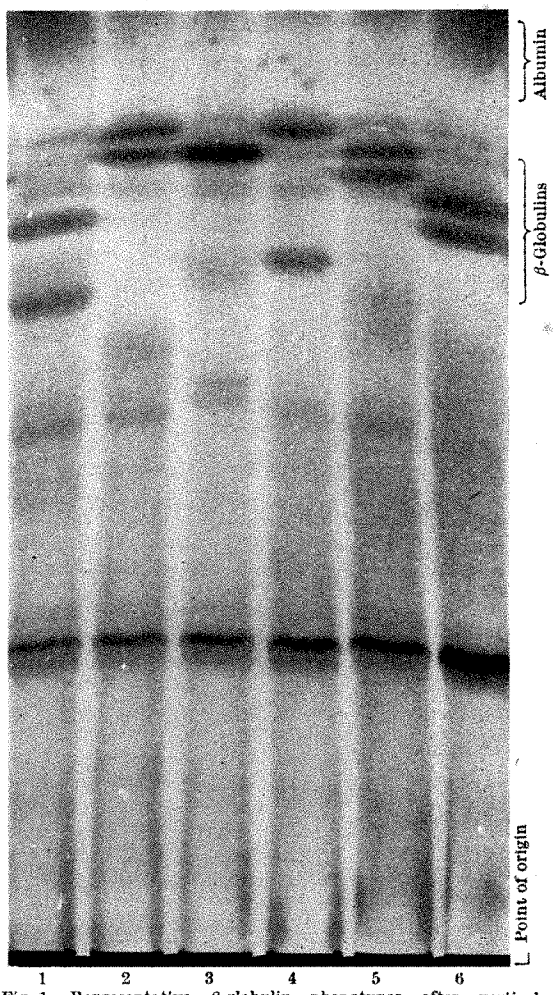

Fig. 1. Representative β-globulin phenotypes after vertical starch-gel electrophoresis of monkey sera. The sera were from left to right: 1, *ADE'FG'*; 2, *A'B'D*; 3, *B'DF*; 4, *A'DEF'*; 5, *AB'C'D*; 6, *ABD'E'*.
(Nos. 1–4 *mulatta* sera, and 5 and 6 *irus*)

Seven distinct β-globulin types were observed. The nomenclature used here is a modification of that of Ashton[3]. The β-globulins are designated by the letters *A* to *G* in order of decreasing mobility, so that *A* is nearest to the albumin and *G* to the point of origin. Three grades of stain intensity were observed. Faintly staining zones are denoted by the capital letter only; moderately staining zones by a single prime and intensely staining zones by 2 primes.

Fig. 1 shows representative patterns of the seven β-globulin variants *A*, *B*, *C*, *D*, *E*, *F* and *G* found in monkeys. In *M. mulatta* these are present in different combinations and proportions to give thirty-four phenotypes. Only fifteen phenotypes have been noted in *M. irus*. The variant of type *E'* and *E''* is most commonly distributed in rhesus monkeys, occurring in 74 per cent (Table 1), while it is found in 31 per cent of cynomologus monkeys. On the other hand, the type *D'* and *D''* β-globulin is present in 33 per cent of the rhesus and 96 per cent of the cynomolgus monkeys. It is interesting to note that type *A* occurs widely in small concentration in both species. However, there is one instance of a phenotype in a rhesus monkey where three intensely staining zones can be demonstrated, one of which is the variant type *A'*. There is also a significant difference in the distribution

Table 1. DISTRIBUTION OF β-GLOBULIN TYPES IN TWO SPECIES OF MONKEYS

	M. mulatta	*M. irus*
A	39	44
A'	6	0
A''	0	0
B	14	33
B'	10	9
B''	2	0
C	0	3
C'	4	6
C'''	0	0
D	26	1
D'	14	32
D''	1	15
E	4	0
E'	28	15
E''	6	0
F	20	1
F'	3	1
F'''	0	0
G	1	0
G'	1	0
G''	0	0
Total No. of animals	46	49

of the *F* types between the two species. The slowest β-globulin variant, *G* type, is very rare and only two rhesus monkeys in the sample possess this, and there is no case in the cynomologus monkeys.

These observations indicate that the two species of monkeys differ appreciably in the frequency of the β-globulin phenotypes. If the β-globulins are divided into two groups, the fast-moving $(A+B+C)$ and slow-moving $(D+E+F+G)$ types, the difference between the two species is highly significant ($\chi^2_{(1)} = 10{\cdot}3$: $P = 0{\cdot}001$).

No attempt has been made so far to study the genetic control of the β-globulin types discovered in monkeys. In comparison with the β-globulin variants in other species of mammals, however, it seems likely that the genetic system controlling the β-globulins in monkeys may be fairly complex[2,7].

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The 'Serial Thrombin Time' Method for measuring Fibrinogenolytic Activity in Plasma

AMONG the techniques described for the measurement of fibrinogenolytic activity, the elegance of the method of Wilhelm, Miles and Mackay[1] seems to have been unnoticed by many workers.

In this technique, a solution of fibrinogen is incubated with the fibrinogenolytic material, and from time to time samples are withdrawn and clotted with thrombin. As the fibrinogen is digested, its concentration in the reaction mixture falls, so that the thrombin clotting time of the samples becomes progressively longer. The rate at which the thrombin times become lengthened depends on the rate of digestion of the fibrinogen, and hence on the activity of the fibrinogenolysin. It is convenient to express the thrombin times as ratios of the value at zero time; and the results may be summarized by the slope of the regression of this ratio against the duration of incubation of the reaction mixture, or by estimating the time taken to achieve a given ratio.

The method is attractive because of its simplicity, the rapidity with which results are available, and because individual readings of thrombin time may be taken at convenient (and irregular) intervals while other work is proceeding. Obviously, the more active the fibrinogenolysin, the more frequently should they be taken; but the appropriate reading-rate can soon be judged as the first few thrombin times are obtained.

Ingram, Norris and Tanner[2] pointed out that this technique could be readily applied to clinical samples of plasma. It is convenient to incubate in parallel samples of citrated plasma (say 2–3 ml.) from the patient and a normal control, starting as soon as possible after venepuncture. Immediately the experiment is set up, 0·1 ml. from each plasma is withdrawn and clotted by the addition of 0·2 ml. calcified human thrombin[3] and the times recorded; unless the fibrinogen concentration is already much reduced in the patient's sample (when purified fibrinogen should be added to both samples to work the test) the ratio between patient's and control plasmas should be near unity. Thrombin times are then repeated on both plasmas at intervals of, say, 5, 10, 20, 30, . . . min. (according to the progress of the test), and ratios obtained between the paired readings; this eliminates error due to decay of activity in the thrombin reagent during the experiment.

The following experiment was carried out to study the relation between the increase in the thrombin time ratio and the digestion of fibrinogen in plasma. Fibrinolysin was prepared from normal human serum by streptokinase[4] and three arbitrary dilutions were made. A portion of each was mixed with nine times its volume of a sample of normal plasma, and the mixture incubated at 37° C. Over a period of 5–6 hr., successive thrombin times were obtained, and a series of samples were also withdrawn for fibrinogen

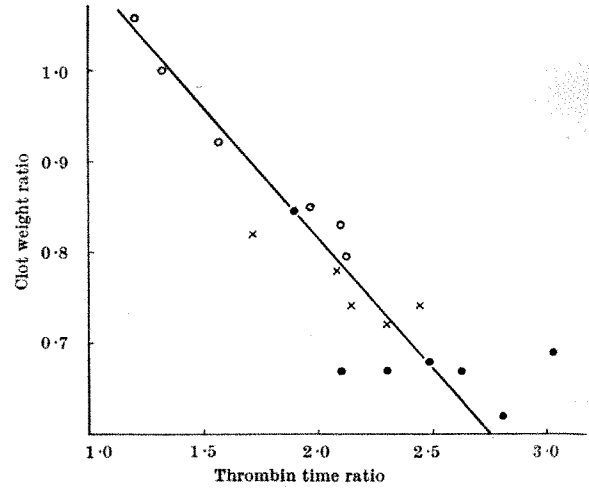

Fig. 1. Ratio of weight of clot to initial reading plotted against ratio of thrombin clotting time to initial reading for three arbitrary dilutions of fibrinolysin. ●, 1/1; ×, 1/2·5; ○, 1/5

estimation by a clot-weight method[5]. For each experiment, the thrombin times and the clot-weights were expressed as ratios of their initial values, and one ratio plotted against the other for corresponding samples. The results of the three experiments are plotted in Fig. 1.

The graph shows a linear relation between proportionate loss of weight of clot and proportionate increase in thrombin clotting time, at least up to a doubling of the thrombin time. Above this level there is a suggestion that the thrombin time ratio rises more rapidly, perhaps due to the Kowalski effect[6], which is thought to depend on a fibrinogen derivative inhibiting the reaction between thrombin and the remaining undigested fibrinogen; but on the whole the results confirm that, when applied to whole plasma, the Wilhelm, Miles and Mackay test provides a satisfactory indication of fibrinogenolysis.

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RADIOBIOLOGY

Labelling of Inulin with Radioactive Iodine

INULIN is used in physiological experiments on renal function and for measuring the volume of extracellular water. Inulin consists of some thirty fructofuranose units linked through C(1) and C(2), corresponding with a molecular weight of about 5,000. The dispersion of molecular weight is thought to be such that nearly all molecules pass freely through capillary walls and the glomerular membrane; apparently inulin is not significantly metabolized during the experiments. Accurate determinations of inulin in biological fluids are required and these are usually colorimetric and involve subtraction of a 'blank' value, due to the presence of other carbohydrates. Radioactive labelling of the inulin could greatly facilitate such experiments. Ideally, labelling should cause the minimum change in the molecule. Carbon-14 could be introduced biosynthetically or tritium by exposure to the gas, but iodine-131 is more conveniently counted in many laboratories. We have experimented with the following reaction sequence on primary hydroxyl groups:

$$\begin{array}{ccccc} CH_2OH & \rightarrow & CH_2OTs & \rightarrow & CH_2I^* \\ | & & | & & | \end{array}$$

(Ts = p-toluenesulphonyl)

A satisfactory product was obtained, but the final labelling step, consisting of refluxing the tosyl inulin with sodium iodide in diethyl ketone, is neither a convenient nor an efficient method of labelling. An alternative procedure is the introduction of an allyl ether group followed by addition of iodine at the double bond:

$$R-OH \rightarrow R-O-CH_2-CH=CH_2 \rightarrow R-O-CH_2-CHI^*-CH_2I^*$$

(R = inulin)

This was done as follows: inulin (5 gm.) in 50 ml. water was stirred under a reflux condenser, and allyl bromide (0·5 gm.) in 3·5 ml. methyl ethyl ketone was slowly added to produce a fine emulsion. The temperature was raised to 65–70° C. and 10·4 ml. N sodium hydroxide solution was added gradually during 30 min. After 6 hr. at this temperature, the mixture was cooled and neutralized with acetic acid. Electrolytes were removed by ion-exchange using a column of 'Biodeminrolite' and the solution was dried from the frozen state. The solid was extracted with hot ethanol, to remove an impurity absorbing ultraviolet light at 232 mμ, yielding allyl inulin (3·5 gm.). The intensity of absorption at 210 mμ, compared with that of allyl ethyl ether, indicated the presence of one allyl group per 14 fructose units. In aqueous solution, molecular iodine was found to react slowly with the double bond; in an iodine solution of approximately 0·0015 N, 100 mgm. allyl inulin combined with 2·5 mgm. iodine in 1½ hr. or 4·5 mgm. in 24 hr., the latter corresponding with one molecule of iodine per 35 fructose units. On oxidation with periodate, the allyl inulin was indistinguishable from the original inulin, 1·0 mole of periodate being consumed per fructose unit in each case. Thus the degree of substitution with allyl ether groups is very small.

The allyl inulin was labelled with iodine-131 using the iodine liberated by addition of 1 ml. of 0·05 N sulphuric acid to a mixture of potassium iodide (4 mgm. in 1 ml.), 75 μc. carrier-free and thiosulphate-free sodium iodide-131 (1 ml.) and potassium iodate (1 mgm. in 0·25 ml.). Allyl inulin solution (102 mgm. in 3 ml.) was added and the reaction was allowed to proceed at room temperature. After 3½ hr. sufficient sodium thiosulphate to react with excess iodine was added, and cations were exchanged for chloride by passage through a column of 'Amberlite *IRA*-400'. Some 25 per cent of the original radioactivity had combined with the inulin, but in a similar experiment this figure was raised to 48 per cent by allowing 24 hr. for reaction. Electrophoresis on paper of the labelled inulin solution in 0·05 M barbiturate at pH 8·6 and 4·5 V./cm. for an hour separated free iodide ions; these were located by an autoradiograph and counted by placing the portion of paper in a well-crystal scintillation counter. In preparations of the type described, about 2 per cent of the radioactivity of the labelled inulin solution was present in the form of free iodide; this percentage could probably be decreased by more efficient ion-exchange. Continuing the electrophoresis for 20 hr. followed by autoradiography showed the labelled inulin displaced towards the cathode by endosmotic flow of buffer solution. Hydrolysis of the labelled inulin in 0·5 per cent oxalic acid at 100° C. for 30 min. followed by electrophoresis of the hydrolysate in borate buffer of pH 10 on paper showed, on autoradiography, several labelled components probably corresponding with various substituted fructoses which have not yet been identified. Thus there seems no reason for doubting that the iodine is firmly attached to the almost unaltered inulin molecule.

In two preliminary experiments in rabbits, the labelled inulin was mixed with the original inulin and injected intravenously. The specific radioactivity of inulin appearing in the urine was measured. In early urine samples, the specific activity was lower and in later samples higher, than that of the injected material, suggesting that the labelled material was being excreted more slowly than the original inulin; the weighted average of the specific activities agreed well with the original value. In an experiment of this kind, molecular weight distribution is an important factor, and it is difficult to ensure that the chemical manipulations involved in labelling do not alter the molecular weight distribution, either by partial hydrolysis or by fractionation, so that the labelled inulin differs from the original inulin used for comparison.

In a subsequent experiment, the labelled inulin was mixed with the same batch of allyl inulin to ensure an identical molecular-weight distribution. Glomerular filtration-rate was measured in a rabbit for seven successive clearance periods, and the same rate was obtained for each period whether calculated from colorimetric determinations of inulin or from the radioactivity of the plasma and urine samples.

The reactions described can be applied to other polysaccharides, and dextran has been labelled in this way; labelled dextran fractions of known molecular weight distribution might be useful in permeability studies.

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Uptake of Radioactive Magnesium in Liver Damage

BRANDT *et al.*[1] injected isotopic magnesium intravenously in the dog and found that kidney, heart and liver have a relatively high activity as compared with skeletal muscle; Rogers and Mahan[2] found a similar distribution in the rat following intraperitoneal administration.

Magnesium-28 has a half-life of 21·3 hr., emitting β- and γ-radiation. The specific activity is relatively low, nominal activity being about 50 μc. per 100 mgm. of carrier. It is supplied as the chloride dissolved in hydrochloric acid by Brookhaven National Laboratories. This solution was neutralized to *p*H 6·5 with sodium hydroxide and diluted with water to contain 0·2 m.equiv./ml. of magnesium. Young male rats (120 ± 5 gm.) were given 0·5 ml. of the solution subcutaneously and killed 2 hr. later by decapitation. Whole heart (opened and rinsed with tap water), left kidney, skeletal muscle of the left abdominal wall, and a portion of the median lobe of the liver were taken and weighed. The samples of approximately 500 mgm. each were counted in a scintillation well. The results are reported as fractional activity: counts per min. per gram of wet tissue divided by the counts per min. of injected dose per gram of animal weight. Thus, if the isotope were evenly distributed and if none were excreted, the fractional activity of all tissues would be 1·0.

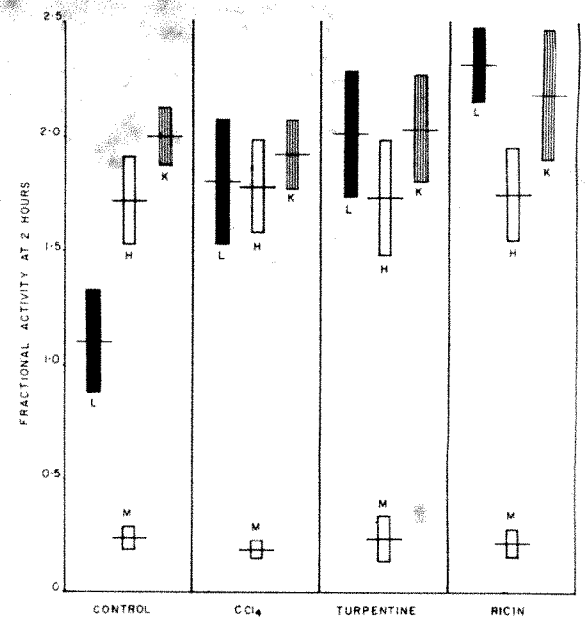

Fig. 1. Fractional activity of liver (*L*), heart (*H*), kidney (*K*), and skeletal muscle (*M*) 2 hr. after subcutaneous injection of magnesium-28. Each horizontal line represents the mean value of tissues taken from 12 animals; the length of the vertical bar indicates two standard deviations

When control rats were killed 2 hr. after subcutaneous injection of the isotope, kidney and heart were found to be relatively active as compared with the moderately active liver and the relatively inactive muscle (Fig. 1). The activity of serum at this time was essentially the same as that of muscle.

In the course of studying the effect of carrier loading on the distribution of magnesium-28, it was noted that the liver of one of the animals appeared to be abnormal. The activity of a sample of this liver was markedly higher than any previously obtained. This observation led to the investigation of the distribution of magnesium-28 following the administration of hepatotoxic doses of carbon tetrachloride, turpentine and ricin.

Carbon tetrachloride and turpentine. Twelve unanæsthetized rats were given 0·25 ml. of carbon tetrachloride subcutaneously. A second group of 12 were anæsthetized with ether and given 0·05 ml. of turpentine intramuscularly. Twenty-four hr. later, 0·5 ml. of magnesium-28 solution was injected subcutaneously. The fractional activity of the liver 2 hr. after giving the isotope was significantly increased over control values in each instance (Fig. 1).

Ricin, a toxic extract of the castor bean, causes widespread tissue damage[3]. The dose of the preparation used, 0·1 mgm./kgm. subcutaneously, had been found to be lethal in 2–4 days. The 12 animals in this series were given the ricin 24 hr. before the administration of the isotope. When the animals were killed 2 hr. after injecting magnesium-28, the heart as well as the liver showed gross and microscopic damage. Whereas the fractional activity was again markedly increased in liver, the activity of the heart was not significantly different from control values (Fig. 1). This would suggest that increased

uptake of magnesium-28 is not a generalized reaction in tissue damage.

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PATHOLOGY

Urinary Selenium and Dental Caries

Cadell and Cousins reported recently on the concentration of urinary selenium and prevalence of dental caries among two groups of children 5–14 years of age in New Zealand[1]. From Table 1 of their article, all but two of the children in both groups had urinary selenium-levels in the range of 0·10–0·49 p.p.m. However, the mean values of urinary selenium given for the first and second group were 0·021 p.p.m. and 0·030 p.p.m. respectively. Obviously there is an error in the presentation of the data.

It is stated by Cadell and Cousins that: "The suggested direct relationship between urinary selenium concentrations and the prevalence of dental caries in American children is not substantiated by an investigation in New Zealand". In view of the data presented by them, this statement seems unwarranted and could lead to erroneous conclusions.

None of their subjects in both groups, having the same magnitude of dental caries, had values of urinary selenium in excess of 0·050 p.p.m. In our work, cited by Cadell and Cousins[2,3], more than half the children in the areas of high prevalence of caries had values of urinary selenium greater than 0·050 p.p.m. On the other hand, in the area with low prevalence of caries, the great majority of the children had values of less than 0·050 p.p.m. Admittedly, the possible dangers to health from the cumulative effects of daily ingestion of small amounts of selenium have been largely unexplored. In one case, however, the presence in the urine of a patient of selenium at a level of about 0·040 p.p.m. was considered to be suggestive of toxic amounts of ingestion[4].

Apparently, Cadell and Cousins are under the impression that a direct relationship could exist between prevalence of caries and all levels of urinary selenium concentration. Such an assumption does not seem correct. It is like claiming that an inverse relationship exists between prevalence of caries and any amount of fluorides ingested, which, of course, is not the case. It is well known that small amounts of selenium are protective against dietary necrotic liver degeneration in rats and also prevent exudative diathesis in chicks[5,6]. On the other hand, the ingestion of excessive amounts of selenium is harmful to animals[7]. If by further work it is shown that selenium is connected with caries, there certainly must be a threshold value of selenium intake, below which there is no influence on susceptibility to caries. Thus it may well be that the ingestion of minute amounts of selenium, such as indicated by the mean urinayr values shown by Cadell and Cousins, does not exert any influence, inhibitory or conducive, on the prevalence of caries.

The description presented by Cadell and Cousins regarding the methods used for assessing caries prevalence in their subjects is quite inadequate. Why did they combine prevalence of caries in primary and in permanent teeth? We have shown that the selenium content of primary teeth appears to be higher than that of the permanent teeth[8]. This becomes an important point in assessing prevalence of caries if the amount of selenium incorporated into the teeth during the period of formation of the crowns influences their future susceptibility to caries.

There is no doubt that further work is necessary for a better understanding of the possible relationship between selenium and caries. However, New Zealand does not appear to be suitable for such investigations since, according to Cadell and Cousins, that country has widespread areas deficient in selenium and also no known seleniferous areas exist there.

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Histochemical Demonstration of Some Hydrolytic Enzymes in Atheromatous Aortas

IN connexion with other investigations made in this Department on the pathogenesis of atherosclerosis, our attention was directed to the histochemical changes in early atheromatous plaques. Barrows and Chow[1] suggested that a disturbance in the relative concentrations of enzymes within arterial tissue may result from arteriosclerosis. Relatively little is known, however, about the localization of enzymes in atheromatous aortas. Paterson *et al.*[2] demonstrated alkaline phosphatase in early atheromatous plaques, using Gomori's calcium–cobalt technique. They assumed that the activity was due to vascularization of the intima in early plaques.

We have made a histochemical study of the phosphatases[3], esterase (with the naphthol *AS* method[4]), and leucyl aminopeptidase[5], in atheromatous aortas. The samples were obtained fresh at autopsy and fixed overnight with cold, neutral 10 per cent formalin: sections were cut in a cryostat at 10μ. The test for phosphatase was made at different *p*H's, and the highest activity was obtained at *p*H 5·8–6·2. This is in good accord with the results of Kirk and Praetorius[6]. This phosphatase was found by histochemical methods in atheromatous plaques only (Fig. 1) and could not be demonstrated in perfectly normal aortas. The activity was most intense at the margins of the plaques.

Fig. 1. Acid phosphatase activity in an early atheromatous plaque

Naphthol *AS* esterase seemed to appear in connexion with the foam cells and its localization corresponded well with the fat droplets visualized by lipid stains. The activity was most intense in the innermost layer of the intima and in the region of the membrana elastica interna. When the whole aorta was involved, distinct esterase activity could even be seen throughout the media (Fig. 2).

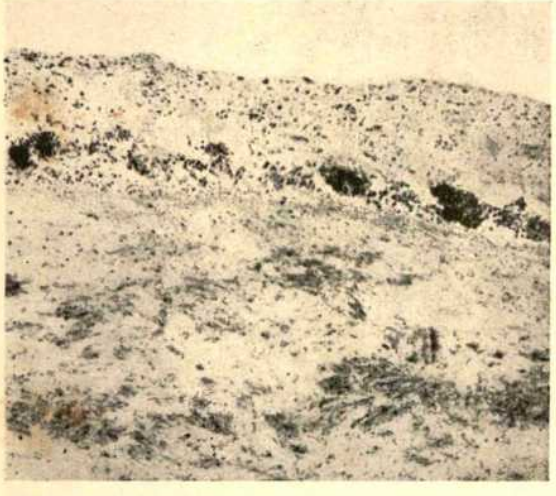

Fig. 2. Naphthol *AS* esterase activity in an atheromatous aorta

In aortas with occasional atheromas, moderate leucyl amino-peptidase activity was seen only in the earliest plaques, mainly in the thickened intima. In severely affected aortas many foci of activity were present even in the media.

It is known that phosphatase and naphthol *AS* esterase are most active in the aortas of those animal species which are least susceptible to experimental atherosclerosis[7,8]. In this connexion the question arises whether the appearance of the two enzymes represents some defensive mechanism in the arterial tissue. Concerning the appearance of leucyl amino-peptidase, it is interesting that Monis *et al.*[9] suggest that its activity is a biological property of proliferating connective tissue cells, and thus this enzyme, too, might be involved in this supposed defensive mechanism or repair mechanism[10].

A more detailed investigation is in progress, the results of which will be published elsewhere.

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Tissue Reaction to Polymethylmethacrylate in Rats and Guinea Pigs

IN 1890 Fraenkel[1] reported on the use of celluloid for the repair of a bony defect of the skull. Since then the increasing availability of plastics with widely differing physical properties has resulted in their use in many surgical procedures, particularly in orthopædic surgery, where the implant is usually intended to remain in the patient for an indefinite period. So far as I am aware, no tumours have occurred in man in association with any of the plastics implanted. In animals, the occurrence of tumours in relation to an implant of a plastic material was first reported by Turner[2] in 1941. He found that fibrosarcomas developed in relation to 'Bakelite' disks implanted subcutaneously in Wistar rats. Since that time, many chemically different plastic materials have been shown to produce tumours when implanted subcutaneously in disk form in rats, mice[3] and hamsters[4]. Originally it was thought that chemical agents were responsible for the development of these tumours[3], but now the form and size of the implant are generally considered to be of greater significance.

In this Department the tissue reaction of the rat and guinea pig to disks of differing diameters of unplasticized polymethylmethacrylate implanted intramuscularly has been investigated. The polymethylmethacrylate sheet used was moulded from a polymer of methylmethacrylate which was prepared by the granular polymerization technique in which benzoyl peroxide was used as the initiator. The method of preparation was similar to that described by Wiley[5].

Disks of three diameters, 18 mm., 12 mm. and 4 mm., and of a thickness $1 \cdot 5 \pm 0 \cdot 5$ mm., were implanted in the gluteal muscles of 153 female Chester Beatty strain rats and 86 female Hartley strain guinea pigs. The age of the rats at the time of implantation was three months, and of the guinea pigs six months. The animals were fed on a standard diet. In each animal the large disk was placed in the left, and the medium and small disk in the right, gluteal muscle mass. Spacing of the disks was such

that there was no difficulty in relating the tumours to the individual disks.

The implantations were completed two years ago. No rat survived for more than twenty-six months after operation, but forty-five of the guinea pigs are still alive. In the rats, thirty-four tumours have occurred in relation to the large- and sixteen to the medium-sized disk (these numbers may be slightly increased when the histology is completed). No tumours have been noted in relation to the small disk. The minimum latent period for the large disk—150 days—was considerably shorter than that for the medium disk—287 days. In only five rats were tumours associated with both the medium and the large disks.

Microscopic examination of the tumours revealed that the majority were fibrosarcomas, but a few rhabdomyosarcomas and osteosarcomas occurred. Tumour deposits, similar in type to those found around the disks, were noted in the lungs of nine rats and were considered to be metastatic deposits.

Tumours can thus be produced by the implantation of unplasticized polymethylmethacrylate in rats, the latent period being shortest with the large disk (18 mm.) which also gave the highest incidence of tumours. The absence of tumours associated with the small disks indicates that either there is a threshold size for disks for tumour formation, as suggested by Nothdurft[6], or that the latent period for the small disk is greater than the survival-time of the rats in this experiment.

Microscopic examination up to eighteen months after implantation has shown no evidence of malignant changes in the fibrous tissue capsules which surrounded the disks in the guinea pigs. Palpation of the disks in the guinea pigs which are still alive—thirty months after implantation—does not reveal any abnormalities. This absence of malignant change in the guinea pigs could be due to a species difference, a greatly extended latent period, or to the disk being below the threshold size required for tumour formation in the guinea pig.

While it is recognized that there is most probably a species difference in response to implantation of plastic materials, the positive findings in rats suggest that there should be a long-term follow-up of patients in which the larger types of plastics implants have been used.

A fuller account of this work will be published elsewhere.

I wish to thank Dr. J. T. Scales, of the Department of Biomechanics, for his advice and encouragement, and Imperial Chemical Industries, Ltd., for technical advice. This work is being carried out with the aid of grants from the Nuffield Foundation and the Medical Research Council.

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BIOLOGY

A Composite Response of Skin Homografts in the Rat

WORK on skin transplantation in rats has revealed a hitherto unreported phenomenon of interest to students of the fundamental biological reactions involved in the destruction of homografts.

A composite response—part survival, part necrosis, part modified necrosis—occurred in 27 of 49 grafts exchanged between members of a closely inbred colony of Wistar albino rats. This colony was started in 1939 from a single pair and it has been kept 'closed' since 1953. Prior to 1953 occasional additions from outside the colony were made. At no time was strict attention to the detail of brother–sister mating made.

Supracarnicular grafts of full-thickness skin measuring at least $2\frac{1}{2}$ cm. × $1\frac{1}{2}$ cm. were removed from the dorsa of the rats. The animals were operated on in pairs, the grafts being exchanged between each member of the pair. Dressings consisting of 'Cellophane' and 'Elastoplast' were removed and first inspections made six days after the transplantation. Close daily observation of the grafts was made and has been continued for periods up to 170 days.

The results of the experiment are summarized in Table 1. Conventional total survival has occurred in three grafts for respective periods of 170, 158 and 148 days. The typical homograft response of total necrosis after 7–11 days of survival was seen in 15 cases, two showed a delayed necrotic process lasting twenty days and in two a prolonged destruction was not complete until the thirtieth day. There was no deviation from the conventional picture of total necrosis in forty-three control grafts, which were composed of two groups. In one group grafts were exchanged between members of a heterogeneous

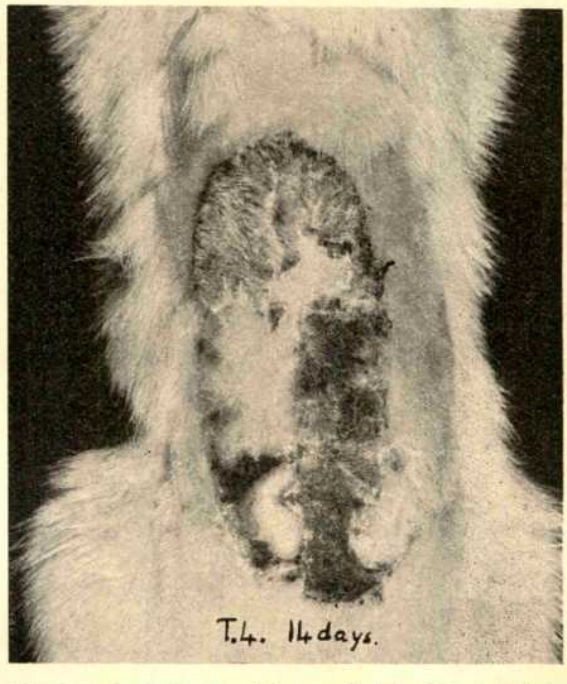

Fig. 1. A large inbred strain homograft at the fourteenth day. A composite response with a geographical line of demarcation

Table 1

Fate of graft / Type of grafts	Conventional response		Composite response				Total No. of grafts
	Total survival	Total necrosis	Survival and necrosis	Survival and modified necrosis	All modified necrosis	Modified and necrosis	
Inbred strain	3	19	11	7	6	3	49
Outbred strain	0	12	0	0	0	0	12
Inter-strain	0	31	0	0	0	0	31

completely outbred population, in the other group interstrain grafts were done, each pair consisting of one rat from the inbred strain and one rat from the outbred strain.

The interesting feature of a graft showing a composite response was that a circumscribed area of the graft, after surviving for 7–8 days, progressed through the whole gamut of the destruction of incompatible skin alongside and abruptly demarcated from another part of the graft which showed no pathological sign; the typical appearance of a composite response at 14 days is shown in Fig. 1; this graft was a 100 per cent 'take' at the six-day inspection with no remarkable characters. The surviving portion produced a good growth of hair, as Fig. 2 demonstrates.

An area of modified necrosis occurred in some cases with an area of unqualified survival, in others beside a part undergoing complete necrosis, and yet another group was observed in which the modified process affected the whole graft. At the usual time of homograft destruction such areas exhibited swelling, exudate and petechial hæmorrhages which developed into scattered points of necrosis; the part survived, but was more indurated than a conventionally surviving part and hair growth was often more sparse and usually 7–10 days later in appearing.

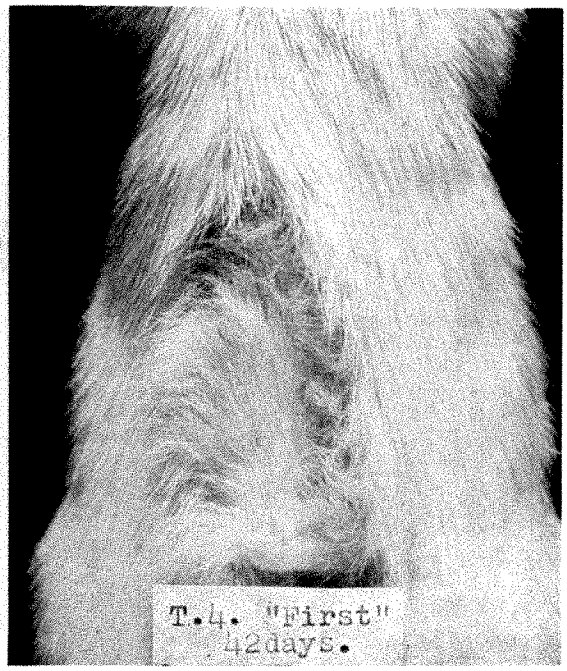

Fig. 2. The same graft as in Fig. 1 at the forty-second day. The graft was rotated through 180° and the surviving part has a good pelt of reversed hairs; it has continued to survive for 86 days. The rejected part on the right half of the graft has contracted a little and shows some residual crusting

Assessment of the survival of a homograft or part thereof was based on the observance of an unquestionable growth of hair with an unorthodox orientation, each graft having been rotated through 90° or 180° around a central vertical axis during transference from the donor to the recipient bed.

An explanation of these observations cannot be offered from the limited scope of the experiments reported at this stage, nor can it be obtained from the hypothesis of actively acquired immunity on which the structure of many arguments concerning the mechanisms of the reactions to homologous tissue seen in all animals above the lowest metazoan species have been based. However, further work on replantation experiments and on more closely inbred strains may indicate the specific factors involved.

I am indebted to Mr. W. J. Dempster for much helpful advice during the course of this work.

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Occurrence of Bivalve Gastropods along the Coast-line of New South Wales

SINCE the descriptions of the animals and shells of two species of Australian bivalve gastropods, *Berthelinia typica* (Gatliff and Gabriel) and *Midorigai australis* Burn, were published earlier this year[1], I have had the opportunity to examine most of the beach drift material of these species in the collections of Mr. C. J. Gabriel, Melbourne, the National Museum of Victoria, Melbourne, and the Australian Museum, Sydney. This material revealed that both the species mentioned are to be found along the coast-line of New South Wales, and they are here recorded for the first time from that area.

(*a*) *Berthelinia typica* (Gatliff and Gabriel), one specimen (left valve only), No. *C*.63121 in the Australian Museum collection, collected in Gunnamatta Bay, Port Hacking, N.S.W., by J. Laseron. This valve is typical of small *B. typica* valves in that it is not as sharply pointed posteriorly as my figures indicate (ref. 1, Figs. 1–2).

(*b*) *Midorigai australis* Burn, one specimen (left valve only), No. *C*.63120 in the Australian Museum collection, collected at Fairlight, North Harbour, Sydney Harbour, N.S.W., by M. Burrows and J. Laseron. This minute valve, 0·8 mm. long and 0·5 mm. high, is very similar to small specimens in the paratype series, although the upper anterior margin is not so high, nor is the upper posterior margin so angled. The protoconch is typically discoidal, and this distinguishes the valve from *Berthelinia*, where the protoconch is described as helicoidal.

Both these species belong to the molluscan order Sacoglossa, family Bertheliniidae.

Careful searching of the green alga *Caulerpa* at various localities in New South Wales during the 1960/61 summer period will, I hope, reveal the living animals of both species, possibly along with other sacoglossans which feed on the same food.

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Northern Limits of *Elminius modestus* in Britain

RECENTLY, Powell[1] reported the occurrence of two specimens of the immigrant barnacle *Elminius modestus* at Keppel Point, Isle of Cumbrae, where the species was reported some four years previously by Connell[2]. This is only the second record of the species north of Loch Ryan, though it has been present in the Loch and farther south for some time[3]. Its presence in very small numbers at scattered points on the south-west coast of Scotland is to be expected, since it has now colonized shores on all sides of the Irish Sea and has been found beyond the North Channel in Loch Foyle[4].

In March 1960 *Elminius* was found sparsely scattered over a wide area in the Gare Loch, Dumbartonshire, north of the Clyde, though no specimens were found in the Clyde estuary itself, nor in the neighbouring Lochs Long and Fyne, nor farther north in Loch Linnhe. It may be significant that there is a naval dockyard in the Gare Loch and shipbreaking yards, as in Loch Ryan. The individuals found in the Gare Loch were mostly small ones which had evidently settled late in 1959, and, though they were seldom seen sufficiently close together to be able to breed, were nevertheless found in numbers at all the piers, jetties and breakwaters which were examined (Fig. 1), the greatest densities occurring towards the head of the Loch. Hydrographic conditions in such a deep and long body of water would be ideal for retaining larvæ liberated by introduced barnacles.

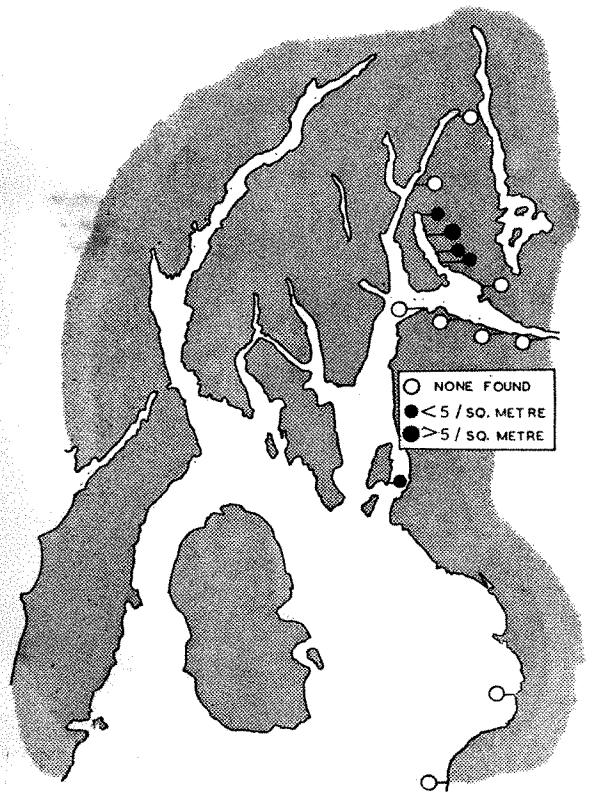

Fig. 1

On the east coast, the Humber has marked the limit of *Elminius modestus* for some years[3]. However, in March 1960 considerable numbers were found to have settled between the Tees and the Humber. On the piers at Saltburn the density reached 20 individuals per square metre. Smaller numbers were found at Scarborough and Bridlington.

The northward spread of the species, both on the west and the east coast, following a period of some five years in which the species had shown little advance, is probably to be ascribed to an increase in the fecundity of the species caused by the exceptionally warm and prolonged summer of 1959.

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Fruit-Setting of Apples using Gibberellic Acid

ATTEMPTS in the past to produce parthenocarpic development of pome fruits with growth substances have had only very limited success[1,2]. Because of a greater natural tendency towards parthenocarpy, experiments with pears have been much more successful than with apples. Luckwill[3], however, recently reported that gibberellic acid sprays caused the initial development of seedless fruitlets on several apple varieties, although with only one, Miller's Seedling, did treated parthenocarpic fruits reach maturity. In experiments at this Division during the 1959–60 season, gibberellic acid, applied as a 1 per cent lanolin paste, has produced mature seedless fruits on four apple varieties—Sturmer, Cox's Orange and two cider varieties, Strawberry Norman and Red Jersey.

Before treatment, petals, stamens and style of flowers on small branches were removed at the pink stage with a sharp blade. Except with Red Jersey at least 80 flowers per treatment were used. Paste was then smeared on the cut surface and around the inside of each receptacle. On Sturmer, additions of 2,4-dichlorophenoxyacetic acid (0·125 per cent) alone or together with kinetin (0·025 per cent) to the gibberellic acid did not appear to enhance the effect of the latter. A single spray of 400 p.p.m. gibberellic acid was as effective as the grease treatment on Strawberry Norman, the only variety on which this method of application was tried.

Subsequent swelling of treated receptacles was rapid and comparable with that of normal seeded fruits. At an early stage the majority of treated flowers appeared to have set. However, many of these fruitlets developed only partially and a heavy drop occurred 5–7 weeks after treatment. The remaining

fruits on three of the varieties, Sturmer, Red Jersey and Strawberry Norman (some 8, 40 and 28 per cent respectively of treated flowers), continued growth and attained a final size at harvest only slightly smaller than the average size of normal seeded fruits from the experimental trees. Treated fruits maturing on Cox's Orange (12 per cent of flowers treated) were only half the size of seeded fruits. With normal pollination, fruit was harvested from 10–15 per cent of flowers on the above varieties. No fruit set on control flowers of any of the varieties on which the petals, stamens, and style had been removed similarly.

In colour development, time of ripening and general quality, parthenocarpic fruits produced by the gibberellic acid treatments were similar to normal fruits. Treated fruits of Red Jersey were noticeably more elongated than normal fruits; but this tendency was only slightly apparent on other varieties. A proportion of the treated fruits of all varieties developed some unevenness, being lopsided or otherwise asymmetric. A characteristic puckering around the calyx occurred particularly on Red Jersey and Strawberry Norman. The gross morphology of the seedless fruits was similar to that of normal fruits. In the absence of seed development, walls of the carpel chambers were sometimes pressed closely together. Undeveloped ovules remained as small brown rudiments no more than 1 mm. long. Treated branches developed flower buds normally during the season.

Although gibberellic acid failed to show any effect during *in vitro* studies of the growth requirements of apple tissue[4], the present results suggest that in normal development of apple fruits the naturally occurring gibberellins may perform a specific role. It is of interest that a similar positive effect of gibberellic acid on fruit set of *Rosa* has been recorded recently[5]. Success of the direct applications of gibberellic acid suggests that such treatments might have considerable practical value in overcoming fertilization problems in apple crops.

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Direct Transmission of a Growth-promoting Substance from Strawberry to Pea

RECENT papers by Guttridge[1,2] have provided evidence that photo-periodically controlled growth responses in the strawberry may be regulated by a hormone, produced in long days, which promotes vegetative growth and inhibits flower initiation; and that gibberellic acid may simulate the action of this hormone in plants growing under short-day conditions[3]. Brian and Hemming[4] found that plants of *Pisum sativum* var. Meteor will respond by increased length of internode to as little as 0·01 μgm. of gibberellic acid.

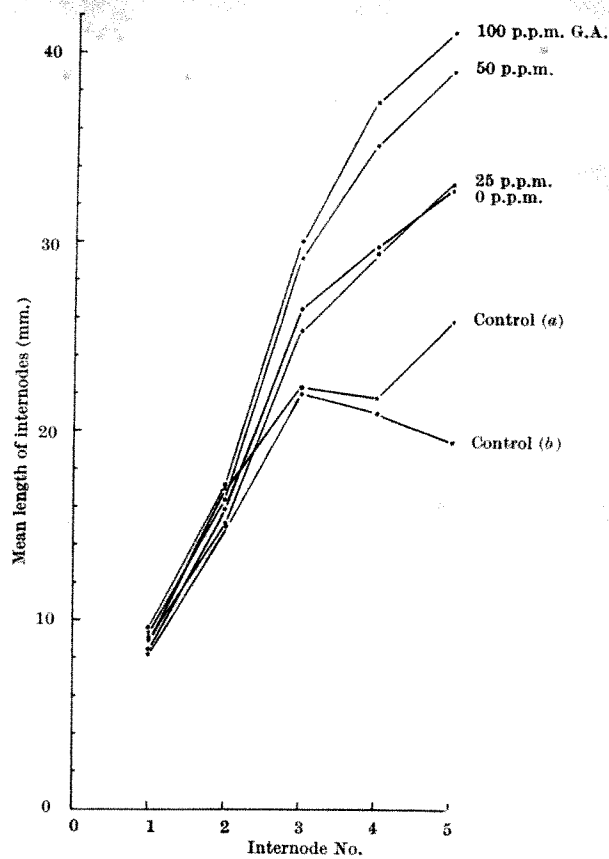

Fig. 1. Effect of grafting *Pisum sativum* var. Meteor on to petioles of strawberries previously treated with gibberellic acid. Control *a* peas retained in pots; control *b* peas treated for grafting

In view of the small quantity of gibberellic acid required to give a measurable response in the pea, an attempt was made to obtain direct transfer of the growth-promoting hormone from the strawberry to Meteor pea plants by making a tongue approach graft between the blanched epicotyl of a pea and a strawberry petiole. After grafting, the roots of the pea plant were placed in a 3 in. × 1 in. sample tube containing Long Ashton mineral nutrient solution[5]. Controls were set up in the same way with their epicotyls cut as for grafting. No graft union was ever formed, and after the sixth internode had expanded the peas were harvested and the length of each internode was recorded.

Fig. 1 shows the mean length attained by successive internodes of Meteor peas grafted on to plants of the strawberry variety Climax, which had been sprayed seven days previously with a solution containing 100, 50 or 25 p.p.m. of gibberellic acid. Fifteen plants were used for each treatment and one pea plant was grafted to each. Also shown is the response of peas grafted on to untreated strawberry plants. Two control series of peas were used; in one, the plants were removed from the pots and treated as for grafting; in the other, they were left to grow undisturbed in their pots.

The internodes of all grafted peas were longer than either the ungrafted controls or the controls which were grown on in their pots. Pretreatment of the strawberry plants with high (50 or 100 p.p.m.) levels of gibberellic acid resulted in additional elongation of the internodes of peas grafted to them.

Brian and Hemming have shown that applications of gibberellic acid have less effect on tall than on dwarf varieties of peas[4]. To determine whether peas responded to grafting in a similar way, 15 plants of each of six different varieties of peas were grafted on to large plants of the strawberry variety Redgauntlet growing in the glasshouse. To confirm the response of these pea varieties to gibberellic acid, 10 plants of each, growing in pots, were either left untreated or treated with gibberellic acid at 0·02 μgm./plant or 0·32 μgm./plant.

Table 1. RESPONSE OF DIFFERENT VARIETIES OF *Pisum sativum* TO APPLICATIONS OF GIBBERELLIC ACID: AND TO GRAFTING ON TO PETIOLES OF STRAWBERRY

Variety	Growth habit	Percentage increase on respective controls:		
		Grafted	Gibberellic acid at 0·02 μgm.	Gibberellic acid at 0·32 μgm.
Meteor	Dwarf	157	155	210
Progress No. 9	Dwarf	149	147	188
Little Marvel	Dwarf	127	140	185
Greenland	Intermediate	137	120	156
Gladstone	Tall	122	116	105
Thomas Laxton	Tall	124	123	115

Table 1 gives the lengths of the first internode to elongate after treatment, expressed as a percentage of the length of the corresponding internode in the control series of each treatment.

The response to grafting of each variety of pea used, with the possible exception of Little Marvel, was similar to its response to an application of 0·02 μgm. gibberellic acid.

The strawberry is a plant in which gibberellic acid can serve as a substitute for the dormancy-breaking effect of winter chilling. After chilling, plants grow very strongly when brought into conditions favourable for growth, in contrast to unchilled plants in which the petioles remain short and prostrate. Fig. 2 shows the mean lengths attained by successive internodes of peas, variety Meteor, grafted on to the petioles of chilled and unchilled plants of the strawberry Redgauntlet, growing in a glasshouse. Each set is the mean of ten plants, each of which was grafted to a different strawberry plant.

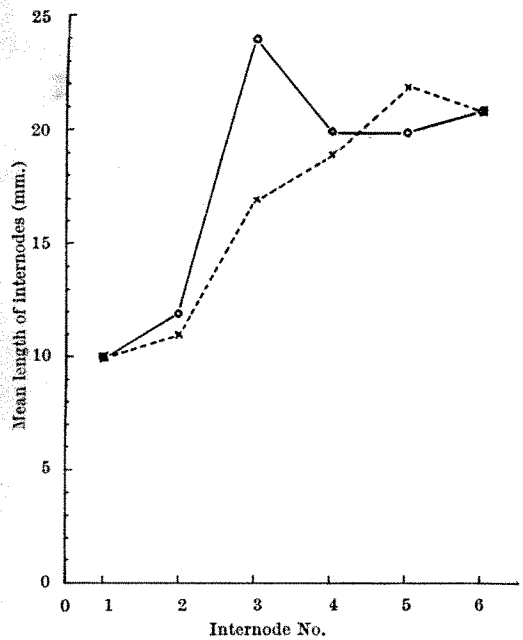

Fig. 2. Effect of grafting *Pisum sativum* var. Meteor into petioles of strawberries growing in the glasshouse. ——, Following winter chilling; – – –, without previous chilling

Grafting peas to chilled strawberry plants resulted in a greater response in internode-length than did grafting to unchilled strawberries.

The experiments show: that Meteor peas respond by increased internode-length when grafted on to petioles of strawberry leaves; that the response is increased when the strawberries have been previously treated with gibberellic acid; that the responses of different varieties of peas to grafting are similar to their responses to treatment with gibberellic acid; and that chilled strawberry plants, in which there may be endogenous gibberellins, promote a greater response than do unchilled plants in which endogenous gibberellins may be low.

Further work is now in progress with the intention of publishing a fuller account of the technique. It is hoped that the method may provide a rapid quantitative technique for the estimation of gibberellic acid-like substances in plants without the necessity either to make an extract or to destroy any part of the plant sampled.

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Intra-ovarian Pollination in *Papaver rhoeas* L.

IN many crosses plant-breeders are confronted with one or more of the following problems: (1) the pollen grains may fail to germinate on a foreign stigma; (2) if they germinate, the pollen tubes may remain short and burst during their passage; (3) even if the tubes grow successfully, their progress may be so slow that the ovary becomes abscissed before they reach the ovules.

Grafting the style on the ovary, shortening it to a suitable length, and removing the middle portion and joining the upper and lower parts of the style together have been tried from time to time to overcome some of these barriers[1].

Intra-ovarian pollination is yet another device. Dahlgren[1] was able to bring about fertilization in the ovules of *Codonopsis ovata* by this method. The experiments of Cappelletti[2] on *Digitalis purpurea*, and of Bosio[3] on *Helleborus foetidus*, *H. viridis*, *Paeonia anomala*, *P. officinale* and *P. peregrina* also indicated the possibilities of this technique. In *Paeonia*, Bosio obtained viable seeds. This communication describes the results of some intra-ovarian pollinations conducted on plants of *Papaver rhoeas*.

The following steps are involved: (1) determination of the time of anthesis, dehiscence of anthers and of pollination; (2) emasculation and bagging of flower buds; (3) collection of pollen grains; (4) determination of the conditions and medium for optimum germination of pollen; (5) injection of a suspension of pollen grains into the ovary.

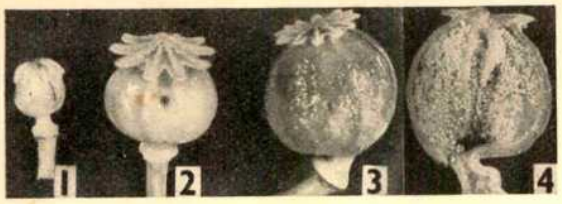

Fig. 1. Ovary injected with pollen suspension. The petals and stamens have been removed to show the hole made by the needle. (× 3/5)

Figs. 2 and 3. Ovaries six and nine days after injection. (× 3/5)

Fig. 4. Nine-day-old ovary cut vertically to show maturing seeds. (*c.* × 3/5)

The pollen suspension was prepared in 2 c.c. of sterile, double-distilled water with 0·01 per cent boric acid, each drop containing nearly 100 pollen grains. An all-glass 'Insuline' syringe (capacity 1 c.c., graduated to 40 units) was used. Before injection the surface of the ovary was wiped with cotton soaked in rectified spirit. A hole was made on one side of the ovary to allow the air to escape, and another on the opposite side through which the pollen suspension was injected until the ovarian cavity was filled with it. The cavity was considered full when the fluid started oozing out from the first prick. Care was taken to shake the syringe before each injection, so that the pollen grains were uniformly distributed. After the operation the holes were sealed with petroleum jelly.

When the calyx, corolla and androecium were all removed the ovaries became pale yellow ; if only the stamens were excised leaving the petals and sepals intact, the development was better, and hence this procedure was always followed after the first few trials.

The growth of ovaries injected with a pollen suspension in sterile double-distilled water matched fairly well with naturally pollinated ovaries. Concomitant with the growth of the ovary, the ovules also developed and the embryos grew faster than in Nature. The cotyledons differentiated within fourteen days after anthesis ; by the third week the plumule and root tip were well differentiated ; and month-old seeds had fully developed embryos.

The experimentally obtained seeds were viable and behaved just like those obtained from naturally pollinated ovaries. When soaked in tap water for 24 hr. and cultured on modified White's medium there was 100 per cent germination, and healthy seedlings were obtained. Counts from the squashed root tips of seedlings from both sets showed 24 chromosomes.

The injected ovaries showed a 40–70 per cent seed set (Figs. 1–4). Seeds also matured in ovaries injected with an aqueous suspension of pollen without boric acid, but were fewer in number.

The technique of intra-ovarian pollination may prove useful in overcoming incompatibility between two plant parents. Further work is in progress.

I am grateful to Prof. P. Maheshwari for guidance and encouragement. Thanks are also due to Drs. S. Narayanaswami and N. S. Ranga Swamy for their help and valuable suggestions.

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MICROBIOLOGY

Misinterpretation of an Agar-Gel Precipitation Pattern

THERE are certain recognized pitfalls in the reading of precipitation patterns in agar-gel immunodiffusion plates[1–3]. Occasionally, a new pitfall is inadvertently introduced by the design of well-pattern employed in a particular plate. Such is the case in the plate depicted in Fig. 2 of the communication in *Nature* of Pepys *et al.*[4].

I reproduce herewith (Fig. 1) the relevant part of the well-pattern employed by Pepys *et al.*, using their numerical notation. In their original paper the two large wells each received the same serum. In well 1 had been placed *Trichophyton rubrum* cell-sap ; in well 3, *Aspergillus fumigatus* cell-sap.

A two-armed band of precipitate, produced by this antigen–antiserum placement, ran continuously between the two antigen wells on one side and the two antiserum wells on the other. One arm extended beyond well 3, the other terminated opposite well 1. The authors assumed that each arm had arisen as an independent band, arms 1 and 3 afterwards fusing in the so-called "reaction of identity". From this they concluded that *T. rubrum* and *A. fumigatus* "possess common antigenic determinants".

What they had failed to take into account was the possibility of antigen from well 3 reacting with antibody from the far antiserum well, as well as from the near, thus being the sole antigen responsible for the entire precipitation band. This seemed to me the more likely explanation, especially in view of the manner in which arm 1 terminated on a level with and failed to extend beyond well 1.

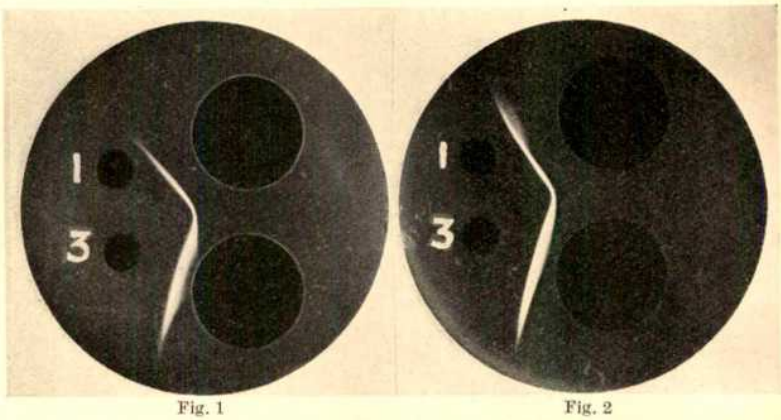

Fig. 1 Fig. 2

Fig. 1. Large wells : rabbit anti-ovalbumin serum ; well 3 : ovalbumin 1 : 1,000 ; well 1 : saline

Fig. 2. Large wells : rabbit anti-ovalbumin serum ; well 3: ovalbumin 1 : 1,000 ; well 1 : ovalbumin 1 : 100,000

To test this view, a plate was set up in which a rabbit antiserum to ovalbumin was placed in both large wells and an ovalbumin solution placed in well 3, while well 1 received only saline. The precipitation band produced (Fig. 1) was identical with that of Pepys *et al.*

To determine the effect of fractional concentrations of antigen in well 1 on arm 1 of the band, plates were set up in which well 1 received tenfold and hundredfold dilutions of the ovalbumin solution in well 3. Fig. 2 shows the perceptible deflexion and extension even a hundredfold weaker antigen produces on the free end of arm 1 of the band. From this it appears to me that, in the original plate of Pepys *et al.*[4], the *T. rubrum* cell-sap could not have contained as much as 1 per cent of an antigen immunologically related to the antigen in the *A. fumigatus* cell-sap responsible for the precipitation band. The photographs are by Douglas F. Lawson from plates by Anne Temple.

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As pointed out by Dr. J. G. Feinberg, the pattern of wells in the agar-gel plate (Fig. 2) of our communication in *Nature* of October 24, 1959 [1], lends itself to misinterpretation. However, the presence of common antigenic determinants in extracts of *T. rubrum* and *A. fumigatus*, which figure in the plate, was demonstrated by inhibition tests. These, together with all the other tests in our communication, were performed on conventional agar-gel patterns (Fig. 1, ref. 1). Nine sera were tested for their capacity to precipitate against these two fungal extracts, after the addition of each of them to the serum. The addition of *A. fumigatus* extract resulted on one hand in complete inhibition of its own precipitation lines with six and partial inhibition with the remaining three sera, and on the other hand in complete inhibition of the *T. rubrum* extract precipitation lines with seven and partial inhibition with a further one serum. The addition of *T. rubrum* extract resulted in complete inhibition of the precipitation lines of the *A. fumigatus* extract with six sera, and of its own precipitation lines with all nine sera.

The problem of related antigenic determinants in extracts which may not produce identical patterns, or may not in some cases produce any precipitation at all, but may nevertheless effectively inhibit the precipitation lines of extracts from sources of known or as yet unknown relationship, has been encountered by us in work on mycobacterial extracts[2] and on the *Aspergillus* genus[3]. It seems reasonable to assume some antigenic relationship from these findings, whether or not reactions of identity are produced by these extracts in agar-gel tests with appropriate patterns.

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Bi-nucleate and Tri-nucleate Conidia in *Colletotrichum gossypii* South

AN isolate of *Colletotrichum gossypii* which was kindly sent from Arkansas by Dr. N. D. Fulton (his No. 6110) produces spores in culture showing great variability in size and shape. This state of affairs has been well known in the genus since the early reports of Alwood[1] and Burger[2].

Cytological work using an acid giemsa technique has shown that in this isolate, under conditions of culture *in vitro*, the variable size of the conidia is apparently associated with a variable number of nuclei per conidium. This is normally one, but may be two or three or rarely up to five per spore. The conidia are abstricted terminally on conidiophores, which in this case are no more than mycelial branches of specialized function, and in slide-culture preparations remain in clusters around the parent conidiophore. Often, but not always, pleurinucleate spores occur together in these clusters.

No evidence has been found for the migration of more than a single nucleus into the conidium before abstriction. What appears to happen is that, after abstriction, the spore may continue to grow to a limited extent, and that in this case the increase in cytoplasmic volume is accompanied by nuclear division. In some cases the bulbous distal end of the larger spores suggests that a setback has been followed by a fresh burst of growth[3]. The cultures were examined after four days growth at 25° C. in the dark. None of the spores was apparently germinating, and the pleurinucleate condition is thought to arise in the development of the spores before hardening of the wall, rather than being associated with spore germination.

The fungus was handled before fixation as a Duncan slide culture or by Dade's method[4]. The agar was removed and the fungus fixed and stained *in situ* on the cover-glass on to which it had grown. Fixation was in Newcomer's fixative[5] over-night. After passing through 70, 50 and 30 per cent alcohol the

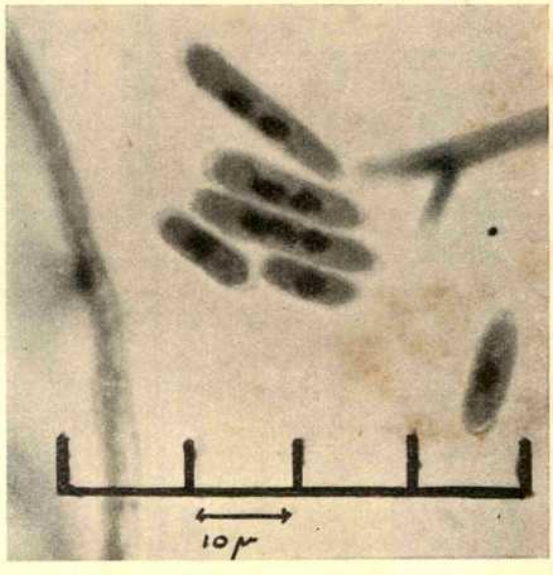

Fig. 1. Conidia of *Colletotrichum gossypii* South on mycelium growing on glass from glucose yeast agar, stained acid-giemsa. Photomicrograph using a × 45, 3·75 mm., N.A. 0·95 objective

preparation was transferred to 1 per cent sodium chloride at 60° C. for 90 min., as suggested by Robinow (personal communication) following Ganesan and Swaminathan[6], to remove the cytoplasmic ribonucleic acid. After hydrolysis for 10 min. in *N* hydrochloric acid at 60°, the material was thoroughly rinsed in Sørensen phosphate buffer at *p*H 6·5. The preparations were stained in Gurr's *R*66 improved giemsa stain at one drop per ml. dilution in the same buffer. No differentiation was necessary and the material was examined as a wet mount in buffer.

The nuclei are very clearly differentiated by this method and are surprisingly large, being approximately 2μ in diameter. The large size of nuclei, as seen by giemsa staining, may be due in part to the staining of protein precipitated around the nucleus, for giemsa contains eosin and cannot be expected to be specific for deoxyribonucleic acid (personal communication from Edward Gurr). Staining and mounting in aceto-orcein in identical material handled in the same way until after acid hydrolysis (a modification of Singleton's method[7]) shows smaller nuclei at the same loci as those seen in the giemsa method. Observation of living material with the phase-contrast microscope shows at distinct loci the nuclei and the guttulæ, which in this fungus are seen in lacto-phenol cotton blue preparations.

The observation reported here is contrary to Messiaen's[8] suggestion that uni-nucleate conidia are a constant characteristic of the genera *Colletotrichum* and *Gloeosporium*. It is suggested that spore size is only rather weakly determined genetically, and may depend on the vigour of growth of the mycelium. The frequently observed production of 'mutants' with small conidia may be the result of nutritional maladjustment. Abstriction and cessation of spore growth are not necessarily fully co-ordinated in this isolate.

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SOIL SCIENCE

A Warburg Vessel for Soil Samples

THE Warburg apparatus has often been used in soil research. Ellinger and Quastel[1] stated that the physical state of a moist sample permits sufficient diffusion of oxygen for aerobic biological processes. Therefore in many experiments soil samples are used in naturally moist state without making a suspension. For such experiments the conventional form of Warburg vessel is not convenient. There are difficulties in filling and washing the vessels, in removing the samples for further analysis, etc. The side arm is useless, for it is not possible to pour off quantitatively the substrate, which must therefore be added directly to the sample at the beginning of the experiment.

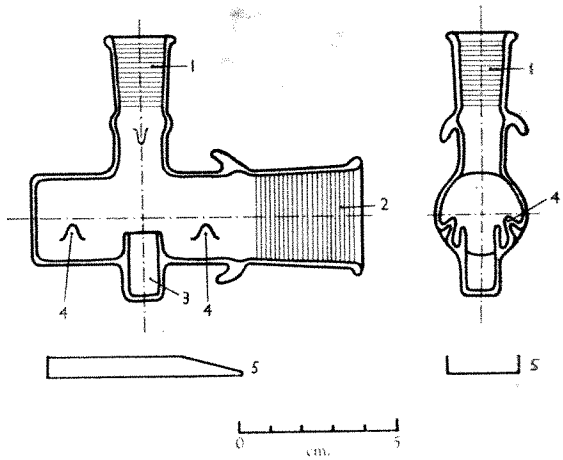

Fig. 1. The Warburg vessel for soil samples.
1, Aperture for manometer; 2, aperture for glass stopper; 3, central well for alkali; 4, support for sample dish; 5, sample dish

For these reasons we use in our Laboratory a Warburg vessel modified after Johnston[2]. The form of this vessel is shown in Fig. 1. The sample is placed on a sample-dish made from plastic or aluminium foil. All dishes have the same weight (that is, the same volume). The volumes of each pair, vessel and manometer, are adjusted to the same value (37 ml.) by means of polyethylene. 0·5 ml. of 20 per cent potassium hydroxide is put into the central well. The advantages of such a vessel are as follows:

(1) The samples are simply weighed direct on the dishes.

(2) The vessels need not be washed after each experiment; the washing of dishes is very simple.

(3) Removing the sample after respiration experiment is easy.

(4) The respiration experiment can be interrupted at any time by removing the dish with the sample which can be put into a wet-chamber in an oven for longer incubation or treated in various ways and then it can be easily returned to the vessel for further respiration measurements.

(5) Since all vessels have the same constant, the calculation of mean values from replicate samples and of net consumption of oxygen for substrate oxidation are very easy, as well as the calculation of the respiratory quotient.

(6) Hydroxide in the central well need not be changed for five days provided no more than 25 ml. of carbon dioxide has been produced. During this time the vessels can be continuously connected with manometers and the exchange of samples can be made only by opening the front glass-stopper.

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Prague.

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Effect of Water-stress on the Absorption of Soil Phosphorus by Wheat Plants

THERE is a limited amount of information on the soil-plant-root interaction with regard to the absorption and accumulation of phosphorus and other ions by plants.

One approach to this problem is to investigate the effect of soil water-stress on the uptake of a particular nutrient ion. From *a priori* reasoning it might be suggested that as the soil water-stress increases the coarse soil pores drain and, therefore, the cross-sectional area for diffusion of ions in the liquid phase is decreased. Hence the rate of absorption per unit area of root surface would decrease. Danielson and Russell[1] present evidence supporting this suggestion. It was found that the uptake of rubidium-86 by maize seedlings from soil decreased with decreasing soil water content. Alternatively, since most nutrient ions are intimately associated with the surface of soil colloids, it is possible that the transfer of ions in the fine pores may be the dominant path for nutrient transfer from soil surfaces to the plant root.

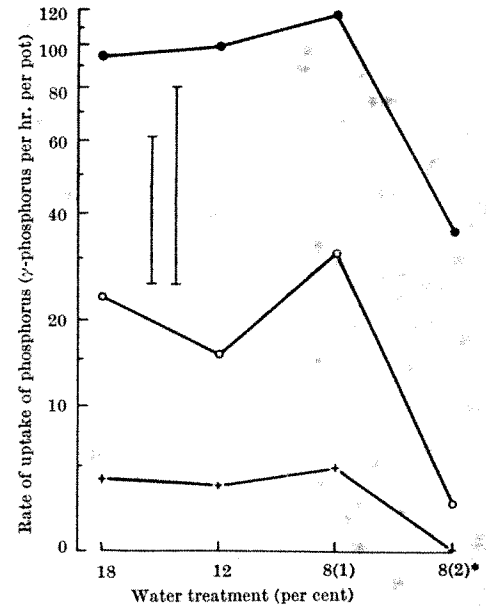
To test the relevance of these ideas, the effect of soil water-stress on the uptake of phosphorus by wheat plants three-weeks old has been studied using phosphorus-32 as a tracer.

Wheat plants (*Triticum aestivium* L. var. Warigo 1957) were grown on a lateritic podzolic soil from Parndarna, South Australia, in a controlled environment room. The interpretation of results was facilitated since this soil was known to be very low in total phosphorus (0·002 per cent) and to have a high capacity for phosphate fixation. Relative humidity and air temperature over the experimental period were as follows: night, 64–65 per cent and 60–62° F.; day, 48–52 per cent and 66–68° F. Day-length was 12 hr. and the light intensity at the top of the pots was approximately 2,000 ft.-candles.

Three levels of phosphorus were used: inadequate (50 p.p.m. phosphorus), adequate (150 p.p.m. phosphorus), abundant (600 p.p.m. phosphorus); 60 μc. phosphorus-32 per gm. phosphorus-31 was used as a tracer. Other nutrients including two micro-nutrients were supplied at levels for normal plant growth. The phosphate and other nutrients were mixed throughout the soil before potting the soil in 'Pyrex' beakers (400-ml.).

Four levels of water stress were imposed as follows: soil maintained at approximately 18 per cent water content (pF 2·3) by frequent watering; soil dried to 12 per cent water content (pF 3·0) then watered to 18 per cent; soil dried to 8 per cent water content (pF 3·7), plants then harvested; or soil dried to 8 per cent water content, then after approximately 12 hr. watered to 18 per cent, dried to 8 per cent water content and the plants then harvested. The water treatments are represented by 18, 12, 8 (1), and 8 (2) per cent respectively. The water-stress treatment during the period from the harvest of the 8 (1) per cent treatment to that of the 8 (2) per cent is represented in Fig. 1 as 8 (2)* per cent. The plants began to wilt at the 8 per cent water content.

All treatments were replicated four times. Nine plants were grown in each pot and all plants were harvested within four days of beginning the water-stress treatments. Additional pots were included to determine the effect of phosphorus-32 on the growth of plants and the uptake of phosphorus. At the beginning of the water-stress treatments, the rate of evapo-transpiration at the adequate and abundant phosphorus-levels was 45 gm. per pot per day and 25 gm. per pot per day at the inadequate phosphorus-level.



Phosphorus-level: 50 p.p.m., +; 150 p.p.m., ○; 600 p.p.m., ●

Fig. 1. Effect of soil water-stress (see text) on the uptake by wheat plants of soil phosphorus. Vertical lines indicate differences for significance at $P < 0·01$ and $P < 0·05$.

Earlier workers have reported that phosphorus-32 may stimulate or retard both the growth of wheat and barley plants and the accumulation of fertilizer phosphorus[2–4]. It is concluded from the present experiment that any effect of phosphorus-32, at the level used, would have been to increase slightly and not decrease phosphorus accumulation by wheat plants. Phosphorus-32 had no effect on the growth of tops and roots at all phosphorus-levels.

The effect of phosphorus-level and water-stress on the rate of phosphorus accumulation is shown in Fig. 1. A statistical analysis was carried out on the results using a log $(x + 10)$ transformation. The analysis showed that the rates of phosphorus uptake for the 18, 12 and 8 (1) per cent water treatments were not significantly different at any one level of phosphorus. However, the reduction in rate of uptake of phosphorus for the 8 (2)* per cent water treatment proved to be significant ($P < 0·05$ to $P < 0·01$) at the adequate and abundant phosphorus-levels. It is to be noted that during the 8 (2)* water treatment, the plants were allowed to wilt for 12 hr. The rate of evapo-transpiration following this period of wilting was significantly less than that prior to wilting. This fact, together with the evidence that the rate of uptake of phosphorus was reduced during the 8 (2)* per cent water treatment, indicates that the mechanism by which phosphorus and water are absorbed by the wheat plants had been damaged by the period of wilting. It is considered that this damage was associated mainly with the roots.

The results, therefore, demonstrate that increasing water-stress did not affect the rate of uptake of phosphorus by young wheat plants provided that the plants were not damaged by wilting.

It is concluded that the available soil phosphorus was mainly held in fine pores that remained full of water even when the plants were wilting. Since these

fine pores would not be so readily drained as coarser pores containing less phosphorus, it is suggested that the concentration of available phosphorus in the fine pores may be considerably higher than has been indicated earlier by workers using displacement techniques.

A more detailed report of this work is being prepared for publication elsewhere.

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[1] Danielson, R. E., and Russell, M. B., *Soil Sci. Soc. Amer. Proc.*, **21**, 3 (1957).
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VIROLOGY

Potato Virus *M* and Paracrinkle

IN a recent communication under this title, Howard and Wainwright[1] confirmed earlier reports[2-4] that potato plants of the variety King Edward contain potato virus *S* plus paracrinkle virus. The communication calls for comment and elaboration because it suggests a uniformity of infection in King Edward plants that conflicts with my experience. During the past two years I have tested many plants from seven different commercial stocks of King Edward, and most contained both viruses; but about 90 per cent of the plants in two of the stocks contained only paracrinkle virus, and one plant contained only virus *S*. This plant is the only one of the many hundreds tested by different workers since Salaman and Le Pelley's[5] original work which did not contain paracrinkle virus.

The origin and behaviour of paracrinkle virus have long continued to stimulate speculation and experiment. To account for the variation in symptoms when Arran Victory was grafted with scions from King Edward, Salaman suggested that King Edward contained two viruses of which occasionally only one was transmitted[6]. However, after it became clear that his suggestion was unacceptable, it became generally accepted that only one virus was involved. For long, too, this virus was thought to be unique to King Edward potatoes and to be transmissible only by grafting. All this is now known to be untrue. Paracrinkle virus was some years ago transmitted by mechanical inoculation of sap[7], and was found to be remotely related serologically to other viruses such as carnation latent virus, which has been transmitted by aphids, and potato virus *S*, which has not[4,8]. Potato virus *S* occurs in many potato varieties, including Arran Victory, so there was the obvious possibility that the severe disease caused in this variety by grafts from King Edward resulted from joint infection with viruses *S* and paracrinkle. My primary purpose in freeing a clone of Arran Victory from potato virus *S* (ref. 9) was to see what symptoms paracrinkle virus alone would cause. To ensure cultures of paracrinkle virus free from virus *S*, I inoculated tomato plants, which are hosts for paracrinkle virus but not for virus *S*, with sap from King Edward leaves and later grafted scions from the tomato plants to virus-free Arran Victory potato plants. Individual Arran Victory plants varied greatly in their reaction; some showed the typical severe paracrinkle, others showed symptoms more resembling those called leaf-rolling mosaic, and still others developed only a chlorotic blotching with little leaf deformity. The range was much the same as when Arran Victory containing virus *S* are infected. Hence, there is no doubt that paracrinkle virus alone can cause a severe crinkling disease in Arran Victory. Virus *S* seems to contribute little to the effects, and the variation in symptoms shown by Arran Victory plants infected with only paracrinkle virus probably means that this, like most other viruses, occurs in strains that differ in virulence.

Plants of several potato varieties suffering from leaf-rolling mosaic have been found to contain a virus that has been called *M* and shown to be closely related serologically to paracrinkle virus[4]. After Wetter and Völk found that virus *M* could be transmitted by the aphid *Myzus persicae*[10], it seemed that the transmissibility of paracrinkle virus by aphids should be re-investigated. The tests I have made show that some stocks of King Edward contain strains of the virus that are transmitted by *Myzus persicae*, whereas from others, which gave similar symptoms when grafted on to Arran Victory plants, the aphid has failed to transmit anything. I am now surveying commercial stocks of King Edward to get some idea of the frequency with which aphid-transmitted strains occur.

The present position can be summarized briefly: most King Edward plants contain paracrinkle virus and virus *S*, some contain only paracrinkle and a few only *S*. The paracrinkle virus in different plants differs in its virulence (some strains are indistinguishable from virus *M*) and in its transmission by *Myzus persicae*.

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THE discovery by Dr. B. Kassanis that 90 per cent of plants in two stocks of King Edward contained only paracrinkle virus and were free from virus *S* suggests that virus *S* entered King Edward stocks later than did paracrinkle virus (virus *M*). The King Edward used by us[1] was possibly derived from Salaman's original material, as the plants investigated were the descendants of occasional Red King mutants found in a stock being propagated by the National Institute of Agricultural Botany and which had originally been supplied by Salaman[2]. Similarly, the King Edward stock investigated by Bagnall, Larson and Walker[3] in the United States, and which also contained both viruses *S* and *M*, was obtained indirectly from Salaman. This suggests that the

stock of King Edward used by Salaman and Le Pelley[4] may have contained both viruses *S* and *M*, although, of course, stocks at the National Institute of Agricultural Botany and those in the United States could have picked up virus *S* at a later date.

We should also like to take this opportunity of saying that in our previous communication[1] we have misinterpreted Bagnall, Wetter and Larson[5]. Although they state that "evidence now indicates that paracrinkle is for all practical purposes a synonym of leaf-rolling mosaic, and that both of these diseases are incited by complexes of virus *S* and virus *M*", Dr. Wetter has pointed out to us that in other parts of their paper they leave it undecided as to the parts played by the two viruses in causing paracrinkle and leaf-rolling mosaic symptoms.

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Influence of a Quaternary Ammonium Salt on the Infectivity of Ribonucleic Acid from Tobacco Mosaic Virus

IN a previous paper, some of us[1] have shown that the quaternary ammonium salts of deoxy- and ribonucleic acids are soluble in organic solvents, and that by the addition of a concentrated solution of sodium chloride a precipitate of the sodium salt of the nucleic acids is obtained. It seemed interesting to us to know if the preliminary treatment of a viral ribonucleic acid with a quaternary ammonium salt produces a structural modification which can be demonstrated by the disappearance of the infectivity of the ribonucleic acid.

Ribonucleic acid preparations were obtained from tobacco mosaic virus by the phenol method of Gierer and Schramm[2]. The solutions in 0·01 *M* phosphate contain about 0·3 per cent ribonucleic acid. The infectivity of these preparations was tested by counting the number of lesions produced on *Nicotiana glutinosa*. At the same time the following controls were made on the solutions: measurement of the sedimentation constant, determination of the molecular weight by light-scattering, serological control of the absence of viral proteins.

Simultaneously, one volume of the solution of ribonucleic acid from tobacco mosaic virus was divided into two parts; an equal volume of 0·2 per cent cetyl-trimethyl-ammonium bromide was added to each part; the precipitates of the ammonium salts of ribonucleic acid were washed three times by centrifuging their suspensions in water. Then, one of the samples was dissolved in absolute ethanol and the other one in dimethylformamide. The ribonucleic acid was precipitated in both solutions by 3 *M* sodium chloride and dissolved in 0·01 *M* phosphate. The concentration of these solutions was determined by measurements of the optical density at 260 mμ with a Jobin–Yvon spectrophotometer. The infectivity tested by the lesions produced on *N. glutinosa* in both cases was compared with the infectivity of the original solution. The results are given Table 1.

Table 1

	No. of lesions per 25 leaves			Concentration of ribonucleic acid (mgm. per ml.)		
Experiment	1	2	3	1	2	3
Ribonucleic acid control	350	166	530	1·00	1·13	1·19
Ribonucleic acid from ethanol solution	369	140	350	1·04	1·03	0·58
Ribonucleic acid from dimethylformamide solution	118	118	270	1·04	0·81	0·96

It was found that 1 ml. of each solution incubated at 4° C. during 10 min. with 2 μgm. ribonuclease gives no lesions on the host.

The present results show that precipitation of the tobacco mosaic virus ribonucleic acid as a quaternary ammonium salt, its solubilization in ethanol or dimethylformamide and its regeneration as a sodium salt do not destroy its infectivity. However, it can be seen that although the infectivity is not significantly altered after treatment with ethanol, it seems to be lowered after the treatment with dimethylformamide.

These results seem to be in general agreement with those obtained by Guerritore[3] on the effect of cetyl-trimethyl-ammonium bromide on the infectivity of aqueous extracts of Rous sarcoma.

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MISCELLANY

A New Shadowing Material for Electron Microscopy

THE high resolving power of electron microscopes at present available makes the granularity of metal-shadowing media the limiting factor in the observation of extremely fine details of surface topography in shadowed specimens.

Platinum has probably been used more widely than any other metal because its high melting point and chemical inertness result in a very stable film. It does, however, have one disadvantage in that it forms a crystalline film which tends to appear granular at high magnification. When a platinum-shadowed specimen is examined at magnifications higher than about × 40,000, the image is seen to consist of many small opaque spots. While this

granularity serves as an excellent test-object for resolution, it begins to limit detail in shadowed specimens.

In our search for a finer grained material, two things led us to try osmium oxide : (i) tissue sections stained with osmic acid often show very fine-grained, extremely opaque detail ; (ii) a heavy metal oxide or mixtures of oxides might provide contrast but yet crystallize less readily than pure metals.

An osmium oxide can be obtained easily by mixing dilute aqueous solutions of osmium tetroxide and ferrous sulphate. A heavy, black, easily filterable precipitate forms at once and can be washed free of iron with dilute sulphuric acid. This black precipitate, although too dense to permit electron diffraction as formed, has been shown to be amorphous by X-ray diffraction. It can be evaporated from a tungsten ribbon to form a film that is not only amorphous to electron diffraction in the same sense that carbon is amorphous, but also exhibits intense scattering in the diffuse halos, as shown in Fig. 1*a*. This results in extreme opacity and requires only a very thin film to provide adequate contrast in the final image. Suitable films of osmium oxide are in fact so thin that they do not change the visual appearance of the specimen.

This black osmium oxide, on heating to red-heat in a closed container, forms brown-red crystalline osmium dioxide, identified by X-ray diffraction. Even this crystalline material forms an amorphous film on evaporation.

In the specific example described here, a small portion (~10 mm.^{3} volume) of moist osmium oxide was placed on a tungsten ribbon filament approximately 10 mm. × 40 mm. and evaporated through a 2-mm. pin-hole placed as close as possible to the filament. The specimen was placed approximately 8 cm. from the source and shadowed at an angle of 30°. After shadowing, the shadowed carbon film was floated in the conventional way from its mica support and picked up on a standard specimen grid.

Fig. 2*b* shows fine crystals of sodium laurate grown from acetone on a carbon support film and shadowed with platinum. Compare this with the same material shadowed with osmium oxide (Fig. 2*a*). Notice how these crystals are more clearly outlined. The granularity in the background is quite different from that of the crystals and probably reflects the granularity of the carbon film. For our work with this type of sample, osmium oxide has proved superior to platinum as a shadowing agent.

The electron-micrographs were obtained on a Siemens Elmiskop I using a beam voltage of 80 kV., and × 40,000 direct magnification. Magnification of micrographs reproduced is × 280,000.

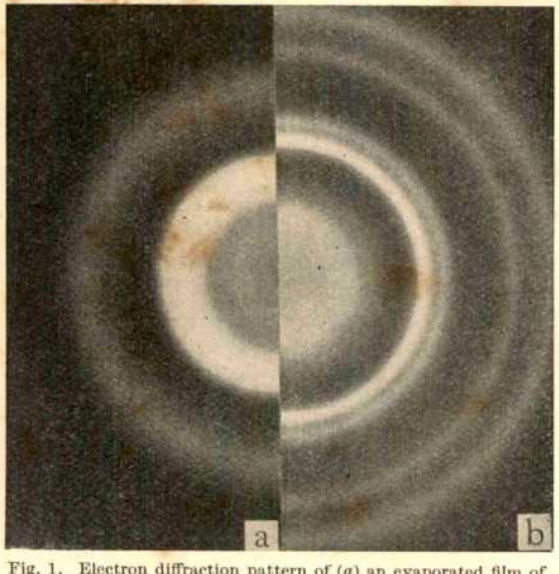
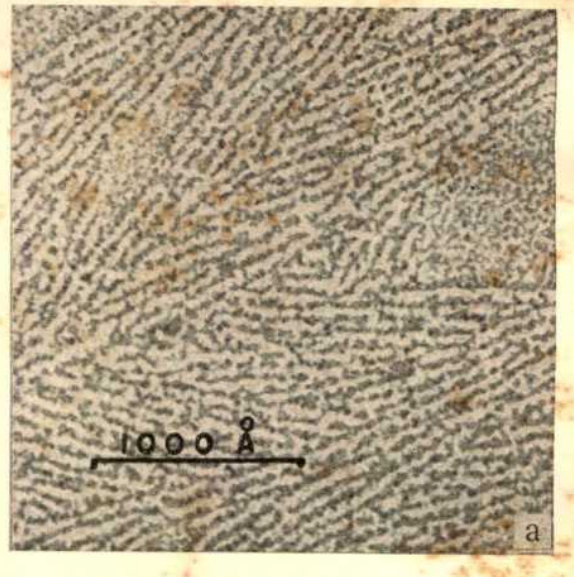


Fig. 1. Electron diffraction pattern of (*a*) an evaporated film of OsO_2 showing diffuse, intense halos, and (*b*) an evaporated film of platinum on a carbon support showing the crystalline nature of the material



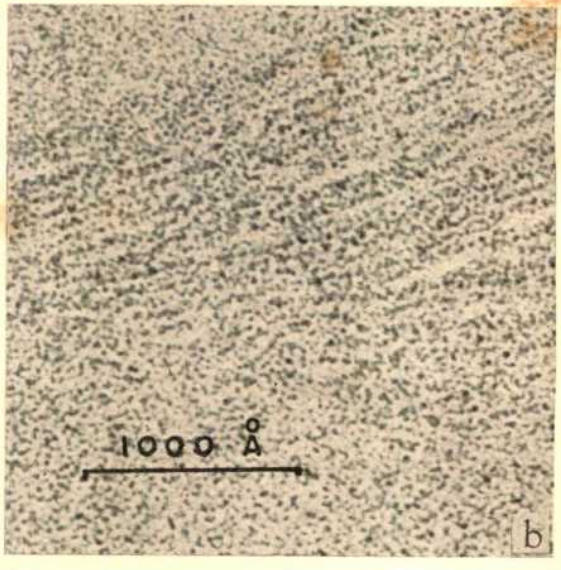


Fig. 2. Electron micrographs of sodium laurate crystals taken at 40,000 × using (*a*) osmium oxide shadowing and (*b*) platinum shadowing

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FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, November 21

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S.W.7), at 5 p.m.—Mr. R. J. Harrison Church. "Problems and Development of the Dry Zone of West Africa".

SOCIETY OF CHEMICAL INDUSTRY, PESTICIDES GROUP (at 14 Belgrave Square, London, S.W.1), at 5.30 p.m.—Mr. L. C. Stones: "Systemic Use of Insecticides in Animals".

UNIVERSITY OF LONDON (in the Anatomy Lecture Theatre, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. John O. Corliss (University of Illinois): "A Modern Approach to Phylogeny and Evolution of the Protozoa".* (First of three lectures on "The Evolution of the Protozoa". Further lectures on November 28 and December 5.)

INSTITUTION OF ELECTRICAL ENGINEERS, LONDON GRADUATE AND STUDENT SECTION (at Savoy Place, London, W.C.2), at 6.30 p.m.—Mr. M. J. Pope: "Magnetic Amplifiers in Power Engineering".

Monday, November 21—Friday, November 25

SECOND INDUSTRIAL PHOTOGRAPHIC AND TELEVISION EXHIBITION (at the Royal Albert Hall, London).*

Tuesday, November 22

SOCIETY OF CHEMICAL INDUSTRY, AGRICULTURE GROUP (at 14 Belgrave Square, London, S.W.1), at 10.30 a.m.—Meeting on "Physiological and Economic Aspects of the Nutrition of Livestock".

UNIVERSITY OF LONDON (at Bedford College, Regent's Park, London, N.W.1), at 5.15 p.m.—Dr. Kathleen Kenyon: "Archæology and History".*

INSTITUTION OF ELECTRICAL ENGINEERS (joint meeting with the INSTITUTION OF CIVIL ENGINEERS, at the Institution of Civil Engineers, Great George Street, London, S.W.1), at 5.30 p.m.—Mr. V. Furuskog and Mr. G. F. Kennedy. "The Aswan Hydro-Electric Scheme".

INSTITUTION OF MECHANICAL ENGINEERS, LUBRICATION GROUP (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Discussion on "Bearing Corrosion".

UNIVERSITY OF LONDON (in the Library of the Institute of Bankers, 10 Lombard Street, London, E.C.), at 6 p.m.—Mr. D. T. Healey: "Case Study in Agriculture". (Fourth of five lectures on "United Europe". Further lecture on November 29.)

SOCIETY OF CHEMICAL INDUSTRY, PLASTICS AND POLYMER GROUP (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Dr. P. H. Plesch: "A Comparison between Cationic and Free Radical Polymerisation".

Wednesday, November 23

UNIVERSITY OF LONDON (at the Postgraduate Medical School of London, Ducane Road, London, W.12), at 2 p.m.—Dr. V. Wynn "Acid-base Metabolism".*

SOCIETY OF CHEMICAL INDUSTRY, FOOD GROUP (in collaboration with the FOOD MANUFACTURERS' FEDERATION, INC., at the Borough Polytechnic, Borough Road, London, S.E.1), at 2.30 p.m.—Meeting on "Protective Clothing in the Food Industry".

GEOLOGICAL SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Dr. R. L. Oliver: "The Borrowdale Volcanic and Associated Rocks of the Scafell Area, Lake District"; Dr. J. H. D. Whitaker: "The Geology of the Area around Leint Wardine, Hereford".

INSTITUTION OF MECHANICAL ENGINEERS (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Mr. H. Headland: "Blaenau Ffestiniog and other Medium Head Pumped Storage Schemes in Great Britain".

SOCIETY OF ENVIRONMENTAL ENGINEERS (at the Imperial College of Science and Technology, London, S.W.7), at 6 p.m.—Meeting on "Vibration Testing and Instrumentation of Large Stores".

BRITISH INSTITUTION OF RADIO ENGINEERS, ELECTRO-ACOUSTICS GROUP (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6.30 p.m.—Mr. F. H. Brittain: "Objective and Subjective Requirements for Loudspeakers".

ROYAL INSTITUTE OF CHEMISTRY (joint meeting with the SOUTH-WEST ESSEX COLLEGE OF TECHNOLOGY CHEMICAL SOCIETY, at the South-West Essex College of Technology, Forest Road, London, E.17), at 7 p.m.—Prof. J. A. V. Butler, F.R.S.: "Nucleic Acids and Heredity".

Thursday, November 24

LINNEAN SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Dr. Wm. T. Stearn. "On the Sesquicentenary of the publication of Rbt. Brown's *Prodromus Novae Hollandiae*"; Dr. Robert F. Thorne "The Queensland Rain Forests".

ROYAL SOCIETY OF ARTS, COMMONWEALTH SECTION (at John Adam Street, Adelphi, London, W.C.2), at 5.15 p.m.—Mr. Peter Runge: "The West Indian Sugar Industry".

UNIVERSITY OF LONDON (at the Institute of Laryngology and Otology, Royal National Throat, Nose and Ear Hospital, Gray's Inn Road, London, W.C.1), at 5.30 p.m.—Dr. E. H. Mercer. "The Fine Structure of the Normal and Malignant Cell".*

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. H. B. Hewitt. "Fundamental Aspects of the Radiotherapy of Cancer".* (Eleventh of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

UNIVERSITY OF LONDON (at Wye College, Wye, Ashford, Kent), at 8 p.m.—Prof. B. Maegraith: "The Effects of Disease and Environment on Economic and Social Development in Hot Countries".*

Thursday, November 24—Friday, November 25

INSTITUTE OF PACKAGING (at the Connaught Rooms, Great Queen Street, London, W.C.2), at 10 a.m. daily—Conference on: "Odour in Packaging".

Thursday, November 24—Tuesday, December 20

ROYAL PHOTOGRAPHIC SOCIETY OF GREAT BRITAIN (at 16 Princes Gate, London, S.W.7)—Autumn Exhibition of Nature Photography.*

Friday, November 25

INSTITUTE OF PHYSICS AND THE PHYSICAL SOCIETY (at the Institution of Electrical Engineers, Savoy Place, London, W.C.2), at 10 a.m.—Symposium on "New Materials of Interest to the Physicist".

BRITISH NATIONAL COMMITTEE FOR HIGH SPEED PHOTOGRAPHY (in the Lecture Theatre, Victoria and Albert Museum, South Kensington, London, S.W.7), at 10.15 a.m.—Report on "The Fifth International Congress on High Speed Photography, Washington, October 16–23".

Friday, November 25—Saturday, November 26

BRITISH SOCIETY FOR IMMUNOLOGY (at the Wellcome Building, 183 Euston Road, London, N.W.1)—Autumn Meeting.

Friday, November 25

At 9.30 a.m.—Symposium on "Stimulation of Antibody Production". Chairman: Sir John Boyd, F.R.S.

Saturday, November 26

SOCIETY FOR THE STUDY OF HUMAN BIOLOGY (in the Department of Anatomy, University College, Gower Street, London, W.C.1), at 10 a.m. and 2.15 p.m.—Symposium on "Recent Developments in the Study of Characters of Anthropological Importance"

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned.

ASSISTANT CATALOGUER (graduate, preferably with library experience) IN THE SCIENCE SECTION of the University Library—The Registrar, The University, Manchester (November 26).

OFFICIAL FELLOW IN MATHEMATICS—The Principal, Hertford College, Oxford (November 26).

LECTURERS (2) (with good academic qualifications and industrial or other experience in one of the following fields: electric power engineering, electrical machines, electrical measurements, control engineering, or microwave engineering) IN THE DEPARTMENT OF ELECTRICAL ENGINEERING—The Registrar, The University, Leeds 2 (December 2).

READER (with a degree in pharmacy, and the qualifications and experience to direct research and postgraduate work in the physical aspects of pharmaceutics) IN GENERAL PHARMACEUTICS—The Clerk to the Governors, Chelsea College of Science and Technology, Manresa Road, London, S.W.3 (December 2).

RESEARCH FELLOWS (honours graduates in chemistry with interests in physical chemistry) IN POLYMER CROSS-LINKING in the Department of Textile Chemistry—The Registrar, Manchester College of Science and Technology, Manchester 1 (December 3).

ASSOCIATE PROFESSORS IN MATHEMATICS AND APPLIED MATHEMATICS at the University of Cape Town, South Africa—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (South Africa and London, December 5).

SENIOR LECTURERS and LECTURERS IN MATHEMATICS at Monash University, Clayton, Victoria, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, December 5).

ASSISTANT LECTURER (preferably with experience in teaching and research, and with training in physical chemistry) IN CHEMISTRY—The Secretary, The Medical College of St. Bartholomew's Hospital, West Smithfield, London, E.C.1 (December 10).

DEMONSTRATOR IN SMALL ANIMAL MEDICINE AND SURGERY—The Registrar, The University, Liverpool (December 10).

BIOPHYSICIST IN THE DEPARTMENT OF MEDICINE, University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, December 16).

LECTURER (preferably qualified in physical geography) IN GEOGRAPHY at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, December 19).

LECTURER IN PSYCHOLOGY—The Registrar (Room 22, O.R.B.), The University, Reading (December 31).

CIBA FELLOWSHIPS to enable graduates of universities of the U.K., Northern Ireland and Eire (who may be at present either at the university or in industry) to carry out research at Continental universities in chemistry, physics or some other allied scientific subject—The Ciba Fellowship Trust, Ciba (A.R.L.), Limited, Duxford, Cambridge (January 15).

CHAIR OF PSYCHOLOGY in the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, January 31).

ASSISTANT BIOCHEMIST (with a first- or second-class honours degree in chemistry or biochemistry) IN THE AREA PATHOLOGY LABORATORY—The Administrative Officer, Stoke Mandeville Hospital, Aylesbury.

ASSISTANT LIBRARIAN (Associate of the Library Association, and preferably with a knowledge of French and German) IN THE DEPARTMENT OF FORESTRY—The Librarian, Department of Forestry, South Parks Road, Oxford.

ASSISTANT (preferably with a medical qualification and previous laboratory experience) IN THE DEPARTMENT OF BACTERIOLOGY, for duties which will include some teaching and virus research—The Secretary, University College Hospital Medical School, University Street, London, W.C.1.

CHEMIST or PHYSICIST (with a first- or good second-class honours degree in chemistry or physics, and preferably Ph.D. or equivalent research experience in the following fields: (a) irradiation metallurgy; (b) ceramics; (c) fluid flow and diffusion through porous materials; and (d) radioactive measurements), to lead a team in experimental work concerned with aspects of radiation and thermally induced changes in structural materials, radiation dosimetry and fuel burning—The Personnel Manager (1778/34), U.K.A.E.A., A.E.R.E., Harwell, Didcot, Berks.

EXPERIMENTALIST (with G.C.E. at "A" level, H.N.C. or equivalent and appropriate experience) IN THE PROTON PHYSICS GROUP of the Nuclear Physics Division, for work associated with the investigation of various methods, such as plating and vacuum evaporation, for producing thin targets for exposure in the proton linear accelerator and also to work on nuclear detectors and to participate in the experimental work of the group which is using the P.L.A. for studying nuclear structure—The Personnel Manager (1824/34), U.K.A.E.A., A.E.R.E., Harwell, Didcot, Berks.

LABORATORY STEWARD, Grade I (with a higher national certificate or higher national diploma in electrical engineering or physics, or equivalent qualifications), to undertake the operation and servicing of the new Phillips E.M. 100 electron microscope and of X-ray diffraction equipment, and to assist in the maintenance and servicing of nucleonic counting equipment and general laboratory duties—The Clerk to the Governors, Plymouth and Devonport Technical College, Education Offices, Cobourg Street, Plymouth.

LECTURER IN AERODYNAMICS; and an ASSISTANT LECTURER IN AERODYNAMICS OR AERO/SPACE PROPULSION, to engage in B.Sc., Dip. Tech. and postgraduate courses and in research—The Secretary, Northampton College of Advanced Technology, St. John Street, London, E.C.1.

MYCOLOGIST (with Ph.D. or equivalent degree), to carry out diagnostic work for the hospital (including collaborative research work with the clinical departments) and research in air-borne fungi in conjunction with the Department of Allergy—The Secretary, Wright-Fleming Institute of Microbiology, St. Mary's Hospital Medical School, Norfolk Place, London, W.2.

READER (with high academic qualifications and research or industrial experience) IN FLUID MECHANICS OR AERO/SPACE PROPULSION—The Secretary, Northampton College of Advanced Technology, St. John Street, London, E.C.1.

RESEARCH ASSISTANT (graduate, not necessarily in a science subject) WITH THE DATA ANALYSIS GROUP, to assist with, and then take charge of, an electronic measuring machine and teleprinter recording data from interactions of high energy particles in a bubble chamber—The Administrative Assistant, Physics Department, The University, Birmingham 15.

RESEARCH ASSISTANT, for chemical and radiochemical analytical work on minerals—Dr. J. R. Butler, Geology Department, Imperial College of Science and Technology, London, S.W.7.

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(not included in the monthly Books Supplement)

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PHYSICS LIBRARY

LIBRARIES AND LIBRARY SERVICE IN BRITAIN

ALTHOUGH the question of scientific and technical libraries was virtually ignored in the recent annual report of the Advisory Council for Scientific Policy, a full session of the Home Universities Conference in December 1959 was devoted to a discussion on university libraries. One of the participants in that discussion, Mr. B. S. Page, was this year's president of the Library Association, and in his annual address to the Association at Scarborough in September—when Dr. D. J. Urquhart outlined the ideas and motives behind the development of the National Lending Library for Science and Technology—he stressed once again the human aspect of librarianship and the demands made on the librarian for scholarship, as well as for human understanding and imaginative insight into the needs of the users of his library. That was, in fact, one of the dominant notes struck in the discussion last winter at the Home Universities Conference*, which was particularly concerned that in the planning and organization of a university library the point of view of the reader, and indeed his weaknesses, should not be ignored. Here, perhaps, as nowhere else, the value of 'browsing' is greatest and special efforts are justified to ensure the maximum access. Prof. J. M. R. Cormack quoted with approval Justin Winsor's principle that books should be used to the largest extent possible and with the least trouble, and observed that it was often the chance find on the shelves that was most useful.

It should not be supposed that either the Advisory Council for Scientific Policy or the University Grants Committee is likely to be altogether unmindful of the human aspects of an adequate library system, whether in the universities or elsewhere, or to forget that however adequate the provision made, its effective use will depend to a great extent on the men and women who operate the service. Men and women of the high calibre and enthusiasm desired will not be forthcoming unless they are given both the tools for the job and accorded the status and respect that go with the scholarship and administrative responsibility involved. These professional demands are growing, and it is important that when the physical needs of university libraries and of a national library service, of which it should be remembered university libraries form an indispensable part —they supplied 28,611 books to the National Central Library in 1959–60 as against the 12,793 they received—are steadily growing, this aspect is not overlooked. Indeed, the co-operation which is essential if an adequate national system is to be developed itself makes considerable demands on the personality and administrative ability of the librarian. It is not simply a matter of techniques and mechanical devices.

The latter, however, is the only aspect to which the Advisory Council on Scientific Policy refers in the section on library work in its current report. Recognizing the immensity of the problem created by the enormous growth of the output of scientific literature in all countries, the Advisory Council suggests that this problem will continue increasingly to impede the utilization of scientific and technical information, and so progress, unless it is recognized as meriting research in its own right; techniques must be devised for recording and presenting scientific information in a form in which its significance can be most readily appreciated by those who have to use it. The Council considers that serious research into the whole problem of collation and dissemination of scientific information should be undertaken forthwith, possibly under the auspices of the new National Science Lending and Reference Libraries and in association with international efforts in this sphere.

The Advisory Council does not mention the Association of Special Libraries and Information Bureaux, of which the terms of current grant from the Department of Scientific and Industrial Research require it to undertake research into the field of documentation; but at least its remarks show that the Advisory Council is aware both of the magnitude of the problem and of the need for co-operation up to the international level. The enormous increase in the output of scientific literature is, however, not reflected in the returns for library expenditure given by the University Grants Committee. While annual expenditure on libraries had risen from £156,000 in 1925–26 to £255,000 in 1938–39, £988,000 in 1951–52 and £1,979,945 in 1959–60, the doubling of expenditure during the past decade has been spread fairly evenly over the different items. Expenditure on salaries and wages rose from £527,238 to £1,070,466; on books from £202,567 to £434,254; and on periodicals from £118,702 to £231,458. The percentage which library expenditure represents to the total expenditure remains at 3·8.

It is, however, the figures for the expenditure of individual libraries that are most illuminating. Apart from the University of London, with expenditure on books of £91,817 (£12,301 was for the Central Library and £13,526 for University College), the only university libraries in Britain spending more than £20,000 on books in 1959–60 are those which are entitled to receive on demand a copy of every published book in the United Kingdom, namely, Oxford (£62,088) and Cambridge (£28,734). Indeed, outside Scotland, where Edinburgh, Glasgow and St. Andrews spent more than £19,000, £18,000 and £16,000, respectively, on books, only Manchester, Leeds, Birmingham, Durham, Liverpool and Sheffield spent more than

* Association of Universities of the British Commonwealth. Conference of the Universities of the United Kingdom—Report of Proceedings. Pp. 104. (London: Association of Universities of the British Commonwealth, 1960.) 5s.

£10,000. The picture with expenditure on periodicals is similar. A quarter of London's expenditure of £63,173 was for the Central Library and that of University College. The University of Cambridge spent £17,400 on periodicals and the University of Oxford £15,461; only three other universities spent more than £10,000—Glasgow, Manchester and Birmingham—though Edinburgh spent only just short of this figure. Furthermore, the proportion which library expenditure bears to the total expenditure also varies widely, especially among the English universities—from 8·3 per cent for Oxford and 7·2 for the Durham Colleges of the University of Durham to 2·0 for King's College of the same University and 0·9 for the Manchester College of Science and Technology; and within the University of London, which averages 3·5, from 36·5 for special institutions like the Courtauld Institute of Art, 7·7 for the London School of Economics and also for the Central Library, to 0·9 for the Imperial College of Science and Technology—a figure attributed to the access enjoyed to the Science Library.

How far these figures are really comparable cannot be judged from the tables supplied by the University Grants Committee, but clearly some account must be taken both of the existing resources of a university and its size. Apart from the fact that some figures like that for the Manchester College of Science and Technology are clearly abnormal—in this instance through inclusion under miscellaneous university expenditure of a surprisingly high figure for interest on overdrafts, etc.—it is common knowledge that expenditure on books for departmental libraries is sometimes included under departmental expenditure and sometimes under library expenditure. It is noteworthy that in the new institutions such as the University College of North Staffordshire (5·7), University of Hull (5·4), University of Exeter (5·0), University of Leicester (5·3) and University of Southampton (4·8) the percentage of library expenditure to total expenditure is above the average. Mr. K. W. Humphreys, librarian of the University of Birmingham, in opening the discussion at the Home Universities Conference, pointed out that already expenditure on libraries exceeds the total Government grant to universities a generation ago. Even at the existing rate of growth, £16 million might well be required for libraries by the late 'eighties, and if any attempt is made to overtake the rapid increase in student population after the mid 'seventies, libraries should absorb an increasing proportion of the general university grant—possibly 10–15 per cent by the end of the century.

So long ago as 1921, the University Grants Committee expressed the view that the character and efficiency of a university might be gauged by its treatment of its central organ, the library. "We regard the fullest provision for library maintenance as the primary and most vital need in the equipment of a university. An adequate library is not only the basis of all teaching and study, it is the essential condition of research, without which additions cannot be made to the sum of human knowledge." In its report on "University Development" two years ago, the Committee recognized that a large part of university expenditure for research of all kinds is expenditure on libraries, and that although between 1951–52 and 1956–57 expenditure on libraries had increased by 64 per cent, this was largely due to increased costs, and the real increase was less than 10 per cent.

Mr. Humphreys recognized that the new National Lending Library for Science and Technology should relieve some of the pressure on the universities inter-lending scheme and provide copies of out-of-the-way periodicals so that science and technology can be better served; but even this passing reference indicates that the universities cannot stand right outside the library services of Great Britain, and Dr. Urquhart, in speaking at Scarborough, reiterated his view that demands for inter-library lending are likely to grow. Mr. Humphreys believes that while the undergraduate population has increased, their book buying has declined; this has been challenged, but even if the Anderson Committee's recommendation that an allowance for books should be included in all maintenance grants and the figure made public has its full effect, the university library is unlikely to benefit substantially. As Mr. Humphreys himself pointed out, the best hope of relieving pressure lies in co-operative action, in the adoption where possible of new techniques and in skilled administration—the same factors that alone can ensure the most efficient use of whatever resources may be available.

Some of these problems were indicated in an illuminating address by Prof. J. M. R. Cormack, who, approaching the problem from the reader's point of view, displayed very clearly not merely some of the opportunities for improvement but also the pitfalls that attend the unwary adoption of new gadgets. It was left, however, for Mr. Humphreys, in replying to the discussion, to refer to some of the implications of the suggestions which had been made in regard to such matters as inter-university co-operation and longer hours of opening. Questions of staff and of finance as well as education may be involved, running well outside the university library itself.

This discussion at last year's Home Universities Conference shows clearly that the universities themselves are well aware of the importance of the university library and the vital contribution it makes to the efficiency with which a university performs its functions of teaching and research. Moreover, those in charge of the university libraries are obviously alive alike to the varied needs of the users of those libraries, whether they be undergraduates or members of the university's staff; and they are no less aware of the important place which the university library holds in the library system of Great Britain as a whole. The way in which criticism advanced in the course of the discussion was received is no less encouraging; weaknesses in the university libraries should not be charged primarily against those

responsible for their administration, but against those responsible for failure to provide the resources commensurate with the growing demands which the universities and the community make on the university libraries.

How far those weaknesses are the responsibility of the University Grants Committee itself or of individual universities can scarcely be judged from the published evidence. All that can be said is that, judged in terms of total expenditure on libraries, expenditure on books, periodicals or staff, or the proportion which library expenditure bears to university expenditure as a whole—or on the expenditure per head of staff and student as noted by Dr. W. S. Mitchell in the discussion—the expansion of expenditure on libraries falls a long way short of that required to meet the ideal formulated by the University Grants Committee more than a generation ago. What is clearly needed is much firmer support from the University Grants Committee and also a wider public understanding generally.

Mr. B. S. Page, in his presidential address to the Library Association, manifestly sought to enlist such support and understanding from the Library Association, and there should be other opportunities in the present Parliamentary session which might be used. In spite of the fact that the Roberts Committee on the structure of the public library service was singularly indifferent to the part played by the universities, that omission should be rectified whenever the Minister of Education advances his proposals for action on the report, though that is unlikely to be in the present session—a fact which itself indicates how little importance the Government attaches to the provision of an adequate library service. It is, however, on the Advisory Council for Scientific Policy and on the Minister for Science that the major responsibility rests. Dr. Urquhart's address to the Library Association shows that he is aware of the inter-relations between the university libraries and the new National Lending Library for Science and Technology, and that he is indeed anxious to foster co-operation and on the proper basis—of ascertained fact. Dr. Urquhart, however, is only responsible for the lending side, and the National Reference Library for Science and Technology also comes into the picture.

It is only as the Minister and the Advisory Council ensure that that project is vigorously and adequately developed, and due account taken not only of the resources and functions of the university libraries and of those of the colleges of technology, but also of the technical libraries provided by at least the major public libraries, that we can hope to see, inside and outside the universities, a library service adequate to meet the needs of the whole community in this age of rapid technological change. It has to be admitted that so far the Minister and the Advisory Council have shown little sign that they are aware of the immensity of their responsibility in this field, or of its far-reaching implications. One remark at least in a discussion at the Library Association's Conference at Scarborough should bring that responsibility home. Commenting on Mr. M. C. Pottinger's address on "Libraries in the Soviet Union", Mr. L. L. Ardern, of the Manchester College of Science and Technology, remarked that the need for a British Scientific Information Centre had been very fairly illustrated, and Mr. Pottinger fully concurred. When all recognition has been made of Dr. Urquhart's readiness to see the new National Lending Library for Science and Technology functioning as part of a truly national system, it is difficult to reconcile its location in Lincolnshire, or the tardiness with which the corresponding reference library project is developing, with any sense at the centre of the inter-relations inherent in a national system, or of the savings which could have been achieved by real planning in relation to the resources of the whole country. Little account seems to be taken of the contributions which the university libraries and those of the learned societies and professional institutions, as well as the National Central Library and the public libraries themselves, could make. In few other fields is piecemeal development more costly in terms of finance and of goodwill.

DARWIN PARTIALLY APPRAISED

Darwin's Place in History

By Prof. C. D. Darlington. Pp. ix+101. (Oxford: Basil Blackwell, 1959.) 9*s*. 6*d*.

PROF. DARLINGTON is perhaps unfortunate in the fact that his essay, dated February, was not published until the late December of 1959, the year when a spate of publications celebrating the centenary of the "Origin" almost overwhelmed the reader. His thesis does not therefore strike home with the originality which its initial composition presumably required. Charles Darwin is shown in this publication to have used the work of precursors in the field of transmutation without sufficient acknowledgment; to have equivocated over the problem of the origin and transmission of variation in Nature; to have "failed to recognize or to relate his own ideas . . . with those of others working in the same field"; and to have used to help achieve his admitted "success in mass conversion" to the evolutionary hypothesis "a flexible strategy which is not to be reconciled with even average intellectual integrity". Darwin is given credit for independence of thought, but this he owed not to any personal quality but to the fact that "by independence of economic position, he had a unique advantage over all his contemporaries".

This remarkable and original view is presented with a pretty wit and a challenging directness. Nobody reading this pamphlet could fail to be stimulated by it. The author is master of the telling phrase, for example, when he refers to Darwin "assembling his forces with a prudent strategy without which he would never have won his battle"; his remark that historians of science "often believe what the discoverer writes about his own discoveries, which, as we see, is not a wise thing to do"; and his comment on Samuel Butler's last anti-Darwin

book "its title *Luck or Cunning* referred not to the causes of Darwin's success but to Butler's views on evolution".

Darlington makes a clear distinction between 'hard' and 'soft' heredity. Hard heredity implies selection after variation and soft heredity direction before variation. In an appendix he supplies an anthology of great value for the student from the writings of protagonists of both views. It is fortunate that the original language is sometimes given so the reader may reach his own conclusion concerning the propriety of translating "genitalia corpora" in Lucretius as "genetic bodies".

Authors are frequently presented in language, admittedly colourful, which carries undesirable overtones of sense acquired in more recent usage. Lawrence, for example, is credited with the use of 'mutation' though he actually wrote "native or congenital varieties". It is somewhat disconcerting to find that Prof. Darlington seems unaware that until the 1850's the word evolution was used in an embryological as well as in its later (post-Darwin) transmutation sense, for he comments (p. 35) that T. H. Huxley's (1878) essay on the history of evolutionary theory was "curiously combined with a history of embryology" although one of his own quotations from Spencer (p. 83) speaks of the physiologist "who knows that every individual being is so evolved" from "their earliest condition" when "the germs of all plants and animals whatever are so similar". Nor is it correct to imply that Darwin did not begin to write the "Origin" until he received Wallace's essay for publication, or that Darwin considered all differences between parents blended in their offspring. On this latter point, Darwin in 1837 wrote opposite Lyell's phrase, "Some acquired peculiarities of form, structure, and instinct are transmissible", the comment "with no tendency to go back" and "the very character of species is character being heredity", an unexceptionable statement of 'hard' heredity[1].

Erasmus Darwin as "the great precursor" is well presented in this pamphlet, though it might be made clear to the reader, since Prof. Darlington places so much weight on Charles's reading of his grandfather's works while at Edinburgh, that he arrived there a boy of sixteen and stayed for less than two years.

The claims of Lawrence as a precursor and advocate of 'hard' heredity are seriously advanced by Darlington. Lawrence's lectures, published in 1819, argue at length, and somewhat repetitiously, to demonstrate "that the human species, therefore, like that of the cow, sheep, horse, and pig, and others, is single, and that all the differences, which it exhibits, are to be regarded merely as varieties". There is no evidence that Darwin read this work before 1847, when his ideas were already fully developed. His copy, at Down House, of these lectures is the 1822 Benbow edition. The notes on the back flyleaf include "Zool. acceptation of Species etc. 225–232", but no comment in written on these text pages. What is useful in Lawrence and Prichard was most likely transmitted to Darwin through Lyell's works, of which Darwin wrote to Horner (August 29, 1844): "I always feel as if my books come half out of Lyell's brains & think I never acknowledge this sufficiently . . .". It seems Darwin did not follow up all Lyell's references until a comparatively late date. He, perhaps justifiably, felt he could trust Lyell.

I have said enough about Prof. Darlington's approach to the writing of history for the reader to realize the need for caution in accepting such statements (p. 52) as: "The cellular basis of reproduction and heredity . . . had been revealed in the previous (to 1864) thirty years". The first published description of the fusion of the fertilizing sperm with the egg and the subsequent behaviour of the male and female pronuclei was given in 1874 by Auerbach from his study of nematode worms. Weismann first published on heredity in 1883, one year after Darwin's death.

This sketch of Darwin's place in history seems to have begun as a brilliant impression; unfortunately, the selective heightening of some strokes by the author has caused the sketch at times to become a caricature. It seems as if the author was using opera glasses the wrong way round, so shrunken and inconspicuous is Darwin's image. The reader often has cause to wonder why so much trouble should be taken to demolish such a minor figure. If, in the pursuit of an answer, he turns yet again to Darwin's writings, good will result from this publication.

SYDNEY SMITH

[1] Smith, S., *Adv. Sci.*, 64, 391 (1960).

MEASURING MOLECULES

Molecular Structure

The Physical Approach. By J. C. D. Brand and J. C Speakman. Pp. viii+300. (London: Edward Arnold (Publishers), Ltd., 1960.) 30*s*. net.

BRAND and Speakman have set out to give an account of the physical methods of elucidating molecule structure "written at a level suited to the honours student, or to the research worker in some other branch of Chemistry". Students in Glasgow must be strong men, however, if the mathematical level of this volume causes them no trouble. To meet the irreducible representations of a group by p. 26 seems over-demanding for a chemistry student Like the authors, I certainly wish that all chemistry students had this sort of understanding of the methods of studying molecular structure; but to start with "Brand and Speakman" would be to push most of them in at the deep end. It is difficult to avoid a comparison with P. J. Wheatley's recent book, "The Determination of Molecular Structure", which covers similar ground. Wheatley kept the mathematics to a much simpler level and provided rather more examples of chemical interest, with numerous illustrations of the shapes of molecules. For an introduction to the subject, students would therefore be well advised to start with Wheatley. The abler ones could then pass to Brand and Speakman, who will take them much closer to the mathematical techniques which are the necessary stock-in-trade of the research investigator. By comparing and contrasting the two books, which often complement each other, good students could reach an excellent appreciation of the subject.

The reader who is not troubled by the mathematics will find Brand and Speakman's account in general admirable. The headings of the various chapters on physical methods will serve to show the range they cover: "The Rotation of Molecules", "Nuclear Resonance Spectra", "The Vibration of Molecules", "Anisotropic Polarisability and the Raman Effect", "Crystal Structure Analysis", and "Electron Diffraction". The stage for these is set by two chapters on symmetry and elementary wave mechanics. The latter, which,

incidentally, has a clear and sound postulatory approach to the subject, provides the quantum mechanical results needed for the spectroscopic chapters. Almost always the book is thorough and clear. The chapter on nuclear resonance spectra, for example, covers nuclear magnetic resonance in solids and liquids, pure nuclear quadrupole resonance and nuclear quadrupole coupling in pure rotation spectra. A separate chapter on the electron diffraction of gases is especially welcome, as the capabilities of this powerful method of structure investigation have been far too little appreciated in Britain. On the other hand, the discussion of electron and neutron diffraction by crystals, which is part of the chapter on crystal structure analysis, is perhaps too brief. Otherwise this chapter gives a very readable account of the methods and of the range of the results of modern X-ray crystallography.

The final chapter of appraisement and conclusions draws the various threads together and makes useful comparisons of the results of the different methods. The last sentence, however, is very curious. As the conclusion of a contrast of diffraction and spectroscopic techniques, it reads: "Because the spectroscopic methods look towards the wave function, they constitute the most fundamental approach to molecular structure". The implication that diffraction techniques are unrelated to the wave functions is, of course, quite false: a glance at James's standard treatise "The Optical Principles of the Diffraction of X-rays" will show the closeness of their connexion. This extraordinary remark is perhaps the result of a certain unbalance in the authors' treatments of spectroscopic and diffraction methods. They give the wave mechanical fundamentals of spectroscopic theory in some detail, but do not even sketch the corresponding parts of diffraction theory: the key relation $\rho = e\psi^*\psi$ is unmentioned.

Nevertheless, "Brand and Speakman" is excellent value. Its price should induce many students to make the mathematical efforts necessary to achieve a deep understanding of the subject.

Minor flaws noted include misprints in the character table for the point group T_d, where the translations and rotations are assigned to the wrong representations. Fig. 3.5.1 omits any scale for x.

D. W. J CRUICKSHANK

PROGRESS IN NUCLEAR PHYSICS

Progress in Nuclear Physics

Vol. 7. Edited by Prof. O. R. Frisch. (Progress Series.) Pp. vii+326. (London and New York: Pergamon Press, 1959.) 84*s*. net.

THE volume under review covers the following topics: "The Bubble Chamber" (D. V. Bugg), "Resonance Fluorescence in Nuclei" (F. R. Metzger), "Spallation" (B. G. Harvey), "Optical Model for Nuclear Scattering" (A. E. Glassgold), "Measurement of Helicity" (L. Grodzins), and "Weak Interactions" (J. J. Sakurai).

Though an article on the bubble chamber was published in the same series two years ago, a progress report seems indicated in view of the technical advances made and the realization that here we have indeed one of the key instruments for future high-energy research. The theory of chamber operation, the practical considerations associated with various liquids, some design features of operating chambers and much of the auxiliary equipment such as magnet characteristics, illumination, photographs and track-measuring devices are included in the account. Since the bubble chamber produces prolific amounts of detailed information, great efforts will be required to develop methods to extract the information contained in the photographs at the same rate as the chamber records events; here the author might have been more generous in attacking such a formidable task, particularly in so far as the general principles are concerned. It would have been useful to provide more information of the financial side of a bubble chamber project.

Dr. Glassgold's review is most ably done; unfortunately it does not include in the analysis the very important results of polarization effects obtained by Dr. L. Rosen at Los Alamos. This and some other aspects might well be a good topic for a future contribution to this series. Again, the article on resonance radiation, though very well done, is just a trifle stale as it misses the impact of the Mössbauer method in the field. The well-written but extensive review on spallation convinces the reader that this field seems a bit dull and is by now probably exhausted. Choice of the highlights of the volume may be a matter of taste, but I feel few will dissent if this distinction is confined to the two articles, "Measurement of Helicity" (75 pages) and "Weak Interactions" (71 pages). Clarity, completeness (including a discussion on unsolved problems in Dr. Sakurai's article) and lively language all contribute to the joy of reading these surveys.

The literature references seem to include the papers up to 1958, but not 1959; the volume is therefore slightly out of date.

E. BRETSCHER

GAS CHROMATOGRAPHY

Gas Chromatography

By A. I. M. Keulemans. Second edition. Edited by C. G. Verver. Pp. xxi+234. (New York: Reinhold Publishing Corporation; London: Chapman and Hall, Ltd., 1959.) 60*s*. net.

THE first edition of Keulemans's "Gas Chromatography", published in 1957, was a landmark in the subject. Prof. Keulemans had played a leading part in the development of both the experimental and theoretical parts of the technique, and was one of the first to direct attention to the importance of operating columns under optimum conditions. The theoretical sections were therefore particularly good and the practical sections gained from a wide practical experience. Since 1957, gas chromatography has developed tremendously, the number of papers having risen from a few hundred to more than three thousand, and in 1958, when the revision of the first edition was presumably being carried out, two highly significant advances occurred. These were the invention of several highly sensitive detectors based on the ionization of the eluted vapours, and of capillary columns. It is now clear that these advances have so altered our outlook on gas chromatography, its aims and potentialities, that any text written before 1958 would require extensive revision to bring it up to date. The revision which has taken place between the first and second editions of "Gas Chromatography" now appears inadequate, although, to be fair, this

was probably not obvious at the time. Only four pages are devoted to the ionization detectors and only four to capillary columns. The Golay equation is not mentioned and there is little in the way of practical information on the operation of capillary columns. There is only the briefest of sections on temperature-programmed gas chromatography and nothing on preparative gas chromatography. Recent work on the improvements in efficiency of packed columns is treated rather sketchily and the katharometer theory remains unaltered in spite of the realization that forced convection is important in determining both the sensitivity and the stability of katharometers. Most of the theoretical sections are still first class, but even here one feels that an improvement could have been effected by more concise presentation now that the initial barriers to the mathematics have been broken down.

My chief impression of the second edition is therefore that modern developments, major and minor, have been given too little space. I am disappointed that so eminent an authority should have failed to make the same mark with his second edition as with his first.

Nevertheless, Keulemans' book is still the best on the subject and can be warmly recommended to those who do not possess the first edition. Those who do must still await an up-to-date account of recent work.

JOHN H. KNOX

LIPIDS AND LIPOPROTEINS

Lipide Chemistry

By Dr. Donald J. Hanahan, Dr. Frank R. N. Gurd and Prof. Irving Zabin. Pp. ix+330. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1960.) 80*s*. net.

AFTER a short introduction, the main chapters have the following sequence: isolation and purification, phosphoglycerides, phosphoinositides, sphingolipids, minor phospholipids, simple lipids, association of lipids with proteins, some naturally occurring lipoproteins. The chapter on sphingolipids is by Prof. Zabin, the last two chapters by Dr. Gurd, and the rest of the book by Dr. Hanahan. Each is an acknowledged authority in his field. Discussion is limited essentially to the chemistry of the lipids present in mammals, while lipid metabolism is the subject of a companion volume.

The three authors differ greatly in style and in approach to their topics. Dr. Hanahan mentions that much of his material has been used for graduate lecture courses, and his chapters gave the reviewer an impression of expanded lecture notes with rather slipshod continuity. On the general level, it is curious to find simple glycerides discussed after the more complex phosphoglycerides, while the minor phospholipids described are all phosphoglycerides and their inclusion with these would have facilitated orderly development. On a more detailed level, there are many points at which the reader is halted by an apparently unjustified conclusion from the preceding argument, later to find the missing material. Two examples must suffice. Near the top of p. 51 "convincing evidence" of optical activity is mentioned, but the relevant data are given near the bottom of the page. About the middle of p. 188 reference is made to "the above chromotropic acid method", which leaves the reader guessing until the top of p. 189. Sometimes there is discrepancy with what has been said earlier; for example, on p. 44 it is reported that β-glycerophosphoric acid is converted quantitatively into the α-form by boiling acid, but on p. 45 we learn that an equilibrium mixture results. A section on p. 73 opens with the words "When confronted with the information cited in Chapter 1". This so-called information is simply a generalized statement repeated almost word for word on p. 73. The whole of Dr. Hanahan's material would benefit from careful editing, even to the reference points in the text for the footnotes on pp. 78, 88 and 91. It is, nevertheless, a valuable source of up-to-date information in a rapidly developing field.

The other contributions are superior in orderly approach and clarity of expression. Presumably they were specially written and not adapted from lecture material. The chapter on sphingolipids is agreeably concise. The two chapters on lipoproteins make up more than one-third of the book and are wholly admirable. Indeed, they redeem this beautifully produced book from the level of the adequate but uninspiring.

J. A. LOVERN

SCIENCE IN THE PRIMARY SCHOOL

Approaches to Science in the Primary School

Edited for the New Education Fellowship by Evelyn Lawrence, Nathan Isaacs and Wyatt Rawson. Pp. xiii+143. (London: Educational Supply Association, Ltd., 1960.) 10*s*. 6*d*. net.

WITH the recent increasing development of science in the secondary school, a growing need has been felt to prepare the way in the primary school. A committee was appointed by the New Education Fellowship to "consider the place of direct observation and experiment in the primary school".

This committee felt that the introduction of science to the curriculum could cause difficulties for the teachers, either through a feeling of inadequacy in themselves or through lack of ideas of approach, so this book was compiled for the teacher. It is not a suggested syllabus, nor is it merely a collection of articles, even though each chapter is written by a different author, including practising teachers who have contributed articles on their own approaches and experiences with different age-groups.

The book deals with the aims and the objects of starting science in the primary school. It explains that such teaching is a necessity not only for the scientifically minded but also for any child who is to grow up in this day and age.

Two chapters are entitled "Diverse Roads to Diverse Sciences": these titles speak for themselves. A further chapter deals with making the most of what one has, whether in the town or the country. Another deals entirely with teachers' needs and difficulties, and suggestions on how to overcome them. One section of a chapter offers leads for science lessons from the children's own, very commonplace, questions. There is a bibliography both for the teacher and the pupil.

The book makes interesting reading, and should act as a helpful guide to the teacher with any doubts.

B. J. G. MAITLAND

Chromatographic Reviews

Progress in Chromatography, Electrophoresis and Related Methods, Vol. 2. Edited by Michael Lederer. Pp. viii+195. (Amsterdam: Elsevier Publishing Company; London: D. Van Nostrand Company, Ltd., 1960.) 46*s*.

APPEARING about a year after the first, this second volume contains six articles. In a preview of gas-liquid chromatography (C. J. Hardy and F. H. Pollard), principles and techniques are dealt with and there are 600 references. Despite the vast literature on the subject, the authors have succeeded remarkably well in covering the essentials so adequately. Starch-block electrophoresis (H. Bloemendahl) is a comparatively short article which provides clear practical details and reviews applications of this important method. G. Biserte and associates write about the paper chromatography of dinitrophenyl amino-acids. This is a most satisfying article, for not only does it supply full data about solvent sytems and R_F values but it also includes details of the preparation and properties of dinitrophenyl amino-acids and describes the dinitrophenylation of proteins and peptides with subsequent treatments for liberating and examining the labelled terminal amino-acids.

Flavonoid pigments are covered by J. H. Harborne, who deals clearly with the paper chromatography of the many substances belonging to this class. The article on human hæmoglobin (H. K. Prins) is a most interesting survey of electrophoretic and chromatographic techniques which have been used with such striking success in the past ten years for demonstrating and isolating a large number of hitherto unknown hæmoglobins. Finally, E. Hayek reviews a special kind of chromatography of inorganic substances based on adsorption and precipitation mechanisms. Like the first volume, all the articles are in English, and were originally published in the *Journal of Chromatography*. This second volume is full of interest, is up to date and maintains the high standards of its predecessor.

R. CONSDEN

Review of Studies in the Flow of Information among Scientists

Vol. 1: Text. Pp. v+62. Vol. 2: Tables. Pp. ii+48. (Washington, D.C.: Bureau of Applied Social Research, Columbia University, 1960.) Available from the National Science Foundation, Office of Science Information Service, Washington, 25, D.C.

THIS review, which was commissioned by the National Science Foundation, is not a review in the ordinary sense. It is rather part of the raw material for such a review. The authors have assembled the statistical material of a number of reports on the flow of information to scientists under the different questions considered. They come to no conclusions. Their purpose seems to have been to leave to others the formulating of conclusions, and only to suggest where further work might be done. The documents will be of value only as an *aide memoire* to those who are planning further surveys.

The subject of the flow of information to scientists is undoubtedly important. So far, however, the efforts to understand this process have led mainly to the collection of curious information. This has resulted in very few measures for improving the situation. The report makes no serious effort to direct attention to what might be useful and what is not. My own paper of 1948 (which is the earliest covered by the survey) is extensively quoted in the tables, although, so far as I know, it never led to any positive action except more surveys. My paper of 1958, which was a detailed survey of the use of serial literature in the Science Museum Library in 1956, is only referred to in one table. But this later paper was used to decide what literature in the Science Museum Library should be duplicated in the National Lending Library for Science and Technology.

Two important results on the flow of information to scientists which we in the Department of Scientific and Industrial Research Headquarters obtained are not mentioned at all. The first was the availability of Russian scientific literature in the United Kingdom in 1956; the second was the extent to which working scientists said they could read French, German and Russian. It matters not. The first result was mainly instrumental in starting the National Lending Library. The second assisted materially in the discussions which led to the starting of the Department of Scientific and Industrial Research's Russian translating programme. Let not the cynic say from this example that in this field "Useful results lead to action. Useless results lead to learned papers". The fundamental problem is going to become more serious as the scientific effort of the world increases.

D. J. URQUHART

Some Problems of Chemical Kinetics and Reactivity

Vol. 1. By Academician N. N. Semenov. Revised and expanded by the author. Translated by Dr. J. E. S. Bradley. Pp. x+305. (London and New York: Pergamon Press, 1958.) 50*s*. net.

PROF. SEMENOV'S pioneering book on chain reactions was published more than twenty years ago, and since then there has been intense activity in the study of chemical kinetics, of which there is now extensive literature. In the preface the author states that he does not think the main problems are completely solved. The number of papers published since 1950, quoted in the references, is very large, and the subject has been brought up to modern publications so far as possible. The Russian work is fully covered, but the literature of all countries has been included and older work of importance finds its place. The treatment is critical, and when complete evidence is lacking or findings are contradictory this is pointed out.

The first part of the book deals with radical reactions in three main branches: uniradical reaction, alternative univalent free radical reactions, and reactions of biradicals. The section on hydrocarbon oxidation reports recent work, including that of Shtern, which suggests that aldehyde formation is more important than peroxide intermediates, but it cannot be said that finality has been reached in this field.

The second and third parts deal with chain reactions. There is a critical discussion of the inhibiting effect of nitric oxide. The initiation and termination of chains on walls are considered from a new point of view, which is also involved in the discussion of heterogeneous catalysis. The appendixes deal with activation energies calculated by the London method.

The translation is very good, and the book reads as if it had been written in English originally. With the later volumes, the work is one which should be carefully studied by all physical chemists.

J. R. PARTINGTON

PORPOISES AND THE BOW-RIDING OF SHIPS UNDER WAY

By ANDREW A. FEJER
Woods Hole Oceanographic Institution and Illinois Institute of Technology, Chicago
AND
RICHARD H. BACKUS
Woods Hole Oceanographic Institution, Mass.

IN recent years there has been a controversy concerning the phenomenon of porpoises dwelling almost motionless near the bows of ships under way while obtaining propulsive power from the moving vessel. In reading the papers[1-5,7] that have been published relative to this matter it is evident that certain observational facts have been overlooked by earlier investigators. In view of this, and on the basis of some new observations made by one of us, we would like to offer an explanation of the phenomenon of bow-riding based on a model which differs from those proposed earlier.

Since Woodcock reported his observations on 'wave-riding' porpoises in *Nature* twelve years ago[1] the several papers published concerning this subject have offered explanations given in terms of the forward-sloping surface of the bow wave—hence the term 'wave-riding'. Woodcock[1] and Woodcock and McBride[2] showed that the component of the submerged weight taken along the wave slope was scarcely sufficient to balance the resistance that the animal experiences as it is moved through the water. Hayes[3] pointed out that near the wave surface the isobars are not horizontal and that the force due to the buoyancy (B) must therefore be normal to the slope of the wave (Fig. 1); consequently the hydrodynamic resistance (D) of the porpoise can be balanced by the component of the body-weight parallel to the wave surface ($W \sin \theta$). Scholander[4], on the other hand, refutes this argument on the basis of drag measurements made on small, streamlined, neutrally buoyant models that were towed in the waves of a vessel. He believes[5] that the porpoise places itself ahead of the bow wave with the tail flukes buried in the forward-facing portion of the wave (Fig. 2) in order to provide the thrust ($L_f \sin \theta$).

Observations by one of us (R.H.B.) of porpoises and their swimming and bow-riding have been distributed over the period of the past ten years, although it is only during about the last two that we have watched these charming animals with the present problem particularly in mind. These observations have been made from vessels having lengths of 100–214 ft. and speeds of 7–14 knots. None of these relatively small vessels generates conspicuous bow waves.

The animals concerned in these observations are the bottlenose porpoise, *Tursiops truncatus*; the saddleback porpoise, *Delphinus delphis*; the white-sided porpoise, *Lagenorhynchus acutus*; *Stenella styx*; and other unsuccessfully identified porpoises including several of the poorly known genus *Stenella*. The largest of these animals is *Tursiops*, which may attain a length of about 11 ft. The others are smaller, generally being, in adulthood, from six to eight feet long. These small cetaceans all belong to the sub-family Delphininae of the family Delphinidae (the 'duodecimo' whales of Herman Melville's classification). It is interesting to note that the next sort of cetacean in point of size (Melville's 'octavo' whales), the Orcinae of the family Delphinidae, most of which reach lengths of 15–20 ft. at maturity—the potheads or pilot whales, *Globicephala* spp.; the killer whale, *Orcinus*; the false killer, *Pseudorca*; *Grampus*; and the like—are not known to be bow-riders nor are cetaceans of still larger size. (The most famous of all individual bow-riders is the porpoise 'Pelorus Jack', which escorted vessels in and out of Pelorus Sound, New Zealand, during the years 1880–1912 and was granted special protection by the New Zealand Government. This animal is supposed to have been a grampus (*G. griseus*), but this is not certain. In our experience grampuses avoid close approaches to a vessel, generally not coming nearer than about 50 or 75 ft.)

Would-be bow-riders, when first observed at a distance of several hundred yards, seem to swim purposefully towards the ship for taking their stations. Sometimes porpoises thus approaching come to within 30 or 40 ft. of the ship but no nearer. On a number of occasions we have watched porpoises

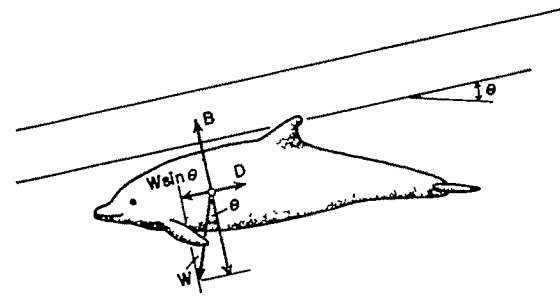

Fig. 1. Model of bow-riding porpoise according to Hayes (ref. 3). B, buoyant force; D, hydrodynamic drag force; W, weight of porpoise; θ, slope of wave

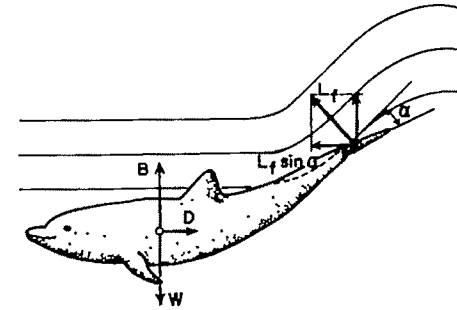

Fig. 2. Model of bow-riding porpoise according to Scholander (ref. 5). Lf, hydrodynamic lift force on flukes; D, hydrodynamic drag force

approach on a nearly reciprocal heading from that of the ship, then turn sharply on to the ship's heading when the range between ship and animal was 20 or 30 ft., and be gently overtaken by the ship as they assume a bow-riding station 1–5 ft. ahead of the ship's stem.

Once at a position at the bow the animals may remain only for seconds or for as long as an hour or more. Often a group of eight or ten porpoises may join the ship together and spend 10–15 min. riding at the bow. Then the group may diminish slowly over the period of 5 min. or so as the animals drop away by ones and twos.

The distance between the ship's stem and the porpoise's flukes is usually between less than a foot to five feet. The lateral spread of bow-riders is generally about 3 ft. to either side of the stem. Sometimes when the porpoise is riding very close to the ship and is to the side of the ship's midline the flukes may be up to a foot or 18 in. behind the ship's stem. The animals are between one or two and five or six feet below the surface and may be arranged in two or even three layers. The animals rise to the surface, of course, as it becomes necessary to breathe and often leap clear, or partly clear, of the water at these times.

While one may detect the swimming motions of porpoises at close range from the ship's side, it is often very difficult to see these motions in bow-riding animals. A novice observer often suggests that this is because of the high frequency and low amplitude of the tail beats; but it appears that it is really due to the facts that: (1) at times the porpoise is not swimming at all; (2) at times the animal is swimming easily with low-frequency and low-amplitude strokes; (3) that the common vantage point of the observer at the top of the ship's stem is a poor one for detecting the vertical swimming motions of an upright porpoise.

Often one sees individuals proceeding on a sinuous course, repeatedly swerving from right to left and back across the very bow while rolling from side to side. Bow-riders may go along on their sides or even upside down and we have seen individuals proceed while slowly revolving about their long axis. One posture assumed by the bow-rider, which we have only recently noticed, seems of particular significance. This was first observed in *Tursiops* from *Chain* on November 20 and 21, 1958, in the ocean area known as the Blake Plateau. From time to time individuals swimming on their side were seen to throw the tail into a strong downward flexure and hold it in this extreme position for two to four seconds. At these times it was hard to observe the angle of attack of the flukes but it was noticed that such porpoises were generally, if not always, so oriented that the back was towards the long axis of the vessel, that is, a porpoise on the starboard bow coasted on its left side and vice versa. It might be assumed that these animals coast in this posture while belly-down or -up; but this, of course, would be less easily seen from the top of the ship's stem. Wrinkles in the skin were noticed on several occasions when the tail was flexed downwards. These were located at the point of flexure and probably do not have a dynamic significance such as the skin folds reported for this species by Essapian[6] may have. On May 12, 1959, off Cádiz, Spain, about two dozen *Tursiops* were observed from *Chain*, and tail-down coasting the same as that described above was seen.

On May 16, 1959, just west of the Strait of Gibraltar and on May 26, 1959, in the Malta Channel this activity was observed in *Delphinus*, animals that are for the most part about 6 ft. long. The tail-down coasting posture of *Delphinus* does not appear to differ from that observed in *Tursiops*; however, it has been observed less frequently in *Delphinus* than in *Tursiops*. That is, after first noticing this bow-riding attitude in *Tursiops*, we saw it in the next two encounters with *Tursiops* but only in two of the next eight meetings with *Delphinus*. Since *Delphinus* is in general smaller and of quicker movement than *Tursiops*, the details of its motion may be more difficult to discern; on the other hand, it may assume this particular posture less frequently. Furthermore, varying states of the sea and the heading of the ship relative to the sea probably affect the behaviour of the animals. In neither species can this activity be described as continuous. Individuals can be watched for periods of many seconds riding close to the ship's bow, but assuming the tail-down attitude only at irregular intervals and then for only a few seconds at a time. On August 27, 1960, tail-down coasting was observed in an unidentified species of the genus *Stenella* from *Bear* near 38° 30′ N., 78° 00′ W. It was noted on this occasion in a porpoise riding on its side at a depth of 5 or 6 ft. in the deeper of two layers of bow-riding animals.

It is readily apparent that some of the observations reported above are not compatible with the bow-riding model proposed by Hayes[3]. The propulsive force required by the porpoise depends in that case on the magnitude of the angle θ between the stream-line and the horizontal (Fig. 1). As this angle decreases exponentially with depth, the explanation offered by Hayes is clearly incomplete when the porpoise is not located in the immediate vicinity of the surface and when small and relatively slow vessels are involved that do not produce bow waves of sufficient size for wave-riding, that is, waves of slopes of 15° or more and large enough to contain the body of the porpoise. It should be pointed out, however, that hydrodynamically, Hayes's explanation, while limited in scope, appears to be correct and that the contradictory data reported by Scholander[4] seem to be the consequence of limitations pertaining to the latter's apparatus, which did not permit him to control and maintain the position and orientation of the model relative to the wave surface.

Considering next the model proposed by Scholander[5], one can determine readily that a propulsive force of sufficient magnitude can result when the animal places its tail flukes in a bow wave in the manner shown in Fig. 2. However, the objection raised by Hayes[7], that the forces and moments do not balance and that consequently the porpoise is not in equilibrium, appears to be sound. Indeed our calculations show that in Scholander's model equilibrium is not attainable: the force on the tail flukes contributes a large moment around the centre of mass and because of the shape of the porpoise and the fact that the pectoral fins are located too near the centre of mass (maximum girth is at the point of insertion of the pectoral fins) it seems impossible that the animal could generate an opposing moment of equal magnitude.

In order to arrive at a model which is consistent with our observations it is proposed to focus attention on the pressure distribution in a horizontal plane ahead of the bow. If one neglects the effect of the

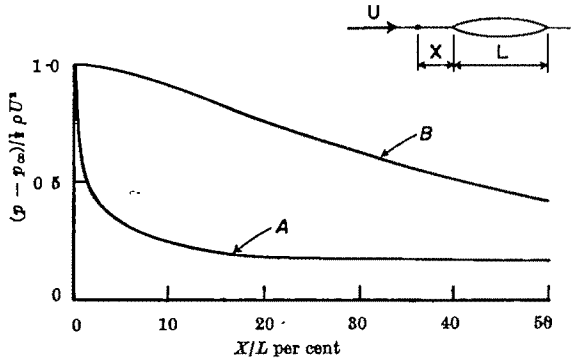

Fig. 3. Pressure distribution in a two-dimensional flow past cylindrical shapes. *A*, ship's water-line profile; *B*, circular cylinder; p, pressure at point X; p_∞, pressure at a great distance from profile; ρ, density of water; U, velocity of flow

surface and keel, that is, considers the flow to be two-dimensional, one can readily determine the pressure field ahead of the bow with the aid of potential theory. Fig. 3 shows the pressure distribution along the centre-line ahead of the bow, obtained in this manner, for a cylinder having a cross-section of the shape of an ordinary ship's water line as taken from ref. 8. For the sake of comparison the distribution for a cylinder with a circular cross-section is also shown. A streamlined body placed in this region experiences a force which is approximately equal to the negative of the average pressure gradient in the field times the volume of the body[9]. It is apparent from the pressure distribution in Fig. 3 that this force is maximum at the bow and decreases gradually as the distance between the bow and the object increases. At a location where the force due to the pressure field equals the drag experienced by the body from the flow around it, the conditions appear to be right for bow-riding. This situation was considered using the dimensions and shape of a female *Stenella styx* which was harpooned from *Bear* on July 27, 1959, at 37° 42′ N., 73° 34′ W.[10]. The resulting curves are presented in Fig. 4 showing the distance d between the bow and the tail of the porpoise as a function of the length L of the vessel for the water-line profile used in preparing Fig. 3. It should, of course, be understood that the distances shown in the

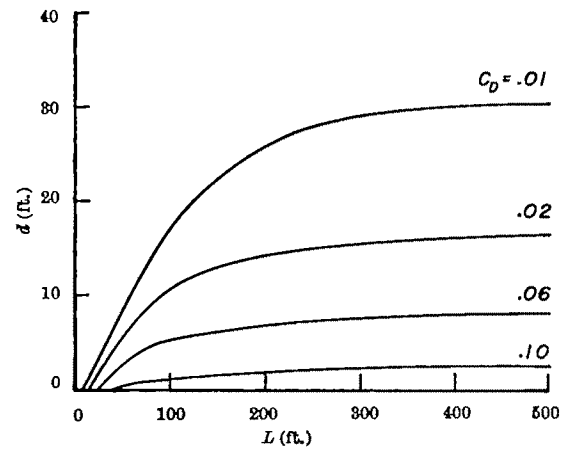

Fig. 4. Dependence of distance between tail of bow-riding porpoise and the bow on length of vessel for various values of the drag. Drag $D = 1/2\ \rho U^2 A\ C_D$; A, frontal area of porpoise; C_D, drag coefficient

figure are larger than one would expect and that this is due primarily to the assumption of two-dimensional flow. Furthermore, it should be pointed out that it is within the power of the porpoise to vary the distance by appropriate changes in posture that will influence its drag, and that the presence of vertical and lateral pressure gradients in addition to those along the centre-line will make it necessary for the porpoise to assume some of the curious positions that have been described above. These positions remind us of the attitude assumed by the sausage-like object employed by G. I. Taylor[9] to demonstrate the equilibrium position of a body in a flow field in which the stream-lines are curved. In reading Dr. Taylor's paper it becomes clear that, due to the complexity of the situation, intuition will be of little help in arriving at the posture and position the porpoise must assume in order to remain motionless in the pressure field ahead of the bow.

In turning sharply on to the ship's heading for bow-riding in the manner described earlier the porpoise could, of course, be guided visually or by echo-location, but it seems most plausible that in manœuvring into bow-riding position and during the bow-riding itself, the animal is responding directly in a tactile way to the pressure field generated by the vessel.

In viewing our results it is of course necessary to realize that the situation to which our calculations pertain is a highly stylized one. In reality the porpoises are now coasting, now swimming to make adjustments in their position relative to the ship or to change their posture, now coasting again. These changes seem to be necessary to counteract fluctuations of the pressure field due to the state of the sea and the resultant motions of the ship, and to correct any mismatch between propulsive force and drag occurring, at times, as the result of a change in the animal's posture. The resulting picture is quite involved, and a more complete and accurate analysis of the bow-riding activity would require detailed information regarding the shapes assumed by the animal and the field of flow ahead of the vessel.

Recently, near 38° 30′ N., 73° 00′ W. on August 26, 1960, we observed what appeared to be the riding of wind waves five to six feet high by a porpoise of the genus *Stenella* the length of which was about 6 ft. In the best-observed instance two porpoises rode side by side in exactly the same posture for several seconds near the top of the forward slope of the wave. Little, if any, of the porpoises' bodies were exposed (possibly the dorsal fins). The heads were down and the tail portions were raised but seemingly not quite to the extent that the long axes of the bodies were parallel to the forward slope of the wave. After proceeding with the wave for several seconds the porpoises fell behind it. This observation is similar to those recently reported by Caldwell and Fields[11] of 'surf-riding' porpoises. They report that the animals rode the top front of the wave with their heads down and only their dorsal fins and a small part of their backs exposed. In these cases Hayes's model is not only appropriate but it seems to be the only feasible one. Our calculations show that even shallow wind waves having slopes of 10–18° and travelling at velocities in the vicinity of 5–6 m./sec. could be utilized for this purpose by porpoises in minimum drag posture; and based on this observation it seems not unreasonable to conclude with the speculation that in regions of the oceans where steady, strong winds are known to raise large waves that move steadily over long distances,

even large cetaceans could very well use wave-riding techniques for migratory travel.

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RADIOCÆSIUM IN HUMAN BEINGS

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THE detection of the long-lived fission product, cæsium-137, in human beings in the United States in 1955 [1], was confirmed for residents of the United Kingdom in 1956 at Harwell[2] and at Leeds[3]. Subsequent measurements of body radioactivity made at the Atomic Energy Research Establishment, Harwell, have demonstrated the presence of radiocæsium in all persons, whether employed at Harwell or not. The results of measurements made in 1956 and 1957 were reported in 1958[4]; a re-examination of all the early measurements has now been made, and some conclusions about the trend of the levels to the end of June 1960 are presented here.

A description of the method of measurement has been given previously[2,4,5] and will not be repeated here, but it should be mentioned that in comparing the levels from subject to subject it is convenient to use the ratio of cæsium-137 content to potassium content. In this way the effects of variations in the sizes of the subjects and in their potassium contents are minimized, and the cæsium content is related to the mass of the muscle, its main site of deposition. In the following results the cæsium–potassium ratio is expressed in μμc. cæsium-137 per gm. potassium.

Results

(a) *Subjects Resident near Harwell*

The data for subjects living in Berkshire and Oxfordshire are presented in Table 1, where the mean values for six-monthly periods to June 1959, are given; since June 1959, measurements have been made in the months shown. Most of these persons are employed at the Atomic Energy Research Establishment, Harwell; none has had any occupational exposure to cæsium-137. In Fig. 1 the trends with time are shown for some individuals who have been measured more than once. In considering the significance of the difference between the mean values for any two consecutive periods, and of small (10 per cent) variations in the results for any one individual, it should be borne in mind that the standard error of counting is at least ± 4 μμc. cæsium-137 per gm. potassium, and that the groups being averaged are small. Further, up to December 1958, the groups were largely composed of different subjects, and the justification for the comparison of the mean values from those different groups is open to question. Also, the inclusion of one extreme value has a pronounced effect on the mean for the group; one subject who has only been measured regularly since July 1959 is in this category, and in Table 1 the mean values in parentheses are those including this man. Apparently, the cæsium-levels in these subjects remained substantially constant until about the middle of 1957, after which they increased to a maximum in July 1959. The mean value for June 1960 shows a significant fall from the December 1959–March 1960 values.

Table 1. Mean Cæsium–Potassium Ratios for Subjects Resident in Berkshire and Oxfordshire

Period	No. of subjects	μμc. Cæsium-137 per gm. potassium
Feb.–June 1956	11	33
July–Dec. 1956	8	80
Jan.–June 1957	11	35
July–Dec. 1957	7 (8)	41 (46)
Jan.–June 1958	6	43
July–Dec. 1958	8 (9)	53 (56)
Jan.–June 1959	12	56
July 1959	11 (12)	63 (66)
Dec. 1959	7 (8)	56 (61)
Mar. 1960	10 (11)	58 (62)
June 1960	10 (11)	52 (55)

(b) *Subjects Resident near Windscale*

The accidental release of radioactivity from the No. 1 Pile at Windscale in October 1957 led to temporary increases in the radiocæsium content of milk from a wide area of England and Wales[6–8]; the biggest increases were close to Windscale[8]. Although no extensive study has been made of the levels in humans in this area, a few subjects have been measured, and the results in Table 2 illustrate the effect of the accident. The pre-accident level was 107 μμc. cæsium-137 per gm. potassium (mean for four subjects); this was 2·5–3·0 times the contem-

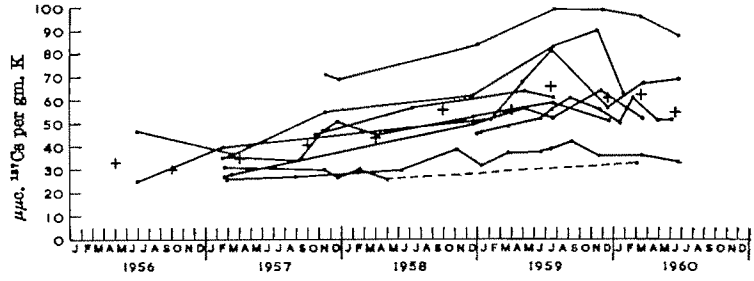

Fig. 1. Trends with time of the cæsium-137/potassium ratios in some individuals who have been measured more than once, compared with the average for all controls. +, Mean values for all control subjects

Table 2. Cæsium–potassium Ratios in Subjects resident near Windscale

Subject	Date measured	μμc. Cæsium-137 per gm. potassium	
		Pre-accident	Post-accident
G.	29. 3.57	138	
	26.11.58		179
C.	25. 4.57	107	
	13. 3.58		443
	21. 7.58		286
T.	27. 6.57	107	
	15. 1.58		370
	3. 7.58		227
	11. 1.60		128
Mrs. *T.*	9. 9.57	77	
*Go.**	2. 4.58		224*
*R.**	7. 5.58		183*
W.	18. 5.60		134

* These two men left Windscale on 10.1.58; their cæsium-137/potassium ratios on that date would have been somewhat higher than the values in the table.

porary average for subjects resident in Berkshire and Oxfordshire. This can be attributed in part to the higher rainfall in the area around Windscale with the resulting higher cæsium-137 levels in milk[8], and in part to slight environmental contamination from the Windscale Works[9]. For this reason the level cannot be regarded as typical for northern England. The cæsium-137/potassium ratio increased roughly fourfold to a maximum around January–March 1958 as a result of the accident, and the level fell to less than twice the pre-accident value towards the end of 1958

(c) *Other Subjects*

Only a few subjects resident elsewhere have been measured; the results are given in Table 3, in chronological order.

Table 3. Cæsium-potassium Ratios for Twenty Subjects with various Residences in Europe and North America

Subject	Date measured	Residence	μμc. Cæsium-137 per gm. potassium
R.	20. 4.56	California	35
H.	14. 5.56	Hampshire	33
B.	28. 9.56	Yorkshire	34
Be.	24. 6.57	London	44
L.	31. 7.57	Devonshire	79
Mrs. *L.*	2. 8.57	Devonshire	71
W.	8.11.57	Yorkshire	63
M.	8.12.58	Buckinghamshire	88
A.	8. 1.59	London	88
Mi.	22. 5.59	Illinois	75
Mrs. *Mi.*	22. 5.59	Illinois	53
Bi.	9. 7.59	Ottawa	93
Me.	17. 9.59	Berlin	73
T.	19.11.59	London	88
W.	29. 4.60	Surrey	51
Mrs. *W.*	29. 4.60	Surrey	45
An.	24. 5.60	New Mexico	53
S.	13. 6.60	Caithness	93
V.	22. 6.60	Dusseldorf	50
Mrs. *Ma.*	28. 6.60	London	56

There is a general increase in the levels during 1956–59, but the data are too sparse for any definite conclusions to be drawn or correlations to be made (for example, with levels in milk). However, it is interesting to note that, with one exception, all subjects measured in 1957, 1958 and 1959 gave values higher than the means in the corresponding periods for persons living in Berkshire and Oxfordshire.

Correlation with Milk Intake

It is known[8] that cow's milk is an important source of cæsium-137 in humans, and a correlation might be expected to exist between the cæsium–potassium ratio in humans and their daily milk consumption. The latter quantity is somewhat difficult to determine and is likely to vary from day to day. However, data on nine subjects resident near Harwell, whose milk intakes were considered to be reasonably constant and to be known, were used. It should be noted that in estimating the milk intake of the nine subjects an attempt was made to include an allowance for milk used in cooking, but not for that in a variety of manufactured foods which are of widespread distribution throughout the country. In Fig. 2 the cæsium-137/potassium ratios (measured in late 1958 or early 1959) are plotted as a function of daily milk intake; two subjects drinking 0·43 litre per day both had 46 μμc. cæsium-137 per gm. potassium. There is apparently a correlation between the cæsium-137/potassium ratio *in vivo* and the milk intake, and it suggests that at that time about 26 μμc. cæsium-137 per gm. potassium originated from sources other than milk. The mean value for all control subjects was 56 μμc. cæsium-137 per gm. potassium, so that milk was responsible for about one-half the average cæsium burden.

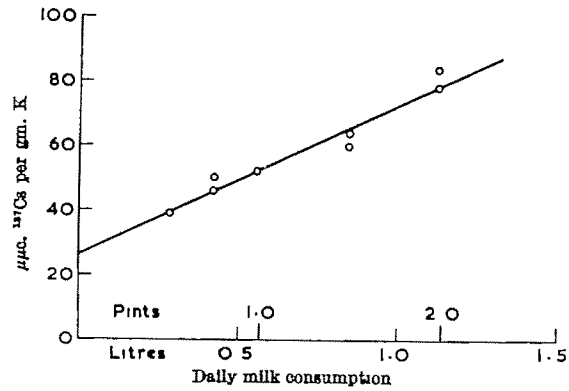

Fig. 2. Correlation of cæsium-137/potassium ratios *in vivo* with daily milk consumption

When the cæsium-137 concentration (in μμc. per kgm. body-weight) was plotted as a function of daily milk intake, a similar correlation was found but with greater scatter. Since for equal body-weights the musculature can vary considerably, and since the greater part of the body's content of potassium and cæsium is in muscle, this is not altogether surprising.

Radiation Dosage from Potassium and Cæsium-137

The radiation dosage to the gonads may be calculated if we assume that the potassium and cæsium-137 are uniformly distributed throughout the body. There is evidence that the potassium content of gonadal tissue is close to 0·20 per cent by weight[10], which is about the same as the average for the whole body (0·21 per cent by weight[4]). There are no data on the distribution of cæsium-137 in individual tissues, but there seems to be no *a priori* reason to suppose that it differs markedly from potassium, and we shall incur no great error in the assumption of uniform distribution.

Taking published values for the β-particle and γ-ray emissions of potassium[11,12], and deriving a value for the 'geometrical factor' for the γ-ray contribution from the calculations of Bush[13], with the application of the theorem of reciprocal relations[14], the dose-rates to the testes from 0·2 per cent by weight of

potassium become 17 and 2 mrads per year from β-particles and γ-rays respectively. These are in agreement with the values of 18 and 2 mrads per year calculated by Spiers[10], who used a value of 0·215 per cent for the mean potassium content of the body.

For the mean value of 63 μμc. cæsium-137 per gm. potassium (July 1959), the dose-rates from the radiocæsium are 0·53 and 0·56 mrad per year from β-particles and γ-rays respectively, it being assumed that the mean β-particle energy is 0·227 MeV.[15]. The total dose-rate to the testes is thus 1·1 mrads per year from cæsium-137 compared with 19 mrads per year from potassium, an increase of about 6 per cent. Compared with the total background radiation of approximately 100 mrads per year, the increase is about 1 per cent.

This calculation was made with the assumption that the metastable barium-137m was in equilibrium with its parent cæsium-137 in the gonadal tissue. The metabolic dissociation of barium-137m from its parent in various tissues of the rat, reported recently[16], would have only a slight effect on the calculated dose-rates. No dissociation of barium-137m was observed in the testes, but there was an excess of barium-137m in the blood. If this also applies in man, the β-particle dose-rate to the testes would be increased very slightly by the electrons from the internally converted γ-rays from the excess barium-137m in the blood present in the gonad, while the γ-ray dose-rate would not be altered significantly.

Discussion

Since the cæsium-137 content of an individual varies with the milk intake, and the concentration of radiocæsium in milk varies with geographical location[8], a comparison of the mean values *in vivo* with those obtained elsewhere is scarcely justifiable. However, it is of interest to compare the trend observed in the groups resident in Berkshire and Oxfordshire with the trends observed in the United States at the Argonne National Laboratory, Illinois, and at the Los Alamos Scientific Laboratory, New Mexico. At the former laboratory, Miller and Marinelli[17,18] have published the mean cæsium-137/potassium ratios in a group of eight to thirteen control subjects; these are set out in column two of Table 4. At Los Alamos results for control groups of 10 subjects measured in 1956, 14 subjects measured in 1957 and 37 subjects measured in 1958 have been reported[19–21] and these are included in column three of Table 4. The 1956 results are taken from Fig. 3 of ref. 19, the 1957 results are taken from Fig. 2 of ref. 20, while the 1958 results are for the 19 subjects who were measured in both the first and second halves of the year[21]. The data show that not only is the trend reported for Chicago substantially the same as that found in Britain, but the mean values are practically identical. The values reported from Los Alamos are very similar for 1956 and 1957, but are somewhat higher for 1958. However, Langham and Anderson[22] reported a mean value of 50 μμc. cæsium-137 per gm. potassium in 500 residents of New Mexico for the whole of 1958.

We may conclude that the radiocæsium found in persons employed at the Atomic Energy Research Establishment, Harwell, is a consequence of world-wide fall-out from nuclear test explosions, rather than of local contamination. Some support for this conclusion may be seen in the fact that the subject

Table 4. MEAN CÆSIUM-137/POTASSIUM RATIOS (IN μμc. PER GM.) IN CONTROL GROUPS RESIDENT IN ILLINOIS AND IN NEW MEXICO (U.S.A.) AND IN BERKSHIRE AND OXFORDSHIRE (U.K.), RESPECTIVELY

Date	Chicago, Illinois	Los Alamos, New Mexico	Berkshire and Oxfordshire
Jan.–June 1956	32	~32	33
July–Dec. 1956	—		30
Jan.–June 1957	35	~32	35
July–Dec. 1957	—	~42	41 (46)
Jan.–June 1958	46	58	43
July–Dec. 1958	51	64	53 (56)
Jan.–June 1959	61 (March)–64 (June)		56
July–Dec. 1959	57 (Sept.)–55 (Dec.)		63 (66) (July)–56 (61) (Dec.)

drinking two pints of milk daily, and with a content of 73 μμc. cæsium-137 per gm. potassium (Fig. 2) has never had any contact with radioactive material and only visited Harwell once, for the purpose of the estimation of his body content. Comparison of the mean values for all control subjects (as set out in Table 1 and plotted in Fig. 1) with either the rate of fall-out or the cumulative fall-out[23,24] at Abingdon, Berkshire, does not enable us to attribute the increase observed during 1956–59 in the levels *in vivo* to either of these parameters exclusively. However, it is clear that the decrease from the maximum level in July 1959 must be associated with the reduction in the rate of fall-out since the spring of that year[25].

With regard to the correlation between the cæsium-137/potassium ratio and the milk intake, it should be noted that there is a correlation between milk and meat consumptions which has an economic basis. Since meat contains cæsium-137, a correlation might still be found as shown in Fig. 2, even if there were no cæsium-137 in milk. For the nine subjects from whom the data in Fig. 2 were obtained there were no major differences in economic backgrounds; but the possibility should be borne in mind.

A correlation between the cæsium-137/potassium ratio *in vivo* and the daily milk consumption was also found by McNeill and Green[26] for 30 subjects in Toronto, Canada. The mean content was 51 μμc. cæsium-137 per gm. potassium in December 1958, which is about the same as found in Britain. Anderson[20] plotted the mean cæsium-137/potassium ratios *in vivo* in 1957 for different regions of the United States against the cæsium-137/potassium ratios in the milk in those regions and demonstrated a correlation; extrapolation to zero indicated that 23 μμc. cæsium-137 per gm. potassium derived from food other than milk. This is similar to the value of 26 μμc. cæsium-137 per gm. potassium deduced from Fig. 2. However, it should be noted that there are substantial differences between the average diets of residents of the United Kingdom and of the United States.

It is not clear to what extent the levels of cæsium-137 *in vivo* are controlled by the daily potassium intake, and the possible influence of naturally occurring (inactive) cæsium-133 is also unknown. That the metabolisms of cæsium and potassium are not identical is shown by the fact that the value of the ratio:

$$\frac{\mu\mu c.\ ^{137}Cs \text{ per gm. K } \textit{in vivo}}{\mu\mu c.\ ^{137}Cs \text{ per gm. K in urine}}$$

in three subjects studied by Miller and Marinelli[27] in 1956 and 1957 when the cæsium-137/potassium ratios *in vivo* were essentially constant, averaged 2·2. A value of 1·95 was found in one subject tested by

me in early 1959 when the levels *in vivo* were increasing, and a value of about 2 for the dietary discrimination factor was estimated by Langham and Anderson[22].

I am indebted to Mr. R. G. Speight for assistance in many of the measurements reported.

Note added in proof. The decrease from March 1960 of the mean cæsium-137/potassium ratio *in vivo* has been maintained. In September the value for 13 subjects resident in Berkshire and Oxfordshire was 48 μμc. cæsium-137 per gm. potassium (cf. Table 1).

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OBITUARIES

Prof. H. W. Swift

HERBERT WALKER SWIFT, emeritus professor of engineering in the University of Sheffield, died near Keswick on October 14. He was born in 1894. From elementary school he won a scholarship to Christ's Hospital and from there an open scholarship to St. John's College, Cambridge, where he read mathematics and physics. He served in the First World War, rising to the rank of captain, and was wounded and mentioned in despatches. After the War he returned to Cambridge and completed the Mechanical Science Tripos as a prizeman with first-class honours and he also won a 'half-blue' for swimming.

Swift obtained his early engineering experience with Hollins Brothers, where he became chief engineer. In 1922 he was appointed assistant lecturer in the University of Leeds. By 1926 he had published papers on several diverse topics and was awarded a D.Sc. by the University of London. For ten years he was head of the Mechanical Engineering Department at Bradford Technical College, and continued to publish in the field of power transmission and lubrication.

In 1936 Dr. Swift was appointed to the chair of engineering in the University of Sheffield, which chair then embraced the Civil, Mechanical and Electrical Departments of the University. During his period at Sheffield he was induced to take a scientific interest in the plastic forming of metal in all manner of forming processes. At a time of empiricism in this field, he made a remarkable impact in bringing logical and scientific thought to the problems involved and was the instigator of a school of plasticity which has had far-reaching subsequent influence through the work of his students.

He was responsible for the planning of both buildings and courses in the enlargement of the School of Engineering at the University of Sheffield. His ill-health brought about his premature retirement just before this task was complete.

Swift was a man of immense energy, deep insight, great enthusiasm and great kindness. He was brilliant, thorough and never mediocre. He had an unquenchable thirst for knowledge. In addition, his students will remember him as a vigorous and inspiring teacher with a readiness to appreciate their personal problems and treat them sympathetically.

J. P. DUNCAN

Dr. H. Zeitlinger

HEINRICH ZEITLINGER joined the firm of Henry Sotheran and Co. in 1894; save for a short break, he remained with it until his death on October 15, in his ninetieth year. A bookseller of distinction, he rendered notable service to science.

The volumes of Sotheran's "Bibliotheca Chemico-Mathematica" were, according to the original title-page, "compiled and annotated by H. Z[eitlinger] and H. C. S[otheran]", and on them Zeitlinger lavished the affection and erudition of the true bibliophile. Almost every famous work on the exact sciences is listed, with comments identifying and characterizing the author, indicating the content, and illuminating the treatment by apt quotation from a wide variety of authorities. An austere bibliographer might wish that these quotations had been dated, since this would have helped in tracing changes in critical estimation, but the defect is slight in such a wealth of scholarship spiced with gentle humour. Where else, for example, can one hope to learn of the only mathematical treatise written to alleviate the pangs of sciatica?

Zeitlinger's expert knowledge of Newton's work enabled him to gather together a considerable portion of Newton's library, which had been lost to sight for some two hundred years and partly dispersed. Several valuable items were recognized from annotations in Newton's handwriting, which Zeitlinger had studied with much care. It was thus possible, for

example, to identify Newton's own copy of Barrow's "Euclid", and first and second editions of the "Principia" with his manuscript revisions and additions. The collection was purchased by the Pilgrim Trust and presented to Trinity College, Cambridge, in the library of which it now rests; but for Zeitlinger's detective skill, scholarly enthusiasm and admiration for Newton, the opportunity of assembling this historic collection might have vanished for ever.

T. A. A. BROADBENT

NEWS and VIEWS

Meteorological Office: Headquarters Reorganization

THE present structure of the Meteorological Office was set up in 1957 as a result of the recommendations of the Brabazon Committee. The forthcoming move of the headquarters sections of the Office, now divided between London, Harrow and Dunstable, to Bracknell during 1961 has provided an opportunity to reconsider that organization in the light of changes which have taken place, and are likely to take place in the future, in meteorology. The division of the Office into two directorates, for services and for research, respectively, with an administrative division controlled by an assistant secretary, will remain unchanged. The balance between the research and services directorates has been improved by the creation of a new deputy director post, which has been filled by Mr. J. S. Sawyer, formerly chief forecasting research officer. He will be deputy director (dynamical research), in charge of climatological research in addition to dynamical and synoptic research. This reflects the view that forecasting work should be closely integrated with climatological investigations. The importance of the relation between the latter and long-range forecasting, in particular, is emphasized by the transfer of long-range forecasting research from the synoptic research to the climatological research branch.

Two aspects of the work of the directorate of services have increased greatly in importance since 1957. One is the rapid growth of public services, and this is catered for by the creation of an assistant director (general services) post, whose main concern will be agricultural services and the Weather Information Centres. The Climatological Services Branch will now be responsible for all climatological inquiries of a routine nature, including world climatology and marine climatology (formerly dealt with by the Climatological Research and Marine Meteorology Branches, respectively). The second development is the increasing complexity of the problems of data processing, and a new post, assistant director (support services), has been created to deal with these problems. The creation of the new branch will facilitate the development of an integrated system of data collection, processing and storage, a problem which has been the subject of much intensive work in the Office during the past few years.

Dr. J. M. Stagg, C.B., O.B.E.

ON September 7, Dr. J. M. Stagg retired from his position as director of services of the Meteorological Office. Dr. Stagg, who comes from Dalkeith, Midlothian, joined the Meteorological Office in 1926, and during 1932–33 led the highly successful British Polar Year Expedition to Fort Rae in Canada. His name soon became well known among geophysicists, and in 1939 he was appointed superintendent of Kew Observatory, where he carried out some notable work in radiation. In 1943, Dr. Stagg was made chief meteorological adviser to the Supreme Commander, Allied Forces, Europe, and it was he who briefed General Eisenhower in preparation for the *D*-day landings in Normandy in 1944. For his war-time services Dr. Stagg was made an Officer of the Legion of Merit by the President of the United States. After the War, Dr. Stagg was made principal deputy director of the Meteorological Office, and in 1957 he was appointed to the newly created post of director of services, responsible for the 'operational' side of the Office. His keen physical insight and excellent administrative qualities made him outstandingly successful in this capacity. He was created a C.B. in 1954. In the international field, Dr. Stagg has taken a keen interest in the activities of the International Union of Geodesy and Geophysics, and he was for a time general secretary of that Union. In 1955, he was awarded the Gauss-Weber Medal for his contributions to geomagnetism. It is understood that he intends to resume his work in this field during his retirement.

Dr. A. C. Best, O.B.E.

ON September 8, Dr. A. C. Best succeeded Dr. J. M. Stagg as director of services of the Meteorological Office. After graduating with first-class honours in mathematics and physics at the University College of Wales, Cardiff, Dr. Best joined the Meteorological Office in 1926 as a junior professional assistant. During his career he has had a wide experience of both the research side and the operational side of the Office, at home and abroad. His early work was in the field of atmospheric turbulence, culminating in the publication of an important Geophysical Memoir on the transfer of heat and momentum in the lowest layers of the atmosphere. His later research has been devoted mainly to cloud physics, and he has written a number of papers on the formation and size distribution of raindrops and cloud droplets. He was awarded the L. G. Groves Memorial Prize for Meteorology in 1952, and made O.B.E. in 1953. Since 1955 Dr. Best has been a deputy director on the services side of the Meteorological Office.

Zoology in the University of Delhi: Prof. B. R. Seshachar

PROF. B. R. SESHACHAR, who has been professor of zoology in the University of Mysore since 1946, has been appointed professor of zoology in the University of Delhi. After a few papers on teleosts, anura and palæontology, he worked during 1932–45 on *Gymnophiona*, describing new species and investigating their development, their germ cells and their cytology. His discovery of a homologue of Bidder's organ is perhaps not universally known. Since 1946 he has been mainly concerned with ciliate Protozoa. India can probably fill many gaps in our existing knowledge of this group. For example, Seshachar has made a

collection of Indian types of *Spirostomum* sp.; this includes different mating types which can readily be induced to conjugate, whereas this has only rarely been seen in Europe. However, his main work has been on the chemistry and physics of the macronucleus. Perhaps Seshachar's greatest service to Indian zoology was to organize a laboratory at Bangalore in which a wide variety of researches went on side by side. Apart from work related to his own, classical comparative morphology and embryology, especially of teleosts, were studied, as were the anatomy and development of *Loris tardigradus*. Endocrinological research was carried out on various Indian vertebrates, and both nuclear and extranuclear cytology were studied in a number of invertebrates. Even when the results of such work are not very novel, it is essential as a foundation for the teaching of physiological zoology in India.

Biology in the University of Malta: Dr. O. L. Thomas

DR. OWEN LEWIS THOMAS, who has been appointed to the chair of biology in the Royal University of Malta, was born in New Zealand and graduated in medicine at Otago University Medical School. While a lecturer in anatomy in the Department of Prof. W. E. Adams, he gained his M.D. (with distinction) in that subject and was awarded a Beit Memorial Medical Research Fellowship. In 1946, he entered Oriel College, Oxford, and studied under Dr. John R. Baker in the Linacre Department of Zoology and Comparative Anatomy, gaining his D.Phil. degree in biological sciences. In 1951, Dr. Thomas was appointed senior lecturer in physiology in St. Bartholomew's Hospital Medical School, London. His main research publications relate to the histology and cytology of the nervous system. He has recently completed his D.Sc. thesis while acting as a teacher of biology in the Napier Girls' High School.

The National Central Library

THE forty-fourth annual report of the Executive Committee of the National Central Library, covering the year ended February 29, 1960, refers to disappointing progress in planning the proposed new building in Store Street (Pp. 20. London: The National Central Library, 1960). The possibility of obtaining additional storage space outside Central London is being investigated. The lending service of the Library has shown a marked tendency to expand, the number of requests for loans increasing by nearly 8 per cent, although books published since January 1, 1959, are no longer supplied to libraries borrowing through the Regional Library Bureaux. To facilitate quick communication in dealing with urgent requests, telex is being installed at the Library. The Executive has also recommended putting in hand a project involving the use of the xerographic process to deal with the arrears of material awaiting insertion in the National and Outlier Union Catalogue, in which finally the great majority of works available for loan in Britain will be recorded. The work done by the British National Book Centre on behalf of British libraries in re-allocating duplicate and other redundant books is now being extended to overseas libraries. The Executive Committee and the Trustees, after considering the Roberts Report, have reiterated to the Minister of Education their view that the inter-library lending system, with its centre at the National Central Library, should be regarded as a whole and financed half by the State and half by the participating libraries. The alterations in the Library's book selection policy are also considered (see *Nature*, 187, 992; 1960). The percentage of applications successfully handled decreased from 76·18 per cent in 1958–59 to 72·22 per cent in 1959–60, probably in consequence of the fact that such requests increasingly relate only to books that could not be traced through the Regional Systems. Of the 76,521 separate issues from or through the Library, 12,793 were to university libraries, 8,318 to special outlier libraries, 2,299 to Government departments, 3,622 to overseas libraries, 3,299 to industrial and research organizations, 33,902 to public libraries and 10,323 to adult classes. University libraries lent 28,611 books, and 3,494 books were lent to 53 countries and 1,871 borrowed from 29 countries, the chief borrowers being Hungary (435), West Germany (352), Czechoslovakia (478) and U.S.S.R. (230), and the chief lenders the U.S.S.R. (414), France (380) and West Germany (362).

Rubber and Plastics Research Association of Great Britain

THE Articles of a new combined rubber and plastics research association for the United Kingdom—to be known as the Rubber and Plastics Research Association of Great Britain—were adopted at an extraordinary general meeting of the executive committee of the Research Association of British Rubber Manufacturers in London on November 15. Seventy members of the British Plastics Federation, about a third of its membership, have already agreed to support the new Association. Speaking at the meeting, Mr. P. W. Howard, president of the Research Association of British Rubber Manufacturers, pointed out that the Research Association of British Rubber Manufacturers was engaged on work of overlapping scientific and technological interest to the rubber and plastics industries, and also on work in the thermoplastics field, much of which was of a similar nature to that envisaged by the plastics industry. The plastics manufacturers who are founder-members will be represented in the Association by a Plastics Research Committee and by representatives on the Council. They become members of the new Association as from January 1, 1961. Both industries will gain much from this joint venture. It has been announced by Mr. David Radford, chairman of the British Plastics Federation, that research will be carried out at the existing laboratories of the rubber industry, at Shawbury, near Shrewsbury, and that work has already begun on new buildings, with an area of 14,000 sq. ft., to house the additional personnel and equipment for plastics research.

Computer Centre at Woolwich Polytechnic

SIR THOMAS SPENCER, chairman of Standard Telephones and Cables, Ltd., and a governor of Woolwich Polytechnic, opened the Computer Service Centre at the Woolwich Polytechnic on November 22. The Centre has a *Stantec Zebra* automatic electronic digital computer, designed by Dr. W. L. van der Poel, of the Netherlands Post Office Research Laboratories, and developed and manufactured by Standard Telephones and Cables, Ltd. The machine is suitable for mathematical, scientific, engineering and statistical calculations and for commercial, financial and industrial applications. A large library of problems already programmed is available to users. The Computer Centre, which is established in the

Mathematics Department of the Polytechnic, will be used for the following purposes: (1) as a service to users in industry and commerce who are invited to discuss their problems with the computer staff and use time on the computer; a fee will be charged for this latter service; (2) for the training of students in the use of digital computers. It is intended that every student of the Polytechnic who is studying for a B.Sc. degree in mathematics, physics, chemistry, engineering or economics, and every student studying for a diploma in technology or a higher national certificate with endorsements, will have an opportunity to write programmes for and to operate the computer; (3) as an aid to research by members of the staff and postgraduate students of the Polytechnic and other educational establishments.

Liverpool Observatory and Tidal Institute

THE Liverpool Observatory and Tidal Institute, which for many years has been administered jointly by the Mersey Docks and Harbour Board and the University of Liverpool, is to become the sole responsibility of the University. The Observatory was founded in 1845 by the Liverpool Dock Trustees, and the Mersey Docks and Harbour Board, on its formation in 1858, took over the operation of the Observatory. The main reason for its establishment was the absence of knowledge at that time concerning nautical astronomy and even the most elementary details of correct determination of chronometer-rates and meteorology. The present Observatory building at Bidston was erected in 1864. The Observatory continued largely as an astronomical and meteorological institution until the death in 1928 of the then director, Mr. Plummer, an officer of the Mersey Docks and Harbour Board. For some years prior to this there had been close association with the Tidal Institute which had been founded by the University of Liverpool, largely through the influence of the late Mr. Charles Booth, a Liverpool shipowner, with whom was associated Prof. J. Proudman, and from January 1, 1929, the Board and the University agreed to combine the tidal work of the Institute and the work of the Observatory at Bidston under the name "The Liverpool Observatory and Tidal Institute", administered by a joint committee of both bodies. Since that time the joint committee has been extended to include representatives of the Admiralty and the National Institute of Oceanography. In addition to the work of tidal prediction, for which it is famous, the Institute has built up an international reputation in the scientific world and is deeply involved in the study of major problems such as the determination of mean sea-level and the investigating of storm surges as well as other matters involving geophysics and oceanography. The activities of the Institute are now far wider than was envisaged when the joint committee was set up in 1929, so the Dock Board has handed over its responsibilities to the University of Liverpool. For the time being the Observatory will be administered by the acting director, Dr. J. R. Rossiter, following the retirement of Dr. A. T. Doodson (see *Nature*, November 19, p. 625).

The Netherlands Universities Foundation for International Co-operation

THE organization known as the Netherlands Universities Foundation for International Co-operation was founded in 1952 to promote international co-operation in academic life at universities and elsewhere. It seeks to do this by functioning as a centre for consultations among institutes and persons at home and abroad; by encouraging the founding and maintaining of special forms of international education in the Netherlands; by keeping those abroad informed about university life and scientific activity in the Netherlands and vice versa; and by lending more general assistance with regard to measures and facilities on behalf of international academic and scientific contact and exchange. The Board of Governors is composed of representatives of all Dutch universities and the honorary president is H.R.H. The Prince of the Netherlands. The Foundation furthers international cultural exchanges in various ways, among others by founding institutions and courses of education on an international basis. Here it is active in a field which has been reconnoitred inadequately, and which presents many problems. It is aware of the need to subject this field of activity to further investigation. As yet, only a modest beginning has been made on this work, but individual research workers have been given commissions to form teams of experts to study comparative education; the problems of inter-cultural communications; the difficulties students from abroad encounter in adapting themselves in the Netherlands; and the evaluation of study in a foreign country. Another subject receiving close attention is European integration, the gradual achievement of which is believed to depend to a considerable extent on voluntary international co-operation within the world of higher education and research, and on the attention given to European affairs in individual institutions of higher learning. A pamphlet prepared by the Foundation describes the detailed work of the organization (Netherlands Universities Foundation for International Co-operation (NUFFIC): Aims and Activities. Pp. 16. The Hague: Netherlands Universities Foundation for International Co-operation, 1960).

The Mauritius Institute

THE annual report of the Mauritius Institute for 1958 notes the increasing demand on the library services, which include a scientific section, which has been combined with the Library of the Royal Society of Arts and Sciences to form a nucleus of works on natural history and biology (Pp. i + 27. Port Louis: Mauritius Institute, 1959. 25 cents). The report includes brief descriptions of the various sections of the Natural History Museum of Port Louis, which was reopened to the public in 1957, as well as of the Historical Museum. A function of the Mauritius Institute is to build regional collections and have them accurately identified, and the annual reports of the Institute should be particularly useful to workers on any group of the Mascarene fauna or flora. This Museum report includes some notes on research in zoology, entomology and botany, a list of publications during the year and also lists of Museum accessions, additions to the fauna of the Mascarene Islands and of library acquisitions. Similar lists are given in the annual report of the Mauritius Institute for 1959, to which are also appended a note on recent advances in the study of the fauna of the Mascarene Islands and one on the Special Collection of the Mauritius Institute Library dealing with the Mascarenes, Madagascar and the Indian Ocean (Pp. ii + 28. Port Louis: Mauritius Institute, 1960. 50 cents).

Public Health and Medicine in the U.S.S.R.

The World Health Organization has issued a useful introductory guide to published material on public health and medicine in the U.S.S.R., based mainly on the holdings of the libraries of the World Health Organization and of the United Nations in Geneva (*Library News*, 13, Supp. No. 2. Pp. 130. Geneva: World Health Organization, 1960). Works published during 1946–60 are included, but the emphasis is on those published since 1954, and on translations, surveys, etc., chiefly in English and French. The material is arranged under nine sections: guides to Soviet medical and scientific publications; periodicals (including a list of cover-to-cover translation journals); abstracting and indexing periodicals; bibliographies; directories; dictionaries and encyclopædias; administrative material; surveys; and miscellaneous material. The section dealing with administrative material is limited to publications issued in the U.S.S.R.; in the remaining sections works published in the U.S.S.R. and works published outside the U.S.S.R. are listed separately. Most of the entries are annotated and there is an alphabetical index.

U.S. Scientific Programmes in the Antarctic

The September issue of the *IGY Bulletin*, published by the National Academy of Sciences, provides a review of the status of the United States scientific programmes in the Antarctic, including many results of the International Geophysical Year and subsequent investigations, as well as descriptions of programmes in progress at the moment. The report contains contour maps showing the thickness of the Antarctic ice-cap and surface elevations; a description of the *Echo I* communications satellite, and of the long-range communications experiment for which it was designed as a 'passive' reflector of radio signals; and a summary of solar activity, geomagnetic disturbances, and decisions of the World Warning Agency during International Geophysical Co-operation 1959, just past the peak of sunspot activity reached during the International Geophysical Year; the relationship of solar activity and its associated terrestrial effects during the International Geophysical Co-operation 59 period to the 11-year-old solar-cycle is also described.

Automatic Data-processing in University Administration

Each year all the students admitted to King's College, Newcastle upon Tyne, are required to register before they start their work. The registration procedure involves the completion of a number of forms giving particulars about the student's date of birth, grant-giving body if any, place of residence, both while at home and at University, which out of a large range of courses he is intending to take, whether he is a new or returning student, an undergraduate or a graduate, and similar information to enable the University administration to have a complete record of the student, to arrange lecture room accommodation and to prepare the statistics required by various bodies. When done by hand this work occupies clerical staff for approximately one term. This year the task has been performed on the automatic digital computer in the University of Durham Computing Laboratory. The information on the forms was transferred to punched paper tape and processed on the computer. In just over two days all the lists and statistics required were produced, and the final lists distributed one week after the start of term. Further information about the tasks performed may be obtained from the Director, University Computer Laboratory, 1 Kensington Terrace, Newcastle upon Tyne, 2.

The Ecological Society of Australia

The Ecological Society of Australia was inaugurated at a meeting of plant and animal ecologists held in Canberra on August 1. The objects of the Society are similar to those of the corresponding bodies in Great Britain and the United States. They include promotion of ecological research and the publication of the results of research, facilitation of exchange of ideas among ecologists working in different fields, and encouragement of the practical application of ecological principles. Management of the affairs of the Society is vested in a Council, of which the executive officers for the current financial year are: *President*, Dr. K. H. L. Key; *Secretary*, Mr. J. H. Calaby; *Treasurer*, Mr. A. G. McArthur. The constitution provides for the annual general meeting to be held in the month of August, with a further general meeting in association with each meeting of the Australian and New Zealand Association for the Advancement of Science; additional meetings may be called at the discretion of the Council. The subscription for the current year has been set at £1. The address of the Secretary is: c/o Wildlife Section, Commonwealth Scientific and Industrial Research Organization, P.O. Box 109, Canberra.

The Institute of Physics and Physical Society: Awards

The Council of the Institute of Physics and the Physical Society has made the following awards: *Duddell Medal*, to Dr. J. B. Adams, director-general of C.E.R.N. (European Organization for Nuclear Research), for his leadership of that team; *Charles Vernon Boys Prize*, to Prof. A. W. Merrison, University of Liverpool, for his distinguished research in experimental physics; *Charles Chree Medal and Prize*, to Dr. S. E. Forbush, of the Carnegie Institution of Washington, for his distinguished work on cosmic radiation. The following appointments have also been made: *Guthrie Lecturer*, Dr. D. Shoenberg, of the Royal Society Mond Laboratory, Cambridge, to be Guthrie Lecturer for 1961; *Thomas Young Orator*, Dr. H. H. Hopkins, of the Imperial College of Science and Technology, to deliver the Thomas Young Oration in 1961.

Royal Society: Awards

Rutherford Memorial Appointment. Under the terms of the scheme to commemorate the late Lord Rutherford of Nelson the Council of the Royal Society has appointed Mr. W. J. Darcey (University of Melbourne) to be Rutherford Scholar for 1960 for three years, to carry out research in experimental nuclear physics at the Clarendon Laboratory, Oxford.

Paul Instrument Fund. Awards of grants by the Paul Instrument Fund Committee have been made as follows: £1,400 per annum for two years, in supplement of a previous grant, to Prof. G. F. J. Garlick, Department of Physics, University of Hull, for the continuation of work on solid state light image amplifiers; £2,000 in supplement of a previous grant, to Prof. D. Gabor, professor of applied electron physics at the Imperial College of Science and

Technology, and Dr. D. Jones, for additional equipment for use in connexion with the development of an electron interference microscope; £1,000 in supplement of a previous grant, to Dr. H. B. Barlow, assistant director of research, department of physiology, University of Cambridge, and Mr. P. E. K. Donaldson, technical officer, Physiological Laboratory, University of Cambridge, for further work on the development of (*a*) a device for automatically improving coding of messages, and (*b*) a diffused storage sequence engine.

The Pugwash International Conferences of Scientists

THE next two conferences in the series of Pugwash International Conferences of Scientists will be held in Moscow during November 27–December 4, and in the United States in the summer of 1961. The subject of both conferences will be "Disarmament and World Security", which will be discussed under two headings: (*a*) problems of disarmament and arms control; and (*b*) the role of scientists in the creation of a stable and peaceful world. About sixty-five scientists from a dozen countries will take part in the Moscow conference, the largest national groups being from the United States and the U.S.S.R. During their stay in Moscow, the participants will be the guests of the Soviet Academy of Sciences. The proceedings of the conference will be private, but a statement will be issued at the end. Further information can be obtained from Wayland Young, 100 Bayswater Road, London, W.2.

The Australian Mathematical Society: Summer Research Institute

THE Australian Mathematical Society has decided to hold its first Summer Research Institute at the Australian National University, Canberra, during January 3–31, 1961. Prof. T. M. Cherry (University of Melbourne) is to be the first director of the Institute, and will be assisted by Drs. H. Levey and J. Gani (University of Western Australia) as secretaries. The Australian National University has agreed to provide working accommodation for the fourteen Fellows of the Institute. Two groups, one in the mechanics of continua, and the other in probability and statistics, will be carrying out research at the Institute; four survey lectures reviewing particular branches of these fields have been arranged, but the Institute will otherwise remain fairly informal. Further information can be obtained from Dr. J. Gani, Department of Mathematics, University of Western Australia, Nedlands, Western Australia.

Symposium on National Health Institutes

A CELEBRATION will be held on December 12 to commemorate the twenty-fifth anniversary of the founding of the Istituto Superiore di Sanità of Rome. This reunion is being held concomitantly with the first international symposium on "National Health Institutes and Actual Research and Medico-sanitary Problems". The symposium is being sponsored by the World Health Organization, under the auspices of the Italian Minister of Health and the Istituto Superiore di Sanità. The topics to be discussed at this symposium will be: (1) organization of national institutes of health and their function in scientific research and in the safeguarding of public health; (2) national institutes of health and government controls; (3) active intervention of national institutes of health in contingent and specific problems. Further information can be obtained from the Istituto Superiore di Sanità, Viale Regina Elena 299, Rome.

Announcements

DR. ALBERT WETTSTEIN, head of the Biological Research of CIBA, Ltd., Basle, has been awarded the 1959 prize of the Marcel Benoist Foundation. The prize, which is awarded annually by the Foundation's administrative committee composed of federal government officials, university professors and the French Ambassador to Switzerland, is given to the Swiss scientist who has made the most useful contribution to human life during the preceding year. Dr. Wettstein received this distinction for his outstanding work in the field of steroid hormones.

DR. PAUL E. GAGNON is to succeed Dr. P. Ribeiro de Arruda (Brazil) as director of the International Atomic Energy Agency's Division of Exchange and Training of Scientists and Experts. Dr. Gagnon was governor of Laval University and also dean of the Graduate School at that University from 1940 until he joined the Agency. In 1947 Dr. Gagnon was elected president of the Chemical Institute of Canada.

PROF. M. V. LAURIE, professor of forestry in the University of Oxford, has been appointed a member of the Steering Committee of the Forest Products Research Laboratory (Department of Scientific and Industrial Research) at Princes Risborough in succession to Mr. Harry Douglass, general secretary of the Iron and Steel Confederation. The appointment is for a period of two years.

UNDER its plastics programme, Princeton University is offering a number of fellowships for engineering study and fundamental research in plastics leading to the degree of master of science in engineering. Applicants must hold a first degree in engineering or physical sciences from a recognized institution. The fellowships are valued at 1,500–2,100 dollars, plus tuition and fees. Opportunities for employment as part-time research assistants at 2,100 dollars per annum are also available to students not on fellowships. Further information can be obtained from Prof. Louis F. Rahm, Plastics Laboratory, Princeton University, Princeton, N.J.

THE University of Texas M.D. Anderson Hospital and Tumor Institute is sponsoring a symposium on "The Molecular Basis of Neoplasia" during February 23–25. Further information can be obtained from the Publications Department, University of Texas M.D. Anderson Hospital and Tumor Institute, Texas Medical Center, Houston 25, Texas.

A JOINT meeting of the Challenger Society and representatives of the Marine Laboratories (Development Commissioners' Scheme) will be held at the National Institute for Research in Dairying, Reading, during January 26–27, 1961. Further information can be obtained from Dr. L. R. Fisher, National Institute for Research in Dairying, Shinfield, Reading.

A PUBLIC conference "Education—18 Plus" is being organized by the Communist Party on December 3 at the A.C.T.T. Hall, 2 Soho Square, London, W.1. The conference will discuss the problem of university selection and expansion. Further information can be obtained from the assistant secretary, W. Alexander, Communist Party of Great Britain, 16 King Street, London, W.C.2.

PHYSICS LIBRARY

PROGRESS IN AERONOMY

AERONOMY is a new word describing a much older branch of science. It was proposed as recently as 1954 by Prof. Sydney Chapman and refers to the study of the properties of the upper atmosphere and the physical processes occurring in it, particularly those due to solar electromagnetic and corpuscular radiation. That the term is already in general use indicates the rapid growth of interest in this field which has arisen out of the development of new experimental techniques (particularly rockets and satellites) and from the success of the recent International Geophysical Year.

The symposium on aeronomy at Copenhagen during July 19–22 was aimed at surveying recent advances in the subject, both experimental and theoretical, and was organized under the auspices of the International Association of Geomagnetism and Aeronomy. If a digression at this point may be permitted, it may be of interest to direct attention to the close and long-standing link between geomagnetism and aeronomy, arising through the interpretation of magnetic disturbance in terms of electric currents flowing in the outer regions of the Earth's atmosphere. As long ago as 1839, Gauss, in discussing the origin of the terrestrial magnetic field, commented as follows: "If we should look for the direct causes completely or partly in the exterior, we could . . . only think of galvanic currents. The atmospheric air is no conductor of such currents, neither is the vacuum. . . . However, the mysterious phenomena of the aurora in which, to all appearances, electricity in motion acts the main part, forbid us to deny outright the possibility of such currents only because of the uncertainty mentioned and it is, in any case, interesting to study how the magnetic effects of such currents would appear near the Earth's surface". The transition from a possibility not to be denied outright to certainty took a century. Nevertheless, as the proceedings of this symposium amply demonstrate, the mysteries of the aurora and associated phenomena in the upper atmosphere increase in fascination in step with the advances in our knowledge and understanding of them.

The reduction of orbital data of the satellites to yield atmospheric densities at heights up to 700 km. was dealt with by three contributors, D. G. King-Hele (Royal Aircraft Establishment), L. G. Jaccia and C. A. Whitney (Smithsonian Astrophysical Observatory). The method is based on the fact that the satellite loses energy, and decreases in orbital period, through collisions with air molecules; the derived densities represent a mean over about 60° of the orbit near perigee. One of the most interesting features revealed is a diurnal density variation above about 400 km., the day- to night-time ratio being of order 10 at 600 km. height. At these heights there is also a correlation between density and solar activity. S. F. Singer (University of Maryland) discussed, from a theoretical point of view, the distribution of density in the exosphere, that is, in the region where the rate of collision is so low that particles follow ballistic trajectories and some escape entirely from the Earth's gravitational influence. From an analysis of the data on satellite drag, Singer places the base of the exosphere at 530 km. for the neutral constituents. R. A. Helliwell (Stanford University) described how the properties of the outer ionosphere may be deduced from studies of 'whistlers'. These are low-frequency atmospherics which result when radiation from terrestrial lightning discharges suffers dispersion along propagation paths following the Earth's lines of force. Since the dispersion is greatest at the uppermost point on the path, electron densities out to several Earth's radii can be derived. How the composition of the atmosphere (both neutral and ionized constituents) has been studied by rocket-borne mass spectrometers was the subject of a paper by C. Y. Johnson (U.S. Naval Research Laboratory).

Solar ionizing radiations (ultra-violet and X-rays) were dealt with in papers by R. W. Kreplin (Washington), H. Friedman and R. Tousey (U.S. Naval Research Laboratory). Because of the opacity of the atmosphere in these spectral regions, rocket and satellite-borne instruments are needed to determine the incident flux of the various components. By combining the variation of observed intensity with height in a particular spectral line with laboratory determinations of ultra-violet absorption in atmospheric gases, we can deduce the variation of density with height of the constituent responsible for the absorption. Measurements of soft X-ray intensities indicate their importance as an ionizing agent in the lower levels of the ionosphere. H. Friedman pointed out that since the Lyman α-wave-length coincides with a 'window' in the O I absorption spectrum, this radiation penetrates to about 70 km. altitude and may contribute to the D-region ionization. Rocket measurements of $L\alpha$ made during solar flares have, however, shown no increases within a factor of two.

P. Mange (U.S. Naval Research Laboratory) and V. C. A. Ferraro (University of London) discussed the importance of diffusion in connexion with the distribution of both neutral and ionized constituents of the high atmosphere. Rocket mass-spectrometer measurements of the argon/nitrogen ratio show that these constituents reach diffusive equilibrium somewhat above 100 km., but below this level vertical mixing prevents their separation. The distribution of ionization depends on the rates of ion production and loss, and on diffusion, which is likely to be of greatest importance in the upper F-region. Ferraro presented some theoretical results which take account of the diffusion term and are consistent with the hypothesis that both $F1$ and $F2$ regions are produced by the same source of ionization.

A comprehensive review by A. Dalgarno (Queen's University, Belfast) of collision processes relevant to the interpretation of upper-atmospheric phenomena was followed by a number of papers on atmospheric emissions. J. W. Chamberlain (University of Chicago) has derived the total rate of emission from the different components of the airglow and from a bright aurora, using observed spectral intensities. He estimates the total input of energy contributing to a bright aurora to be in the vicinity of 400 ergs cm.$^{-2}$ sec.$^{-1}$. The altitudes of the nocturnal airglow emissions have been the subject of controversy for a number of years, and, in view of their importance in relation to the emission mechanisms, it was particularly gratifying to hear about direct rocket measurements, reported by D. M. Packer (U.S. Naval Research Laboratory). These referred to various radiations

from O_2, O, OH and Na(*D*); in all these cases the peak-emitting levels occurred between 80 and 100 km. The variations in the 5577 and 6300 Å. airglow emissions were discussed by F. E. Roach (U.S. National Bureau of Standards) and D. Barbier (Institut d'Astrophysique, Paris). According to the latter author, the 6300 Å. line from O I is the only radiation which is emitted from altitudes greatly in excess of 100 km. Of particular interest was Barbier's recent discovery of stable red arcs emitting the 6300 Å. line at the low latitude of Tamanrasset (in the Sahara). The sodium twilight-glow was the subject of a paper by T. M. Donahue (Observatoire de Meudon, France). At Tamanrasset (21° N.) there is little seasonal variation in abundance of sodium, with about $4 \cdot 5 \times 10^9$ atoms per cm.^{2} (vertical column), whereas at Haute Provence (41° N.) the abundance varies between 2×10^9 and 25×10^9 atoms per cm.^{2}.

Spectra of atmospheric emissions contain information about the temperature of the upper atmosphere, but difficulties in both measurement and interpretation are considerable. However, D. M. Hunten (University of Saskatchewan) demonstrated that a temperature profile between 70 and 250 km. can be satisfactorily constructed, using rotational temperatures from N_2^+ negative bands in auroræ and Doppler widths of forbidden lines in the night and twilight airglow.

A general scheme of solar and terrestrial disturbance was presented by T. Obayashi (Hiraiso Radio Observatory, Japan). High-energy protons (10–100 MeV.) reach the Earth several hours after solar flares associated with type-IV radio outbursts. These particles cause prolonged polar cap radio-blackouts in the region within geomagnetic latitudes 60–65°. They are followed after a day or so by the corpuscular cloud of low-energy particles travelling at a speed of the order of 1,000 km. sec.$^{-1}$. The interaction of this conducting cloud with the geomagnetic field produces the main part of geomagnetic storms. Various detailed mechanisms proposed to explain the morphology of geomagnetic disturbance and the nature of the different types of fluctuations were surveyed by E. H. Vestine (The Rand Corp., Santa Monica, California) in a paper entitled "Problems of Geomagnetism in Relation to Aeronomy". Of great interest in this connexion are the results of rocket and satellite experiments in which many of the features theoretically inferred have actually been measured; for example, the detection of the equatorial current in the *E*-region by Singer, Maple and Bowen, of the interplanetary fields by *Sputnik III* and the Soviet Moon rocket, and perhaps most exciting of all the discovery of trapped high-energy particles in the Van Allen belts. A particularly interesting finding has been the large magnetic disturbance in interplanetary space at the time of a terrestrial magnetic storm, made by the U.S. *Pioneer V*. Field values of the order of 50γ which were found may be compared with a general background field of 2γ or so.

The influx of interplanetary dust, as determined by various methods, was discussed by me. There remains a gap between the smallest particles producing observable telescopic or radio meteors, and the range of particle sizes detected by rocket and satellite investigations. Satisfactory comparison between the distribution of meteor magnitudes and the distribution in particle momentum or energy as derived from rockets and satellites requires rather more detailed knowledge of the structure of the particles, their orbital distribution, and of the nature of their interaction with the atmosphere than we possess at present.

I wish to conclude by thanking, on behalf of the participants, our Danish hosts, the chairmen of the various sessions, Prof. J. Kaplan (president of the International Association of Geomagnetism and Aeronomy) and Prof. M. Nicolet (chairman of the Association's Committee on the High Atmosphere) for arranging and conducting such a stimulating and rewarding meeting. The papers contributed will shortly appear in the *Annales de Géophysique* and afterwards as a bound volume which, it is hoped, will be available at a price to suit the purse of individual research workers in this rapidly expanding field.

T. R. KAISER

LATTICE DEFECTS AND THE MECHANICAL PROPERTIES OF SOLIDS

THE second symposium of the Fifth Congress of the International Union of Crystallography was held in the Guildhall at Cambridge. It opened with an introductory lecture on August 20 by Prof. N. F. Mott, who surveyed the development of our knowledge about lattice defects and their relation to mechanical properties, and outlined outstanding problems in the field. The symposium, organized by Dr. P. B. Hirsch, occupied August 22–24, and about one hundred papers were presented by contributors from eleven countries. On two days the sessions continued (with a substantial audience) until 10 p.m.; the supposedly free afternoons were, of course, usually fully occupied by private discussions. One may criticize meetings of this kind for the mental indigestion and exhaustion they produce, and argue that fuller discussion on a more restricted subject is to be preferred. Nevertheless, these larger gatherings do have a value of their own in presenting a broad picture of current progress in many associated fields, and in providing an opportunity for the assembled specialists to assess the impact of related developments on their own particular interests.

The papers of the symposium were grouped under twelve main headings, and it is clearly not possible in the present short review to refer to the significant content of all contributions. Summaries of the papers are printed in the Congress Abstracts of Communications, and the papers will appear in full in the usual scientific journals.

Four sessions were devoted to "Yield Strength" and "Work-hardening", which are perhaps the central problems of the field. Ideas on work-hardening are still in a state of flux, and discussions took place on a number of mechanisms which may be important in determining the flow stress: the stresses due to dislocation groups (Seeger); the debris left behind by moving dislocations (Gilman, who discussed the

velocity of dislocations as a function of stress); also, in a new theory, the associated accumulation of defects by dislocations as they move (Hirsch, Warrington and Hirsch); and the interactions arising from the intersections of dislocations with one another (Baird and Gale, Saada, Hale and McLean). The last authors, and also Howie, and Bailey and Hirsch, reported detailed correlations between observations on thin films and macroscopic treatments and measurements in various metals; and flow-stress measurements were discussed by Christian, Masters, Mitchell and Pargeter, and by Basinski. Other topics treated were the theoretical strength of metals (Richards) and dislocation reactions in body-centred iron (Crussard), while considerable attention was given to the mechanical behaviour of ionic crystals (Newey and Pratt; Pratt; Silverstone and Pratt; Westwood) and of semi-conductors (Bell and Bonfield; Suzuki, Kayano and Watanabe; Bernard, Berth, Burgeat, Devaux, Mme. Soula and Tsoucaris). In the sessions on "Stacking Faults" and "Twinning", two papers were concerned with the direct measurement of stacking fault energies (Howie and Swann) and associated calculations (Bilby, Grinberg and Swinden), and a number of others described the behaviour of faults and twins as observed in thin films and under stress in the electron microscope (Phillips; Price; Fourie, Weinberg and Boswell; Catlin, Walker and Lawless; Pashley and Presland). The last authors also directed attention to fine defects ('black death') produced, probably indirectly, by the electron beam. Two papers discussed the theory of twinning (Christian; Venables) and others treated kinking in cadmium (Blasdale, King and Puttick) and in alkali halide crystals (Mme. Klassen-Neklu-dova), and the interplay of twinning and slip in iron (Sleeswyk) and silicon iron (Hull).

In contrast to the situation in work-hardening, the survey of probable mechanisms of "Fracture" could be given (Cottrell) without provoking instant controversy. The influence of minute surface imperfections was emphasized in papers on the Joffe effect (Stokes, Johnston and Li) and on the fracture of glass (Murrell). The former authors also illustrated in another paper the interrelation of fracture and deformation in magnesium oxide. Other papers treated the fracture of zinc (Barnby and Pratt) and silicon iron (Cuff), the fracture of thin metal films (Fujiwara and Yoshida, Fisher and Nutting), and the propagation of cracks (Mme. Shaskolskaya) and the influence of inhomogeneities on this process (Bethge and Schmidt) in alkali halides. The session on "Fatigue" was opened by Thompson, and included reports on thin-film studies of the defects produced (Partridge and Segall), the role of cross-slip (Broom) and a theory of the dependence on temperature (Hirsch and Segall). Grosskreutz described experiments on crack propagation in single crystals.

There were two sessions on "Dislocations and Point Defects"—one on "Quench Hardening" and one on "Climb and Creep". The effects of irradiation and/or cold work and the course of subsequent low-temperature recovery (usually assessed by resistivity measurements) were reported for several materials: in copper and its alloys (Pritchard and Pratt, Sosin), in molybdenum and niobium (Johnson, Peacock and Wronski) and in titanium and zirconium (Smith and Stagg). Effects of straining and ageing on the mechanical and electrical properties and the etching behaviour of alkali halides were also discussed (Slifkin, Kabler and Layer; Curien and Mihailovic; Bethge and Frohlich; Davidge, Whitworth and Pratt), and an extension of the general theory of strain-ageing reported (Bullough and Newman). Changes in impurity concentration around precipitates at dislocations and other sites in doped silicon were revealed directly by the formation of annular p–n junctions made visible by etching (Newman, Wakefield, Willis and Bullough). Internal friction studies on cold-worked gold and copper (Hasiguti and Okuda) and on quenched aluminium (Gelli and Federighi) were reported, as well as the influence of pressure and plastic deformation on point defects (Lazarus) and their contribution to stored energy and volume changes (Åström). Quench hardening was introduced by Maddin, and a thin-film study of the vacancy clusters produced in aluminium reported by Westmacott, Barnes, Smallman and Hull. The role of solute atoms and vacancies in the ageing of aluminium alloys was studied in thin films (Nicholson), by calorimetric and resistivity measurements (Borelius and Larsson), and by small-angle X-ray scattering (Gerold and Schweizer). An introductory paper on climb and creep (Friedel) was followed by a direct thin-film investigation of the shrinkage-rates of dislocation loops in zinc by climb (Price). An example of the direct and subtle experiments now possible was afforded in a paper by Dash, who was able to argue that climb observed in silicon due to the introduction of gold was due to vacancy deficiency, since left-hand screw dislocations formed right-hand helices. In similar vein, Barnes and Mazey showed that certain dislocation loops in copper foils induced by α-particles were formed by condensed interstitials, since in a foil where the particles come to rest the loops grow during the precipitation of helium bubbles, which is a process requiring vacancies. Other papers in the two sessions on "Radiation Damage" included work on copper and other face-centred cubic metals (Blewitt, Coltman, Jamison and Redman; Silcox; Makin, Whapham and Minter; Seeger, Mader and Essmann), on graphite (Williamson and Baker; Fujita and Izui) and on fission in uranium steel (Baker and Nutting). A general discussion of dislocation-point defect interaction was given by Sosin.

The session on "Recrystallization" and related phenomena included thin-film investigations on silver (Bailey) and work with other techniques on a titanium molybdenum alloy (Schofield and Bacon) and on aluminium (Weissmann, Imura and Nakayama; Fujiwara and Takano). Grain-boundary motion in sintering was discussed by Horustra and van Bueren. In the session on "Alloy Hardening", A. Kelly reviewed the yield strength of alloys, and thin-film observations on the dislocations in ordered alloys were discussed in two papers (Pashley and Presland; Marcinkowsky, Brown and Fisher). Work was also reported on the order and precipitation hardening in a nickel (24 per cent), chromium (15 per cent), aluminium (3·5 per cent) austenitic steel (Blackburn and Nutting), and of dislocations and precipitates in an austenitic steel containing niobium (Arrowsmith and Nutting).

The final session, on "Martensitic Transformations", was introduced by Read, who also discussed the plasticity of metals undergoing polymorphic transformation. Again, important work using the thin-film technique is revealing here the fine details of the transformation process. P. M. Kelly reported thin-film work on high- and low-carbon steels and on

iron–nickel alloys, and suggested correlations between the twinning and different morphologies observed and the martensite hardness. Venables has worked on thin films of stainless steel transformed by cold work, where stacking faults, regions of hexagonal ε-phase and regions of body-centred cubic α'-phase can be seen. Other papers in this session described extensions to the crystallographic theory (Wechsler and Otte) and etch-pit investigations of dislocations in the austenite (Reed and Greeson).

Thus, the subject of defects in crystals continues to expand at an ever-increasing rate, particularly under the stimulus of the development of experimental techniques permitting direct observation of dislocation lines, of which the dominant one is now the use of the electron microscope to examine thin metal films by transmission. With these high-resolution studies, our knowledge of the detailed behaviour of individual dislocations and other lattice defects is increasing rapidly, and the next ten years will see a great extension in work of this kind. While possible differences in the behaviour of defects in thin films and bulk specimens must always be borne in mind, it is clear that much valuable information about the basic mechanisms controlling bulk mechanical properties will be obtained in this way. Such information must indeed play an essential part in the solution of the more difficult problems concerned with the development of theories about the bulk mechanical properties of practical interest. B. A. BILBY

CO-ORDINATION CHEMISTRY

A SYMPOSIUM on Co-ordination Chemistry with an international attendance was held in Prague during September 5–8. It was organized by the Czechoslovak Chemical Society and by the Faculties of Inorganic Chemistry of the Charles University and the Technical University and sponsored by the Czechoslovak Academy of Sciences.

The introductory paper by Prof. A. A. Grinberg (Leningrad) consisted of a survey of the development of co-ordination chemistry in the past decade and a general review of the present position of the subject. This was followed by a general discussion of the applications of polarography by Dr. A. A. Vlček, a member of the Polarographic Institute at Prague. Dr. Vlček emphasized, in particular, the importance of searching for new complexing agents which would permit the electro-deposition of a wider range of metals than can at present be utilized in this way.

The other scientific meetings were grouped into three sections, concerned with modern preparative methods, with the physico-chemical properties and structure of complexes, and with direct methods of structure determination, respectively. Prof. S. Herzog opened the first main session with a paper on the properties of low-valency co-ordination compounds of metals with dipyridyl and phenanthroline. He described some remarkable substances, for example, zero-valent *tris*-dipyridyl derivatives of titanium, scandium and even niobium. The existence of such compounds and of magnesium and lithium dipyridyl derivatives was shown to raise a number of important problems in valency theory which were discussed in some detail. Whether these compounds are to be regarded as true low-valency compounds of the metals, or as complexes of the dipyridyl anion radical, was the interesting question which emerged in discussion.

Among the contributed papers one can mention only a few. Prof. E. O. Fischer (Munich) described the preparation of a variety of mixed diene-carbonyl complexes of zero-valent metals and discussed some very remarkable rearrangements which they undergo. Prof. I. I. Chernaev (Moscow) described his extensive work on the nitro complexes of tetravalent platinum. Dr. K. Isslieb (Jena) described a large number of novel complexes of transition-metal ions with primary and secondary phosphines. Complexes of tri- and tetra-dentate arsenic ligands were discussed by a group from Oxford.

The section on physico-chemical methods was opened by Dr. L. E. Orgel (Cambridge), who gave an elementary account of the principles of ligand-field theory and of modern methods of determining the spatial distribution of unpaired *d* electrons in transition-metal complexes. This was followed by an entertaining paper by Dr. L. G. Sillen (Stockholm), who summarized the extensive research of his school on the varied hydrolysis reactions of metal ions in aqueous solution.

Madame B. Jezowska-Trzebiatowska (Warsaw) described the use of optical and magnetic measurements in discussing the electronic structure of a variety of co-ordination complexes. The *trans* effect in a variety of complexes of divalent platinum, trivalent cobalt and divalent copper was treated in a series of papers.

A further group of papers dealt with applications of polarographic methods. Prof. K. B. Yatsimirskii (Kiev) described ingenious methods of using the catalytic polarographic currents to study complexes in solution; Miss D. Wagnerova (Prague) discussed the polarographic reduction of ruthenium nitrosyls, and Dr. E. Fischerova described similar work on trivalent chromium complexes.

The final section was opened by Prof. Porai Koshitz (Moscow), who gave a concise summary of the present state of our knowledge of the environments of metal ions in co-ordination compounds as determined by direct X-ray studies. There followed a series of papers describing structural studies on individual compounds. One may mention in particular papers on the periodate of trivalent copper, on the dipyridine adduct of the dimer of copper acetate, and on $(NH_2.CH_2.CH_2.NH_2)\,CuBr_2$. Another paper in this series by Czech crystallographers discussed the mechanism of the substitution reactions of cupric compounds.

The meeting as a whole provided an excellent opportunity for the exchange of ideas and information between scientists of all countries. For those from the Western countries it was a particular pleasure to meet and talk with their opposite numbers from Eastern Europe. Apart from the main scientific business of the meeting, foreign delegates were most hospitably entertained—a tour of the medieval city of Prague, an excursion to neighbouring points of interest and the various social activities in the evenings were greatly enjoyed by those present. L. E. ORGEL

ADMISSIONS TO BRITISH UNIVERSITIES

THE second report of an *ad hoc* committee of the Committee of Vice-Chancellors and Principals of the Universities of the United Kingdom on Procedure for Admission of Students (pp. vi+31. London: Association of Universities of the British Commonwealth, 1960. 2*s*.) deals first with the action taken by the universities on some procedural recommendations of an earlier report published in May 1958 by an *ad hoc* committee. Although the new system has been in operation for only one full year, it is already clear that a marked improvement has occurred. Indeed, 86 per cent of heads of schools answering the independent inquiry of the Joint Committee of the Four Secondary Associations about delays by universities were satisfied that there was no unreasonable delay, and 66 per cent were satisfied with the decisions themselves. Throughout the universities, all those concerned are showing the utmost willingness to co-operate in making the selection and admission of students as simple, fair and rapid a process as possible. As all those concerned, in universities and schools, become more accustomed to the new procedures, the improvement should continue, and to this end the Committee recommends that the normal date for the receipt of applications should continue to be January 31 of the year in which entry is desired (the preceding November 30 for medicine, etc.); constant care should be exercised to preserve standards of precision in letters making offers of places, and the great importance of making as many early decisions as possible is specially emphasized. The Committee also reviews some continuing problems such as multiple interviews and clearing houses, and recommends that experiments should be tried, worked by volunteer professors in limited fields such as chemistry, physics, biology, medicine, dentistry, veterinary science, agriculture and law. Finally, it recommends that the admission of students generally be kept under review. The Committee of Vice-Chancellors and Principals has already invited this *ad hoc* committee to continue its consideration of future problems.

Figures for applications and admissions for 1959 show that applications to university institutions in England, Wales and Scotland were 117,300, 7,600 and 9,100, respectively, and the corresponding admissions to first-degree courses were 14,960, 1,650 and 3,720, respectively. As between the main categories, applications were distributed as follows: arts, 50,900; pre-science, 40,700; technology, 21,700; medicine, 13,100; dentistry, 4,500. The ratio of applications to the number of places available varies widely between individual universities; for example, from 6·0 to 11·4 in England, 3·8 to 6·2 in Wales, and 1·9 to 3·0 in Scotland, but no clear pattern, according to age or type of institution, emerged from more detailed examination of the figures.

Appended to the report is a brief guide for the sixth-former entitled "Getting into a University", containing the minimum information which any intending candidate needs before discussing matters with those who will give him advice and before completing his application.

INTERNATIONAL UNION FOR CONSERVATION OF NATURE AND NATURAL RESOURCES

R. LEVEQUE was appointed by Unesco to undertake a new mission to the Galapagos Islands. The purpose was to consolidate the basis for the establishment of a research laboratory, the primary objective of the Charles Darwin Foundation. He has now presented a report which contains a wealth of information about the destruction being wrought on the exceptional fauna of the archipelago*.

In his inventory of the present state of the animal populations, Levêque recalls that the sea-lion has succeeded in holding its own in face of the depredations of fishermen, but the fur-bearing seal (*Arctocephalus australis*) is prey to exploitation which will soon lead to extinction if drastic measures are not taken. Biological study of the species must be a priority in the programme of research.

Concerning the bird populations, the maintenance of which is bound up with the survival of the shrub cover of the islands, Levêque is less pessimistic. The larger species call for attention: albatross, flightless cormorant, penguins and especially the flamingo, which is in keen demand for its feathers, and consequently vulnerable.

The author has nothing essential to add to the excellent material on reptiles previously compiled by Mr. Eibl-Eibesfeldt. Wild pig destroy the eggs of the sea iguana, but apart from this the latter species is practically without enemies; the land iguana is holding its own.

By far the most threatened species is the giant tortoise; the local position is desperate. The massacres continue, with the destruction of eggs by feral pigs, by trading shells, and extraction of oil. It appears necessary to destroy the feral pig if the tortoise is to be saved. Levêque calls for the establishment of a large park to be fenced off with barbed wire, and gives suggestion for its boundaries.

Crayfish are being captured on a reckless scale; a single boat recently brought in three tons of crayfish tails in a few days; a thorough study of the biology of the species is required. Likewise, overfishing of the bacaleo will soon result in a serious depletion of this species.

The author lays strong emphasis on the disastrous consequences resulting from the introduction of exotic species to the Islands: dog, donkey, but especially pigs, "the worst enemy of the indigenous

* *Bulletin of the International Union for Conservation of Nature and Natural Resources*, 9, Nos. 1–2 (1960).

agriculture, flora and fauna", and feral goats, which are on the increase and destroy numbers of plants. It would seem advisable to encourage unrestricted hunting of these animals; the fate of the Galapagos Islands, otherwise, will be similar to that of the Mexican island of Guadeloupe. Levêque emphasizes the mistake of prohibiting hunting of feral animals introduced to the Islands. The result is contrary to the objective pursued; the defenceless native fauna, the destruction of which does not require the use of fire-arms, pays the consequences and serves as food for the settlers.

A number of sound recommendations conclude the survey: engagement of an experienced botanist to undertake methodical inventory of the plant species represented; careful study of the biology of the land tortoise, and, later, of both iguanas, *Amblyrhynchus* and *Conolophus*; efforts in the fields of oceanography and meteorology resulting in a marine research scheme and the establishment of climatological stations.

INDUSTRIAL HEALTH

THE annual report of the Chief Inspector of Factories on Industrial Health in 1959 follows the pattern of the two previous separate reports, and this year includes a special chapter on "Dusts and Their Effects on the Lungs"*. The establishment at headquarters of the new pathological laboratory permitted a substantial increase in the number and variety of tests, and the combined chemical and pathological work has made possible the examination of an increasing number of workers. The Chief Inspector again emphasizes his anxiety to foster the liaison between the medical branch of the Inspectorate and members of the medical profession generally, which he regards as of great importance if due weight is to be given to significant occupational factors in the health of work people. The 532 cases of industrial poisoning or diseases, notified under the Factories Act, 1937, and the Lead Paint Act, included 64 non-fatal cases of lead poisoning, 6 cases (1 fatal) of anthrax and 25 non-fatal cases of aniline poisoning; 226 notified cases of epitheliomatous ulceration included 9 fatalities, and there were 192 cases of chrome ulceration, while 14 of the 206 gassing accidents were fatal.

The First Aid in Factories Order, 1938, was superseded by the First Aid Boxes in Factories Order, 1959, on January 1, 1960, which brings the contents more into line with modern practice than under the 1938 Order. Interdepartmental discussions on the general principles of first-aid treatment were attended by independent medical experts nominated by the Medical Research Council and members of the Advisory Panel in Ophthalmology were consulted on the first-aid treatment of eye injuries, while at the two meetings during the year of the Industrial Health Advisory Committee the possibility of developing and extending medical supervision in factories was the main subject discussed.

Publication of a new booklet, "Toxic Substances in Factory Atmospheres", was approved. The special chapter on dusts and their effects on the lungs points out that it is now becoming increasingly doubtful whether it is safe to assume that any finely divided dust is harmless if inhaled in sufficient quantity over a sufficient period. Certain dusts, too, may produce an acute inflammatory response in the lungs when they are breathed, and others, usually after many years, may bring about a cancerous development in some part of the respiratory tract. The chapter outlines some general principles on measures required to protect workers against inhaling injurious dusts as well as briefly summarizing existing knowledge about the action of particular classes of dusts.

* Ministry of Labour. Annual Report of the Chief Inspector of Factories on Industrial Health, 1959. Pp. iii+60. (Cmnd. 1137.) (London: H.M. Stationery Office.) 3*s*. 6*d*. net.

X-RAY DIFFRACTION STUDIES OF THERMALLY DECOMPOSED PERMANGANATES

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THE thermal decomposition of crystals of silver[1], potassium[2], rubidium[3], cæsium[4] and barium[5] permanganates in high vacuum yield pressure-time plots which are sigmoid in form. The plots for the decomposition of crystals of potassium permanganate (13·6 mgm.) and silver permanganate (20·6 mgm.) at 217° C. and 110° C., respectively, are shown in Figs. 1 and 2. The acceleratory and decay portions of the curves for the above permanganates, except silver permanganate, are described by the Prout–Tompkins equation[2]:

$$\log [p/(p_f - p)] = kt + c$$

where p_f is the final pressure. The plots for the decomposition of silver permanganate obey a modified form of the equation[1], namely:

$$\log [p/(p_f - p)] = k \log t + c$$

These equations follow if it is assumed that at the commencement of the acceleratory period strain exists in the crystal at the interface between the product formed prior to acceleration and the undecomposed material. This strain produces micro cracks in the reactant surface, and the reaction progresses inwards by a mechanism of branching planes of reaction. Mechanical disruption of the crystal, as in the case of potassium permanganate, is a consequence, not the cause, of branching. Silver permanganate, for example, does not disintegrate during reaction. It is of interest, therefore, to examine the Laue photographs of potassium permanganate and silver permanganate at different stages during decomposition when lattice distortion would be expected for both substances. Such distortion will be shown by asterism of the diffraction spots. Fig. 3, *A*, *B*, *C*, *D*, *E*, *F*, *G* were taken at 40 kV. and 20 m.amp. using

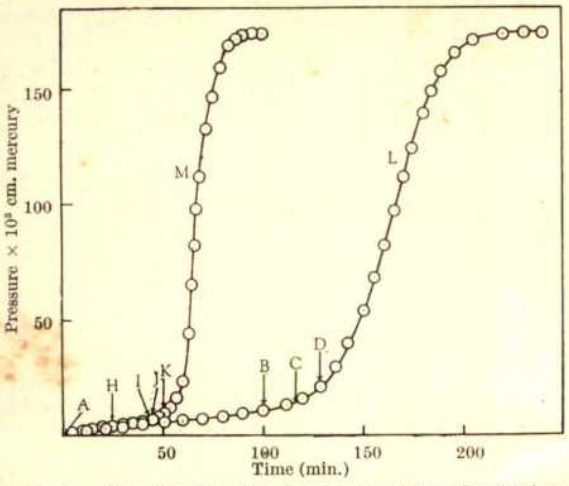

Fig. 1. Pressure-time plots for decomposition of potassium permanganate at 217° C. Curve *L*, unirradiated crystals; curve *M*, γ-ray irradiated crystals. Laue photographs taken at times of interruption indicated by arrows. Fig. 3, *A*, *B*, *C*, *D* and Fig. 4, *H*, *I*, *J*, *K* correspondingly lettered

copper radiation filtered through iron. The silver permanganate crystal was mounted about the needle axis. The crystal of potassium permanganate was similarly mounted before disintegration, but after this there was no known orientation. The corresponding times of interruption of the reactions are indicated in Figs. 1 and 2.

Asterism is not exceptionally pronounced immediately prior to acceleration, but with both silver and potassium permanganates there is a marked increase in the lattice distortion immediately after this.

Fig. 4, *H*, *I*, *J*, *K* are Laue photographs of pre-irradiated potassium permanganate (γ-ray dose in spent fuel facility at Harwell, 10 Mrads; $p - t$ plot in Fig. 1) under the same conditions as for Fig. 3. The Laue photograph of undecomposed irradiated material does not differ in any marked respect from that for undecomposed unirradiated potassium permanganate (Fig. 3*A*). It is seen that the amount of strain is extremely high at the end of the induction period. This is in accord with the suggested mechanism of decomposition of pre-irradiated potassium permanganate[6], which presumes that at the end of the induction period there are centres of decomposed material throughout the crystal and that these produce a high degree of strain in the solid.

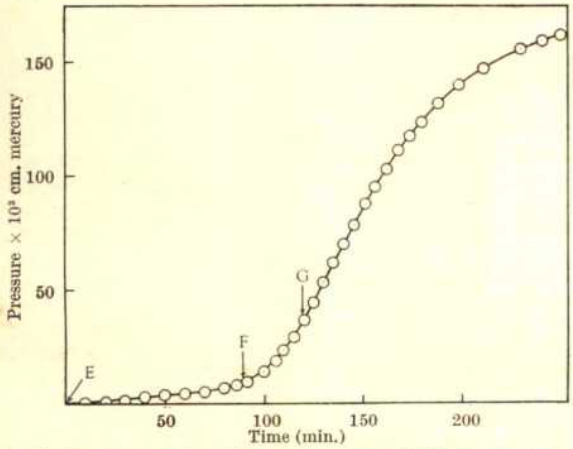

Fig. 2. Pressure-time plot for decomposition of silver permanganate at 110° C. Laue photographs of Fig. 3, *E*, *F*, *G* taken at corresponding times of interruption shown by arrows

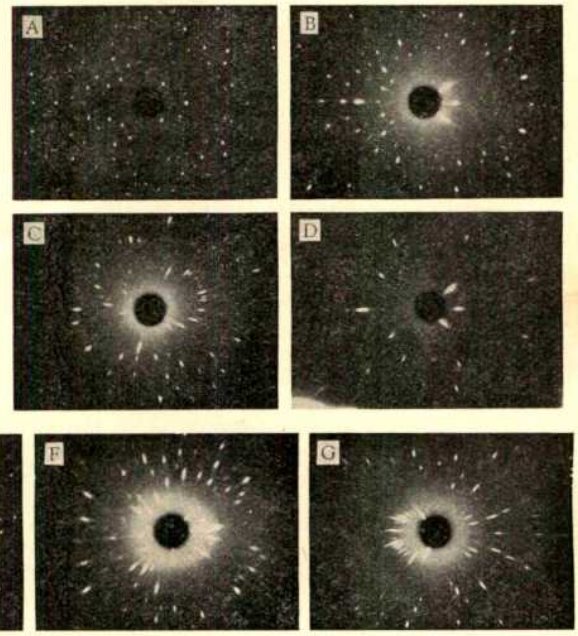

Fig. 3. Laue photographs of unirradiated potassium permanganate and silver permanganate. See legends for Figs. 1 and 2

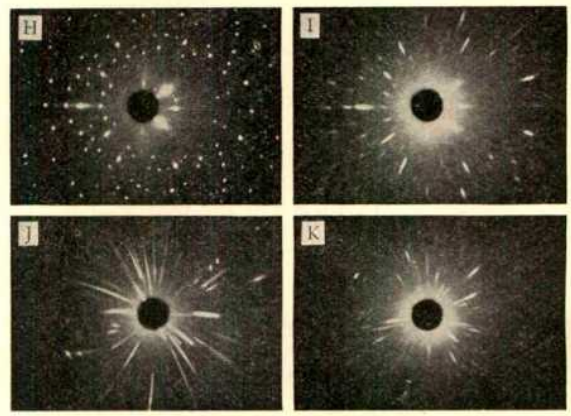

Fig. 4. Laue photographs of pre-irradiated potassium permanganate. See legend for Fig. 1

More detailed X-ray studies of unirradiated and irradiated permanganates are in progress, and the results will be published elsewhere in due course. We wish to acknowledge financial assistance from the Council for Scientific and Industrial Research (South Africa) and for a scholarship held by one of us (P. J. H.).

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A CONNEXION BETWEEN P_c AND THE F REGION

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THE two most promising theories of the origin of geomagnetic micropulsations of the P_c type are: (1) they originate as standing hydromagnetic waves within the ionosphere[1], or (2) they originate as standing hydromagnetic waves in the outer atmosphere[2].

Each of these theories has at least one major difficulty to overcome. The first must explain how phase stability can be produced over distances large compared with the thickness of the ionosphere; and why the modulation envelope of P_c wave trains should often be so similar at places as widely separated as College, Alaska, and the Borrego Desert in California. The second must explain how the electromagnetic field appears to be propagated through the lower ionosphere without serious attenuation; indeed, how there can be a maximum of activity on the sunlit side of the Earth where the shielding has been thought to be greatest. This paradox is the main subject of this communication.

White[3] has published a curve showing the high harmonic content of the diurnal variation of the ionospheric electron density near the equator. Afanasieva[4] has reported a similarity between P_c and f_0F_2 (although measured at different places), and a high correlation (0·75–0·97) between P_c amplitude and f_0F_2. On the other hand, Benioff[5] reports that his type A oscillations (0·3–2·5 sec. period, and thus not P_c) occur only when the electron density in the F region is unusually low.

These conflicting reports suggested that, averaged over a year, there might be a world-wide relationship between P_c and ionospheric electron density $N(h)$ which is obscured by local effects. A preliminary study of this relationship is now possible since the publication of Miss Hutton's data on the diurnal variation of P_c on the equator[6], and those of Jacobs and Sinno for the International Geophysical Year[7]; together with the most recent results of $N(h)$ during the International Geophysical Year by workers at the Cavendish Laboratory (Croom, S., Robbins, A., and Thomas, J. O., private communication) and by Schmerling[8].

As yet there are only enough data to suggest that the diurnal variation of P_c is inversely related to the diurnal variation of the true electron density at 280 km.

Figs. 1*a* and *b* respectively show the ratios of the 12-hr. and 8-hr. harmonic components to the 24-hr. component of the diurnal variations of P_c occurrence, and of $N(h)$ at 280 km. over stations covering a large range of geographical latitude. The symbols for the stations are shown along the top of each diagram.

It will be noted that the 8-hr. and 12-hr. ratios are comparable for both P_c and $N(h)$ at all latitudes, although there is considerable dependence on latitude. The harmonic vector lies in the quadrant indicated below each point relative to the 24-hr. vector.

Three different zones are suggested: (1) an equatorial zone, where the corresponding P_c and $N(h)$ vectors are in opposing quadrants; (2) a middle zone, where the effect of the ionosphere is not clearly displayed by this treatment; (3) an auroral or polar zone, where the 8-hr. vectors are in phase, although the 12-hr. vectors oppose one another.

Unfortunately, only the behaviour at the equator is reliably indicated by the present data. The harmonic content in the middle latitudes is so small that slight errors in the data would cause large phase changes, and the high-latitude data are only available from stations in opposite hemispheres.

The simplest interpretation of the equatorial behaviour is that the source of P_c oscillations lies above the ionosphere. At the surface of the Earth the amplitude is reduced by conventional ionospheric

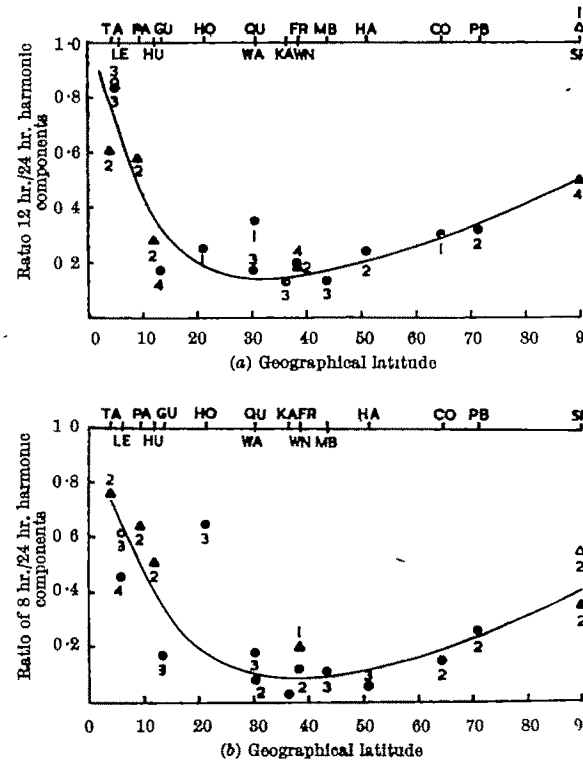

Fig. 1. *a*, The ratios of the 12-hr. to the 24-hr. harmonic components of the diurnal variation of the occurrence of P_c (dots) and of $N(h)$ at 280 km. (triangles), averaged over the International Geophysical Year, for stations the symbols of which are found at the top of the figure and geographical latitudes at the bottom. The hollow circle is Miss Hutton's (ref. 6) May–July 1957 data. The hollow triangle is Knecht's (ref. 10) f_0F_2 data for the South Pole. *b*, The ratios of the 8-hr. to the 24-hr. harmonic components of the diurnal variation of the occurrence of P_c and of $N(h)$ at 280 km. at a number of stations. The symbols are the same as in Fig. 1*a*

shielding as discussed by Ashour and Pryce[9]. The rather complicated diurnal and latitudinal variations of $N(h)$, together with the too simple assumption of a uniform external disturbance field, have hitherto obscured the ability of their theory to explain the role of the ionosphere in the diurnal variation of P_c.

At high latitudes the 12-hr. phases of both $N(h)$ and P_c are opposed, as they are at the equator. However the 8-hr. components are in phase. Possibly this is due to occasional incursions of solar corpuscles, themselves the source of the hydromagnetic disturbance of the outer atmosphere, which are confined to the auroral zones. It must be noted, however, that not only are the polar data from different hemispheres but also that Knecht[10] observed 3-hr. phase differences between the 12-hr. and 24-hr. components of the F_1 layer and their counterparts in the F_2 layer. Thus considerably more data are required to clarify polar behaviour. Despite the occasions mentioned by Afanasieva[4] and Campbell[11] when the ionization increases during P_c events, a demonstrable effect of the polar ionosphere appears to be that of shielding.

On this basis one may venture to predict that a daily minimum in P_c occurrence will be found corresponding to the daytime maximum in ionization reported by Croom, Robins and Thomas[12], centred on 70° N. during December 1957, and in the southern hemisphere in July. The remarkable absence of P_c during the polar night noted in the International Geophysical Year literature[4,13] may be associated with this anomaly the origin of which is not understood.

The fact that P_c are found at night at both the equator and at the poles, and can have coherent phases over a thousand kilometres[14], suggests that they can extend simultaneously over the whole surface of the Earth, but with varying amplitude. If this is so, why are they so seldom seen at night in the middle latitudes ?

The simplest explanation appears to be that as the average summer month electron density is a maximum at about 20° latitude[15], the P_c field penetrates the local $N(h)$ minimum at the equator. The $N(h)$ diurnal variation is very large at the equator, and it controls the P_c-level. It does not appear to be necessary to postulate a P_c source which is highly dependent on latitude, although Kato and Watanabe's[2] expression for the outer atmospheric oscillation can have this property.

It is necessary, however, to postulate a source of P_c in the outer atmosphere which is stronger on the sunlit side of the Earth in order to explain the generally low level of night-time P_c. Scholte's study[16] of the propagation of hydromagnetic waves associated with giant pulsations concludes that energy from a rotational transverse disturbance is propagated along the magnetic field without attenuation, and hence is confined to the originating field lines. However, a part of the irrotational disturbance can act to build up a resonance along the magnetic field, and this part falls off inversely as the distance from the source of the disturbance. Thus energy from a localized source travelling with the Sun would be propagated weakly to the dark hemisphere. The amplitude of this 24-hr. component is much greater than the amplitude of the 8-hr. and 12-hr. 'shielding' components in middle latitudes. However, Figs. 1*a* and *b* show that they become comparable where the electron density exhibits particularly large diurnal variations, that is, at the equator and at the poles.

The present results do not exclude the possibility that localized hydromagnetic resonance in the upper F region is the source of some P_c disturbances, although the outer atmospheric source seems necessary to explain their large geographical extent. Local oscillations are necessary to explain the phase-changes and differences in wave-form sometimes observed over distances of a few kilometres[5,13,17]. One would expect them to be excited according to Lehnert's[1] theory.

The equivalent current system for a number of P_c calculated by Jacobs and Sinno[7] show the disturbance to be concentrated in the auroral zone. Such a picture would be consistent with P_c originating as a hydromagnetic resonance in the auroral F region, and being propagated through the F region to lower latitudes as an increasingly attenuated Alfvén wave. The occurrence of P_c at night on the equator rules out this type of propagation as attenuation would have occurred in the middle-latitude part of the path. Again, we are drawn to the outer atmospheric oscillation as the mechanism producing P_c.

Matsuchita[18] has shown that in general the electron density decreases during the main phase of a magnetic storm, although what happens to the total ionization is not yet clear. A decrease in ionospheric shielding would explain why P_c are generally of larger amplitude during such times, without postulating a change in their source energy. As Matsuchita's effect is dependent on latitude, further study of present data should clarify this point.

If the data of Figs. 1*a* and *b* are re-plotted on geomagnetic co-ordinates the similarity between P_c and $N(h)$ disappears. This suggests that the principal attenuation occurs in the lower ionosphere, where there is greater symmetry about the geographical equator. The damping of hydromagnetic waves in the ionosphere depends on the density of the neutral particles as well as on the charged particles. Thus the lower part of the ionosphere should be more effective as a shield than is suggested by its electron density alone. However, the diurnal variation of $N(h)$ is greater in the upper ionosphere. Further study of $N(h)$ data at different heights is required to clarify this very important question of symmetry.

If P_c were produced at the same heights as the S_q currents, one would expect them both to be governed by the ionospheric conductivity, and hence by the symmetry of the geomagnetic field. Thus, on the basis of the present data, I am led to discard the S_q current theory of Terada[19] and to accept a higher source for P_c.

The above arguments show that further documentation of the relationship between the occurrence of P_c and $N(h)$ (better, perhaps, the integrated density over the whole ionospheric column) may rule out one or more of the postulated sources of P_c. In particular, the study of the variations of the upper F region will help decide the question of how local oscillations occur.

The data on which Figs. 1*a* and *b* are based are rather scanty. The magnetic data are averaged from October 1957 to September 1958. The $N(h)$ data, although covering the same period, are derived only from ten International Quiet Days in each month, together with Regular World Days of the International Geophysical Year. Furthermore, the $N(h)$ curves pertain only to the 280-km. level because the ionosonde records are most complete for this height. Even so, a number of extrapolated values have been

used, especially in the late evening hours. Only four $N(h)$ stations are complete. The data from the South Pole are only for the month of September 1958[9]. Knecht's[10] values for f_oF_2 are also shown for comparison. They are averaged for the whole year.

There are large seasonal variations in both $N(h)$ and P_c occurrence. Miss Hutton's[6] P_c data from Legon show that in the summer the 12-hr. component is smaller than the 8-hr. component, although it is larger averaged over the whole year. Similarly the 1939 and 1944 $N(h)$ records from Huancayo show seasonal reversals. The ratios are shown in Table 1. There appear to be even larger changes from year to year, and for this reason care has been taken in this communication to compare data only from the same year.

Table 1. RATIOS OF 12-HR. TO 8-HR. COMPONENTS

$N(h)$	1939	June	1·9	March	0 71
	1944	June	1·6	March	0 59
P_c	1957	May–July	0 72		
	1957	October to			
	1958	December			1 8

I have not distinguished between P_c occurrence and P_c amplitude variation in this discussion, nor considered the effect of the U.T. component of their daily variation. Furthermore, the P_c data include a range of periods which several authors[4,5,13] would now treat as containing different classes of P_c.

Nevertheless the present data have indicated that P_c are less frequently observed when the electron density at 280 km. is high, providing a P_c source with 24-hr. periodicity is postulated.

This work was done at the Cavendish Laboratory, and the help of J. A. Ratcliffe, Dr. R. Knecht, Dr. J. O. Thomas, Miss A. Robbins and Mrs. S. Croom is gratefully acknowledged. It was supported by a grant from the Defence Research Board of Canada.

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REGENERATION OF INSULIN ACTIVITY FROM THE SEPARATED AND INACTIVE *A* AND *B* CHAINS

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IT is generally accepted that when insulin is split into its *A* and *B* chains by breaking the disulphide bonds, hormone activity is abolished[1]. Recent reports[2-4] have indicated, however, that preparations of the isolated chains may possess low levels of activity, but the possibility has not been excluded that traces of intact insulin might be responsible for the effects observed. A variable factor in this work has been in the mode of cleavage of the disulphide bonds. Nicol[2] used the performic acid method of Sanger (which converts the cystine sulphur into the stable sulphonic acid, cysteic acid) and found low activity in both chains. In contrast, Langdon[4] employed reductive cleavage followed by conversion of the resulting sulphydryl groups to phenylmercuric mercaptides. He found that the substituted chains were inactive, but the preparation of *B* chain developed hormonal activity on removal of the mercury compound with thiol. This suggested that the free sulphydryl form of the *B* chain carried the hormonal activity, and it was postulated that insulin might be converted to this form at its site of action.

The present work was started with the object of cleaving the disulphide bonds of insulin by a method which would give the two chains as stable derivatives, readily separable from each other and from unmodified insulin. These requirements were met by the sulphite method of Swan[5], which yields the *A* and *B* chains as S-sulphonates ($R.SSO_3^-$). These derivatives can be separated readily by ion-exchange chromatography and purified by paper ionophoresis. It was of interest, in the light of Langdon's report[4], to convert the S-sulpho chains into their free sulphydryl forms by treatment with excess thiol and to examine the products for insulin activity. Experiments have shown that the chains as the S-sulphonates are inactive, either separately or mixed, which rules out the possibility of the preparations being contaminated with intact insulin. When the S-sulphonates were separately incubated with excess thiol, cysteine or mercaptoethanol, to convert them to the sulphydryl forms, again no insulin activity was detected. However, incubation of a mixture of the two chains with excess thiol gave rise to definite insulin activity. Since this activity had an ionophoretic mobility similar to that of intact insulin and could be neutralized with a specific anti-insulin serum, it appears that a resynthesis of insulin from the separated chains had taken place.

Preparation of the A and B chains. Ox insulin (1 gm.) was dissolved in 20 ml. of a reagent containing 0·2 *M* sodium sulphite, 0·08 *M* cupric sulphate and 8·0 *M* urea, which had been adjusted to *p*H 10·2 with ammonia. As judged by ionophoresis, these conditions gave complete splitting within a few

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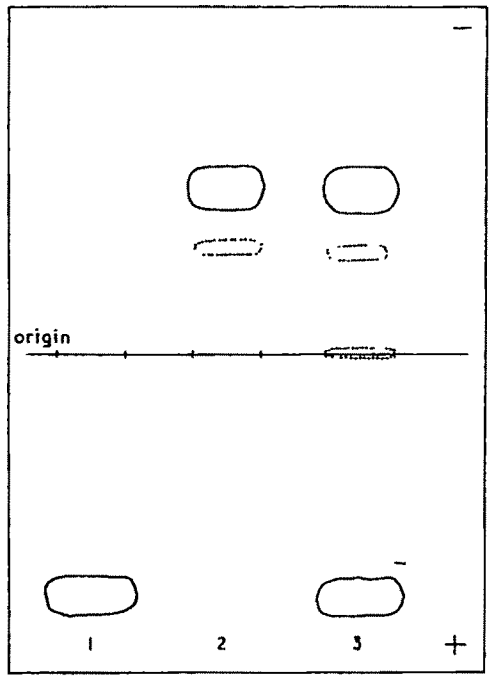

Fig. 1. Tracing of an ionophoretogram of S-sulpho *A* and *B* chains of insulin. The paper (Whatman No. 3) was wetted with a buffer consisting of 1 ml. of pyridine, 10 ml. acetic acid, 48 gm. urea and water to 100 ml. Ionophoresis was for 60 min. at 75 V./cm. in an apparatus cooled with 'Varsol *D.X*3641' (Imperial Oil, Canada). After drying the paper, the urea was washed out with 95 per cent ethanol. The components were stained by spraying with 1 per cent diazotized sulphanilic acid in 5 per cent sodium carbonate, when the *A* and *B* chains appeared as bright orange bands. 1, S-sulpho *A* chain; 2, S-sulpho *B* chain purified as described in the text; 3, impure S-sulpho *B* chain prepared by unmodified procedure of Mycek *et al.* (ref. 6). The minor component in 2 has been shown to be derived from S-sulpho *B* chain during elution with 1 *M* ammonia and is likely to be a desamido derivative produced by the alkaline *p*H

minutes. The solution was left at room temperature for 2½ hr., then acidified with formic acid to *p*H 3·2 and the mixture of chains precipitated by adding 10 volumes of 95 per cent ethanol. The chains were fractionated initially by the procedure of Mycek, Clark, Neidle and Waelsch[6]. However, when the preparations were examined by high-voltage ionophoresis on paper, it was found that although the *A* chain appeared pure, the *B* chain contained appreciable amounts of *A* chain (Fig. 1). The contamination of the *B* chain with *A* chain was thought to be due to adsorption of *A* chain on to the *B* chain which was insoluble in the formic acid solution used by Mycek *et al.* When the procedure was modified to include 8 *M* urea in the buffer[7], the *B* chain stayed in solution. Paper ionophoresis of *B* chain prepared in this way showed that it was free of *A* chain (Fig. 1). The modified procedure is as follows: 100 mgm. of the chain mixture was dissolved in 2·0 ml. of buffer solution containing 2 6 *M* formic acid and 8 *M* urea and applied to a 2·2 × 9 cm. column of 'Dowex-50*X*2' (200–400 mesh) in the H^+ form which had been equilibrated in the same buffer. The *A* chain, which was not retained by the column, was eluted and then precipitated, together with urea, by adding excess acetone. The urea was redissolved by adding a few drops of ethanol. The *A* chain flocculated on standing overnight. The *B* chain was eluted from the resin with 1 *M* ammonia in 8 *M* urea and appeared at the alkaline front, leaving the copper behind as a blue band at the top of the column. Urea was removed from the *B* chain solution by passage through a 'Sephadex *G*-50' column equilibrated with 1 *M* ammonia and the *B* chain was precipitated by acidification with formic acid.

Treatment of S-sulpho chains with thiols. *A* and *B* chain preparations were treated with thiol to remove the sulphonate and regenerate the free sulphydryl group as shown:

$$\text{Chain—S—SO}_3^- + R.\text{S}^- \rightleftharpoons \text{Chain—S—S—}R + \text{SO}_3^= \quad (1)$$

$$\text{Chain—S—S—}R + R.\text{S}^- \rightleftharpoons \text{Chain—S}^- + R\text{—S—S—}R \quad (2)$$

The reaction was carried out by making a 50 mgm./ml. solution of the chain preparation in a 0·02 *M* formate buffer, *p*H 3·5, containing 8 *M* urea, and transferring 0·02 ml. (1 mgm.) into a reducing system made up in freshly boiled water. The total volume was 1·0 ml., and the final concentrations were: chain preparation, *c.* 0 00033 *M*, *tris*, 0·025 *M* and an amount of thiol (0·0062 *M*) which was a 20-fold excess with regard to the molarity of the chain; the final *p*H was 8·5–9·0. After standing for 30 min. at room temperature the mixture was diluted into a balanced salts solution, 'medium *A*'[8], for biological testing. In biological tests under anaerobic conditions (see below) the medium *A* was gassed with nitrogen before the reduced chains were added to it.

Biological tests. The preparations were examined for insulin activity by the mouse convulsion test, using the rotating cylinder apparatus of Young and Lewis[9], and also by a sensitive *in vitro* procedure using mouse hemidiaphragms. The latter test, which is described fully elsewhere[8], is based on the ability of insulin to stimulate the synthesis of glycogen by muscle tissue incubated in a modified Gey and Gey medium. To test the sulphydryl forms of the chains it was desirable that anaerobic conditions be used, and advantage was therefore taken of the observation that pre-exposure of hemidiaphragms to insulin, at 0° under nitrogen, sensitized the tissues so that they exhibited an insulin effect when afterwards incubated under the usual aerobic conditions of the test. The pre-exposure was done by adding three hemidiaphragms to each reaction tube, which contained 5 ml. of test solution under nitrogen. After 15 min. the tissues were transferred to vessels containing 3 ml. of modified Gey and Gey medium which was gassed with 95 per cent oxygen + 5 per cent carbon dioxide. The tubes were incubated for 90 min. at 37°, when the tissues were taken out and each hemidiaphragm analysed for glycogen by an anthrone method[8]. With each batch of hemidiaphragms, usually 30 per batch, control tests were made to determine the basal level of glycogen synthesis during incubation and also the responsiveness of the tissues to different levels of insulin.

Activities of A and B chain preparations. In early experiments with chain preparations obtained by the unmodified procedure of Mycek *et al.*, it was shown that neither the S-sulpho *A* nor S-sulpho *B* chain possessed insulin activity. However, when the S-sulpho *B* chain was treated with a thiol, cysteine or mercaptoethanol, insulin activity appeared (Table 1). This seemed at first to confirm Langdon's report[4] that *B* chain in the sulphydryl form has insulin activity. But ionophoresis of the S-sulpho *B* chain preparation revealed that it contained appreciable quantities of S-sulpho *A* chain (Fig. 1), and when this

Table 1. ACTIVITY OF THE *A* AND *B* CHAINS OF INSULIN COMPARED WITH INTACT INSULIN IN A MOUSE HEMIDIAPHRAGM TEST

Preparation	Concentration of chain (μgm./ml.)	Insulin effect* ± *S.E.*	No. of hemidiaphragms
S-sulpho *A*	40	11 ± 5	6
S-sulpho *B* (crude†)	40	1 ± 4	12
S-sulpho *A* + thiol	40	10 ± 5	12
S-sulpho *B* (crude†) + thiol	40	61 ± 7	18
S-sulpho *B* (crude†) + thiol	10	21 ± 3	12
S-sulpho *B* (purified‡) + thiol	40	6 ± 5	12
S-sulpho *A* + *B* + thiol	40 + 40	82 ± 6	18
" " "	13 + 13	75 ± 10	6
" " "	4 + 4	46 ± 6	6
Insulin	0·4	74 ± 6	6
"	0·2	49 ± 5	18
"	0·04	23 ± 4	15
"	0·008	6 ± 4	12
Thiol control	—	4 ± 4	15

* Percentage increase in the amount of glycogen synthesized by the experimental tissues over that synthesized by the control tissues.
† Prepared by unmodified procedure of Mycek *et al.* (ref. 6).
‡ Prepared by modified procedure described in the text.

was removed by the method described, the S-sulpho *B* chain no longer showed activity in the presence of thiol (Table 1). Next, the significant observation was made that when S-sulpho *A* chain was added back to the purified S-sulpho *B* chain and the mixture treated with thiol, there was a reappearance of insulin activity in a yield of 1–2 per cent. These experiments were all made by the pre-exposure technique using anaerobic conditions although it was found later that the activity was still present when tested under aerobic conditions. These aerobic tests were made by diluting the chain mixture plus thiol into 'medium *A*' (1·0 ml.), oxygenating and adding 1 ml. 'medium *B*'[8] to complete the incubation mixture. Mouse hemidiaphragms were added, and, after gassing with 95 per cent oxygen + 5 per cent carbon dioxide, were incubated for 90 min. at 37° prior to glycogen analysis. In this test, as in the pre-incubation test, the yield of insulin activity from the chains was in the region of 1–2 per cent.

The *A* and *B* chain preparations were also tested by the mouse convulsion method and showed the same pattern of results, that is, no activity of the separated chains in either the S-sulpho or sulphydryl forms, but reappearance of activity (1–2 per cent yield) in a mixture of the S-sulpho chains plus thiol (Table 2).

Table 2. ACTIVITY OF THE *A* AND *B* CHAINS OF INSULIN COMPARED WITH INTACT INSULIN IN A MOUSE CONVULSION TEST

Preparation	Dose of chain per mouse (μgm.)	No. of mice convulsing / No. of mice injected
S-sulpho *A* + *B*	50 + 50	1/36
S-sulpho *A* + thiol	50	0/36
S-sulpho *B* + thiol	50	2/36
S-sulpho *A* + *B* + thiol	50 + 50	55/72
Insulin	1·6	56/72

Nature of the regenerated insulin activity. It seems probable that the regenerated insulin activity is due to the resynthesis of insulin itself from the separated chains. It was thought possible at one stage that the regenerated activity, observed after thiol treatment, might have come not from separated chains but from insulin molecules in which only one of the inter-chain bridges had been broken by the original sulphite treatment. However, this seems to be excluded by the finding that ionophoretically purified preparations of *A* and *B* chain remain inactive when they are treated with thiol separately, but develop activity when they are treated with thiol in a mixture. This finding would also appear to exclude activity being due to complexes such as *A*-*A*, *B*-*B*, *A*-mercaptoethanol or *B*-mercaptoethanol, although it is possible that each of these species is formed during the thiol treatment.

Evidence of a more direct nature that the regenerated activity in the reduction mixtures was due to insulin itself was obtained by ionophoretic and immunological tests. The ionophoresis was done in starch gels prepared with a buffer containing 8 *M* urea, 0·05 *M* formic acid and 0·01 *M* sodium hydroxide at *p*H 3·7 which was known to give good resolution of insulin (Smithies, O., personal communication). When a portion of the gel corresponding with a marker of bovine insulin was dialysed to remove urea and extracted with acid-alcohol, insulin activity was detected. Adjacent portions of the gel tested in this way were inactive.

The immunological tests were made with an anti-insulin serum prepared by immunizing guinea pigs with ox insulin in Freund's adjuvant, as described by Moloney and Coval[10]. The serum neutralized the hormone activity of ox and other mammalian insulins but not that of the codfish. The potency of the serum in a mouse hemidiaphragm test[8] was such that 1·0 ml. neutralized 600 milliunits (24 μgm.) of insulin. It will be seen from Fig. 2 that 0·06 ml. serum was required to neutralize the insulin activity present in a mixture of 40 μgm. each of S-sulpho

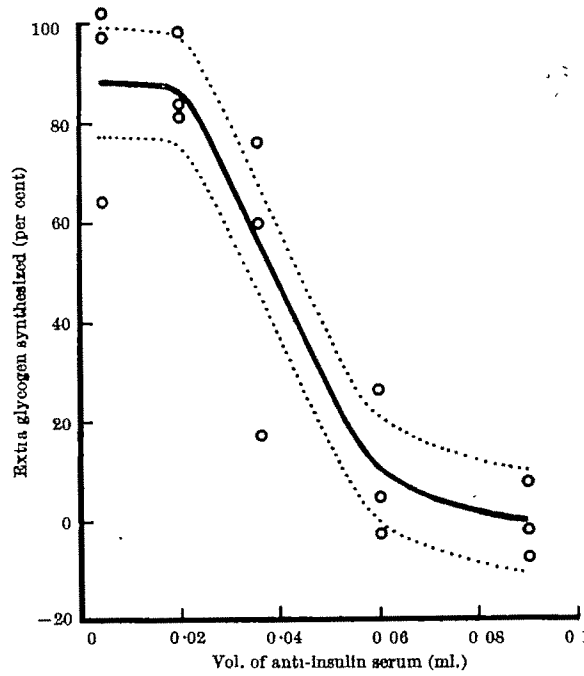

Fig. 2. Neutralization of reformed insulin activity by specific anti-insulin. The figure shows the relative amounts of glycogen, above the mean basal level, synthesized by individual hemidiaphragms incubated (in groups of three) in mixtures of increasing volumes of anti-insulin with constant aliquots of a solution containing 40 μgm. S-sulpho *A*, 40 μgm. S-sulpho *B* and mercaptoethanol. The dotted lines are at ± 1 *S.E.*

$A + B$ chains, treated with thiol and oxidized with air. This indicates that from the 80 μgm. of chain mixture 1·44 μgm. insulin was produced, which corresponds to a yield of 1·8 per cent. The fact that there is such close correspondence in the estimates of yield by hemidiaphragm tests with and without antiserum indicates that the resynthesized material has an immunological specificity indistinguishable from that of ox insulin. Had the immunological specificity of the molecule been changed, then larger quantities of antiserum would be required for neutralization (as is the case with codfish insulin[8]) and the estimates of yield given by tests with and without antiserum would differ. It is likely, therefore, that the resynthesized activity is due to a small amount of material, identical in its folded structure with insulin, rather than to a large amount of material of altered structure and lower activity.

Since resynthesis of insulin appears to occur in mixtures of separated chains, it is essential that before isolated chain preparations, particularly in the sulphydryl form, are tested for insulin activity, they be free from cross-contamination with the other chain. Preparations which met this criterion appeared to be without significant activity (<0·1 per cent of the same weight of insulin) at the levels tested (Table 1).

Mechanism of resynthesis. It was shown by starch-gel electrophoresis as described above that the isolated S-sulpho chains, on treatment with excess thiol, lost their negatively charged sulphonate groups and were converted quantitatively into more positively charged species which are interpreted as the sulphydryl forms (equations 1 and 2). One mechanism of disulphide bond formation would therefore be the recombination of the reduced chains in the presence of oxygen. An alternative mechanism of resynthesis could be the result of a displacement of a sulphonate group on one chain by the sulphydryl group on another :

$$\text{Chain—S}^- + {}^-\text{O}_3\text{S—S—Chain} \rightleftharpoons \text{Chain—S—S—Chain} + \text{SO}_3^{=} \qquad (3)$$

No final decision can be reached as to which mechanism of resynthesis is operating here, but in experiments carried out with anaerobic solutions, to minimize oxidation, the yield of insulin activity was the same as when the solutions were deliberately oxidized before testing. It must be realized, however, that even when the test solutions are anaerobic, the freshly dissected diaphragm possesses an undetermined content of oxygen. However, there is no evidence that the diaphragm exerts any specific catalytic influence on the resynthesis.

The yields of insulin obtained are not considered to be unduly low in view of the large number of possible molecular species which could be produced by random reformation of disulphide bonds in a system as complex as a mixture of A and B chains with thiol. Experiments are in progress to determine whether the disulphide bridges tend to reform in certain preferred orientations, as with ribonuclease[11], and whether recombination can be influenced so as to increase the yield of insulin. However, even with the present yield, it can be said that if chemically synthesized A and B chains were available in mgm. amounts it should be possible to obtain insulin by the above method and thereby provide the terminal step in the total synthesis of a protein with biological activity.

We wish to thank the Insulin Testing Department for the mouse convulsion tests.

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SEMICONDUCTIVITY IN PROTEINS AND HÆMOGLOBIN

Enhanced Semiconductivity in Protein Complexes

DRY proteins show a very high resistivity and energy-gap, typical values being $10^{16}\,\Omega$ cm. (20° C.) and 2·8 eV.[1,2]. Decreases in this resistivity value by a factor 10 have been achieved by H atom bombardment[3], following a suggestion to convert the protein into a free radical by chemical means[4]. We have now found that a very large effect may be achieved, following an analogy with the effect of chloranil in forming highly conducting complexes with donors such as dimethyl aniline[5,6] and phthalocyanine[7]. An aqueous solution of bovine plasma albumin was shaken with *p*-chloranil, the excess *p*-chloranil filtered off, and the solution evaporated to form a bovine plasma albumin–chloranil complex film. Such a film contained a very small amount of chloranil, approximately 0·5 per cent, corresponding to 3 chloranil molecules to 1 molecule of bovine plasma albumin. This plasma–chloranil film in the dry state had a room temperature resistivity of $3 \times 10^{12}\,\Omega$ cm. and energy gap of 1·06 eV., compared with values for a control dry film of bovine plasma albumin of $8 \times 10^{17}\,\Omega$ cm. (extrapolated) and 2·80 eV. Thus the chloranil has raised the specific conductivity of the protein by a factor 3×10^5. The bovine plasma albumin–chloranil complex showed a weak but definite electron resonance signal, with a g-value of 1·998 and a line-width of 6 gauss. There was no optical absorption or photoconductivity at a wave-length corresponding to the energy-gap of 1·06 eV. Bromanil and iodanil complexes gave very similar results. Admission of water vapour at a vapour pressure chosen to give approximately a Brunauer–Emmett–Teller monolayer over the (relatively small) available surface of the bovine plasma albumin–chloranil complex gave a twelve-fold increase in resistivity. This is in marked contrast to the effect of water vapour in decreasing the resistivity of pure dry proteins, including bovine plasma albumin.

These results may be explained on lines well known for inorganic semiconductors. The chloranil molecules are taken to accept electrons from the protein, creating positive holes in its conductivity band[8]. On the other hand, water is an electron donor, and by neutralizing positive holes lowers the conductivity of the bovine plasma albumin–chloranil complex. Ammonia gas shows a similar electron-donor behaviour to water, as would be expected. The twelve-fold increase in resistivity is consistent with a filling up of the positive holes (10^6 increase) followed by a donating of electrons into the conductivity band (10^5 decrease). It seems probable, therefore, that in the living cell proteins may show *N* (negative) or *P* (positive) behaviour, depending on their environment, whether aqueous or lipoidal, presence of electron acceptors, free radical sources, etc. It is possible that further work will show that such changes in conductivity may result in steady-state values sufficiently high to be significant for models of electron-transport[1], carcinogenesis[9] and other phenomena in the living cell.

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Semiconductivity in Hydrated Hæmoglobin

Hæmoglobin is regarded as a model for a large class of oxidation enzymes, where electron mobility may be of biological significance[10]. In the dry state its very low specific conductivity, about 10^{-16} Ω^{-1} cm.$^{-1}$ at 30° C., is attributed to electron and hole mobility[1] in the CO . . . . HN bridge system[8]. Water is adsorbed on natural, or methanol-denatured, hæmoglobin, corresponding to a Brunauer–Emmett–Teller '*BET* monolayer volume' V_m of 319 moles/10^5 gm. protein, whereas a close-packed monolayer of water molecules over all the molecular surfaces throughout the crystal would involve 1,160 moles/10^5 gm. protein[11]. The molecular dimensions for the latter calculation are taken from X-ray data[12] which also show that water molecules do not penetrate within the actual molecules, but only over the molecular surfaces. We have studied the effect of adsorbed water on the semiconductivity of a solid specimen of methanol-denatured hæmoglobin, allowing three days for equilibrium for each point. The result in Fig. 1 shows that there is a large increase in conductivity which reaches a constant value at about V_m. Thereafter, there is little change until a relative vapour pressure of about 0·9, corresponding to $4V_m$, when the conductivity increases sharply to about 10^{-8} Ω^{-1} cm.$^{-1}$ at 30° C.

Following the result of the previous communication it, is suggested that initially water molecules are held on special sites and donate electrons into the conductivity band of the protein molecule giving an '*N*-type (negative) protein', where a high mobility is expected throughout the crystal[8]. To accord with earlier suggestions[13], and the increase in conductivity, these sites may be CONH groups adjacent to polar side chains. This view differs from that of Baxter[14], who suggested that electrons tunnelled from one adsorbed water molecule to the next. As the physical surface becomes filled up around $4V_m$, we expect proton conduction to set in within the monolayer of adsorbed water, along lines suggested by Riehl[15]. Proton conduction, with 10^{-9} Ω^{-1} cm.$^{-1}$, has been

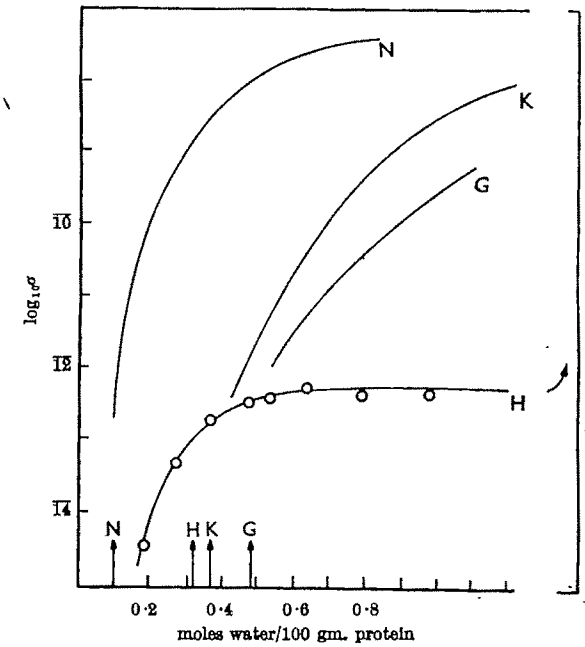

Fig. 1. Specific conductivity σ, Ω^{-1} cm.$^{-1}$ as a function of adsorbed water for nylon at 25° C. (*N*) (ref. 9), keratin at 25° C. (*K*) (ref. 9), gelatin at 32° C. (*G*) (ref. 11) and hæmoglobin (*H*) at 30° C. The arrows mark the values of the Brunauer–Emmett–Teller monolayer adsorption (refs. 11 and 17)

demonstrated for keratin with 15 per cent water[16], about $2{\cdot}5V_m$ [17] (see Fig. 1). Similar 'high' specific conductivities may be calculated for gelatine with $2{\cdot}5V_m$ adsorbed water[18]. It may be that the relatively marked effect of water on the conductivity of these two fibrous proteins, and its even more marked effect on nylon[16,19] point to the operation of yet a third effect due to adsorbed water on flexible chain molecules containing CONH groups, that is, the plasticizing effect of water molecules on chain movement, facilitating transfer of protons between NH and CO groups in different chains, first described by Baker and Yager[19].

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EVIDENCE FOR THE INVOLVEMENT OF A TRYPTOPHAN RESIDUE IN THE REACTION OF DI*ISO*PROPYLPHOSPHOROFLUORIDATE WITH α-CHYMOTRYPSIN

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THE inhibition of chymotrypsin by di*iso*propylphosphorofluoridate was first reported by Jansen, Nutting, Jang and Balls[1]. In this stoichiometric reaction[2,3] an aliphatic hydroxyl group of a serine residue in the active centre of chymotrypsin is implicated[4]. Evidence is presented in this communication which indicates that a tryptophan residue is also involved in the reaction of di*iso*propylphosphorofluoridate with α-chymotrypsin.

The difference spectrum of di*iso*propylphosphoryl-α-chymotrypsin versus α-chymotrypsin (three times crystallized α-chymotrypsin, Worthington Biochemicals, Freehold, New Jersey) at *p*H 6·7 is illustrated in Fig. 1*a*. Identical solutions of α-chymotrypsin are added to the sample cell and to the reference cell of a Cary model 14 self-recording spectrophotometer. Approximately three times the stoichiometric amount of di*iso*propylphosphorofluoridate in dilute *iso*propanol is added directly to the sample cell while an equivalent aliquot of dilute *iso*propanol is added to the reference cell. The solutions are scanned 3 min. after addition of di*iso*propylphosphorofluoridate and at intervals up to 30 min. later. No spectral changes are observed on standing, indicating that the reaction is complete in 3 min. at this *p*H, and that the spectral change is due to the addition of di*iso*propylphosphorofluoridate and not to any progressive change of the control solution due to autolysis.

Nitrogen[5] and phosphorus[6] determinations on exhaustively dialysed samples of di*iso*propylphosphoryl α-chymotrypsin prepared using 3 and 10 times the stoichiometric amount of di*iso*propylphosphorofluoridate showed a phosphorus content of 1·16 moles per mole of enzyme, based on a molecular weight of 25,000 and a nitrogen content of 16·5 per cent. This is in good agreement with the previously reported value[2].

The difference spectrum of di*iso*propylphosphoryl-α-chymotrypsin versus α-chymotrypsin appears to be due to the specific reaction of an acylating agent with the active site of the enzyme. When α-chymotrypsin denatured by 8 *M* urea or α-chymotrypsinogen are treated with a ten-fold excess of di*iso*propylphosphorofluoridate, and these samples are scanned versus their respective control sample, difference spectra are not observed. The difference spectrum of di*iso*propylphosphoryl-α-chymotrypsin versus α-chymotrypsin is essentially the same as the difference spectrum of one of the monoacetyl-α-chymotrypsins[7] versus α-chymotrypsin (Fig. 1*b*). Above *p*H 6·0, where monoacetyl-α-chymotrypsin deacylates, the difference spectrum disappears with time. The rate of change of ΔD 290 appears to follow the known rate of deacylation of monoacetyl-α-chymotrypsin at the same *p*H and temperature.

A series of experiments were carried out in order to differentiate between various types of interactions which could result in the appearance of the difference spectrum of di*iso*propylphosphoryl-α-chymotrypsin versus α-chymotrypsin. (1) The relationship between ΔD 290 and concentration of di*iso*propylphosphoryl-α-chymotrypsin follows Beer's law up to a concentration of 1·15 mgm. of di*iso*propylphosphoryl-α-chymotrypsin per ml. (Enzyme concentrations were determined spectrophotometrically at 280 mμ using E(280, 1 per cent) = 20·0 to relate extinction to enzyme concentration[8].) (2) The difference spectrum is stable over the *p*H range 1–11, both in water and in 8 *M* urea. Large changes in ionic strength do not

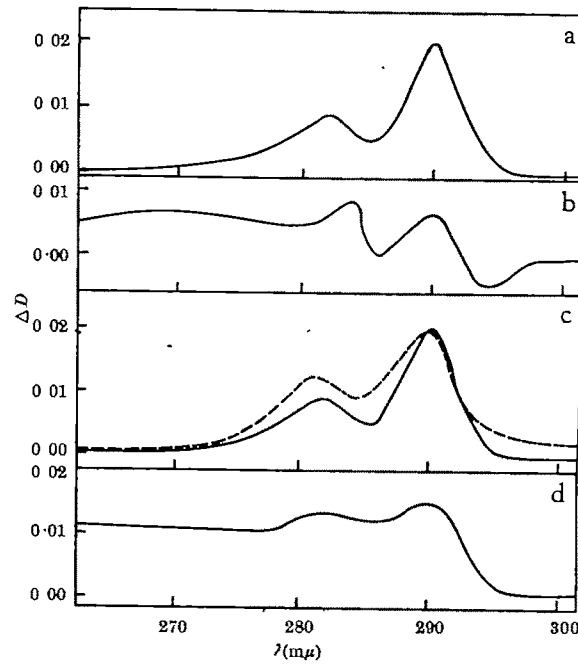

Fig. 1. Ultra-violet difference spectra. *a*, Di*iso*propylphosphoryl-α-chymotrypsin versus α-chymotrypsin, enzyme concentration ≈ 3 6 × 10^{-5} *M*, *p*H 6·7, 0·033 *M tris* hydrochloric acid, 0·033 *M* calcium chloride, 1 1 × 10^{-4} *M* di*iso*propylphosphorofluoridate, 25° C.; *b*, monoacetyl-α-chymotrypsin versus deacylated control, enzyme concentration ≈ 2 4 × 10^{-5} *M*, *p*H 6·7, 0·033 *M tris* hydrochloric acid, 0 033 *M* calcium chloride, 25° C. Spectrum obtained 6 sec. after adjusting *p*H of monoacetyl-α-chymotrypsin solution to 6 7; *c*, effect of ionic strength on difference spectrum of di*iso*propylphosphoryl-α-chymotrypsin versus α-chymotrypsin, enzyme concentration ≈ 3 6 × 10^{-5} *M*, 25° C. The enzyme samples were dialysed at 4° C. for 72 hr. against several changes of de-ionized water. The ionic strength was adjusted by addition of sodium chloride. ———, μ = 0·5 *M*; – – –, μ = 6 × 10^{-4} *M*; *d*, di*iso*propylphosphoryl-α-chymotrypsin versus α-chymotrypsin in 8 *M* urea, enzyme concentration ≈ 3 6 × 10^{-5} *M*, *p*H 7 0, μ = 0 2 *M*, 25° C.

appreciably affect either the magnitude or the position of the principal peak of the difference spectrum at 290 mμ (Fig. 1c). (3) The difference spectrum of di*iso*propylphosphoryl-α-chymotrypsin versus α-chymotrypsin persists after denaturation of the enzymes in 8 *M* urea at *p*H 7·0 for 48 hr. at 37° (Fig. 1*d*). It has been demonstrated[9], using optical rotation as criterion, that both chymotrypsin and chymotrypsinogen are completely denatured in 7 *M* urea at 0° C. after 2½ hr. Di*iso*propylphosphoryl-α-chymotrypsin is more rapidly denatured in urea than chymotrypsinogen[10].

The data presented so far suggest that the spectral shift responsible for the 290-mμ peak is not due to some form of intermolecular interaction, intramolecular hydrogen bonding, a simple dipole–dipole interaction, a change in dielectric constant of the medium surrounding the chromophore, or a charge effect.

The findings are consistent with a strong interaction involving either a tyrosine or a tryptophan residue in di*iso*propylphosphoryl-α-chymotrypsin, since both these residues absorb strongly in the 280–300 mμ region. In order to differentiate between these two amino-acid residues, advantage is taken of differences in their spectral behaviour at high *p*H. The characteristic 282 mμ absorption peak of tryptophyl residues in proteins undergoes only slight shifts with changes in *p*H (ref. 11). The absorption maximum of unionized tyrosyl residues in proteins is approximately at 278 mμ, of ionized tyrosyl residues at 295 mμ. The observable increase in optical density at approximately 295 mμ with ionization of tyrosyl groups makes possible a spectrophotometric titration of these groups[12]. Thus abnormalities in the behaviour of tyrosyl groups in proteins due to interaction with other groups are detectable. To determine whether a tyrosyl group ionizes differently at any *p*H in di*iso*propylphosphoryl-α-chymotrypsin than in α-chymotrypsin, pairs of samples are compared in both aqueous buffer and in 8 *M* urea at *p*H's between 7 and 13.

Table 1. ΔD 295, DI*iso*PROPYLPHOSPHORYL-α-CHYMOTRYPSIN VERSUS α-CHYMOTRYPSIN

Enzyme concentration, 3.6×10^{-5} *M*, $\mu = 0.2$ *M*, 23°. A Beckman model *G* *p*H meter was used for *p*H determinations

8 *M* urea		Aqueous	
*p*H	ΔD 295	*p*H	ΔD 295
7.4	+0.002	7.2	+0.001
7.8	0.000	7.9	0.000
9.8	+0.010	9.3	0.000
9.8	−0.006	9.8	+0.018
12.3	+0.004	11.8	+0.005
13	+0.002	12.6	+0.003

As can be seen from Table 1, there is no significant difference between di*iso*propylphosphoryl-α-chymotrypsin and α-chymotrypsin in the ionization behaviour of tyrosine residues. The data suggest that a tryptophan and not a tyrosine residue is modified in di*iso*propylphosphoryl-α-chymotrypsin.

This suggestion is supported by studies of the reaction of N-bromosuccinimide with di*iso*propylphosphoryl-α-chymotrypsin and α-chymotrypsin. According to previous reports the reaction conditions used in these experiments lead to the selective oxidation of the tryptophan residues to the corresponding oxindole[13]. The reaction was carried out in 8 *M* urea after the enzymes were allowed to stand in 9 *M* urea for 24 hr. Under these conditions all tryptophan residues should be equally reactive. It was found, however, that oxidation of tryptophans

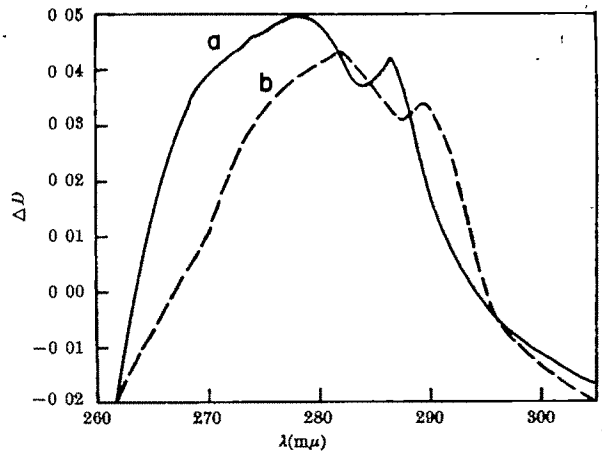

Fig. 2. Ultra-violet difference spectra in 8 *M* urea following reaction of enzyme preparation with N-bromosuccinimide. Enzyme concentration $\approx 3.6 \times 10^{-5}$ *M*, *p*H 4.0, 0.07 *M* sodium acetate buffer, 25° C. The sample cell contains an enzyme preparation in which 4·0 moles of tryptophan residues were oxidized by N-bromosuccinimide per mole of enzyme; the reference cell contains an enzyme preparation in which 4·5 moles of tryptophan residues were oxidized per mole of enzyme. Curve *a*, di*iso*propylphosphoryl-α-chymotrypsin versus α-chymotrypsin; curve *b*, α-chymotrypsin versus α-chymotrypsin

by N-bromosuccinimide occurs less readily in di*iso*propylphosphoryl-α-chymotrypsin than in α-chymotrypsin. Addition of the same amount of N-bromosuccinimide to identical solutions of α-chymotrypsin and di*iso*propylphosphoryl-α-chymotrypsin leads to the oxidation of 4·5 ± 0·1 residues in α-chymotrypsin and only 4.0 ± 0.1 residues in di*iso*propylphosphoryl-α-chymotrypsin. The difference spectra of N-bromosuccinimide-treated di*iso*propylphosphoryl-α-chymotrypsin versus N-bromosuccinimide-treated α-chymotrypsin, and N-bromosuccinimide-treated α-chymotrypsin versus N-bromosuccinimide-treated α-chymotrypsin are illustrated in Fig. 2. The sample cell contains di*iso*propylphosphoryl-α-chymotrypsin or α-chymotrypsin in which 4·0 moles of tryptophan are oxidized per mole of enzyme; the reference cell contains α-chymotrypsin in which 4·5 moles of tryptophan are oxidized per mole of enzyme. In both cases the difference spectra correspond closely in shape to an absolute spectrum of tryptophan, but they differ both in position and in the relative intensities of the absorption peaks. The data indicate that the reaction of N-bromosuccinimide with di*iso*propylphosphoryl-α-chymotrypsin leads to the accumulation of a reaction product which is not found in the reaction of N-bromosuccinimide with α-chymotrypsin.

The results presented suggest that the 290 mμ absorption peak observed in the difference spectra of monoacetyl-α-chymotrypsin versus α-chymotrypsin, and di*iso*propylphosphoryl-α-chymotrypsin versus α-chymotrypsin, is intimately associated with the specific acylation of the active site of α-chymotrypsin. Since these difference spectra seem identical, it appears that their origin is probably not due to a direct interaction with these substituents, but due to a reversible rearrangement of the active site of the enzyme. The results support the view that this rearrangement involves a strong interaction, resembling a covalent bond, with a tryptophan residue in the enzyme.

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DETECTION IN INVERTEBRATES OF INDUCIBLE, REACTIVE MATERIALS RESEMBLING ANTIBODY

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THOSE reactive substances that are produced by vertebrates in response to foreign materials, and to which the term 'antibody' is generally applied, constitute a collection of proteins of somewhat varied properties. The outstanding common characteristic of these proteins is their reaction with the inducing antigen, although the occurrence of this reaction may be manifested in a number of different ways. Apart from assay methods which involve biological response, for example, toxin neutralization, sensitization, etc., quantitative detection is generally dependent on either the production of a change in state of one or both of the reactants, such as precipitation and agglutination, or the consumption of a third measurable component by the antigen antibody reaction as in complement fixation.

The choice of a method of detection for studies on invertebrates might therefore be made from any of the above procedures. However, there are certain difficulties inherent in each of these approaches. Deviations in behaviour sufficient to be scored as biological responses are not readily judged in such animals as sea anemones. Precipitation and agglutination may be dependent on rather unpredictable conditions in the reaction mixture, for example, the concentration of electrolyte or protein. There is variation in the ability of antibodies from various animals to fix complements of heterologous species.

The methods described here were developed in an attempt to circumvent some of these difficulties. These procedures allow the rapid detection of antibody formation in a variety of invertebrates. In essence, we aim at the detection of any combination between induced substances in the invertebrate and the inducing agent. Such combination is detected through the use of a standardized rabbit antiserum prepared against the inducing antigen. Measured amounts of rabbit antiserum and antigen are added to invertebrate preparations. Any deviation from the expected amount of precipitate due to the combination of rabbit antibody and antigen is taken as presumptive evidence of a combining substance present in the extract of the invertebrate. Further evidence is obtained by demonstrating a relationship between the injection of antigen into the animal and the subsequent increase in activity of extracts. Finally, a certain degree of specificity must be demonstrated by showing a difference in the effect of the invertebrate extracts on a precipitating system in which a different antigen and rabbit antibody are used.

Investigations on the anemone, *Anthopleura elegantissima*, are reported here. Individual animals were given an injection of 1 mgm. of Armour bovine serum albumin fraction V, contained in 0·1 ml. of artificial sea water[1]. In each case an attempt was made to introduce the antigen into the mesoglœa, but success or failure was difficult to judge. Most of the animals were placed in a 30-gallon aquarium in which sea water was maintained at 13° C. At the same time, six anemones were placed in small, individual jars containing 50 ml. of artificial sea water and maintained at the same temperature. Since cœlenterates are nonvascular animals, extracts were prepared from the whole animals as follows: 5 anemones were removed from the aquarium at desired intervals of time and individually macerated in a Waring blender with artificial sea water containing 1/10,000 merthiolate. The volume of sea water employed was 100 ml., including the volume of the anemone. The water from the six small jars containing individual anemones was collected after the same time intervals and replaced by fresh artificial sea water. The extracts and sea water samples were centrifuged at 15,000 r.p.m. in a high-speed 'Serval' for half an hour at 5° C., and the supernatant filtered through Whatman No. 1 filter paper. The filtrate was then tested for antibody activity.

Two methods of testing for activity have been employed. The scheme of the first is shown in Table 1. Each of the mixtures was set up in duplicate. Incubation was at 5° C. for 24 hr. The mixtures were then centrifuged at 5° C. for 15 min. at 2,000 r.p.m., and the precipitates washed twice with artificial sea water at 5° C. The precipitates were dissolved in 0·1 *N* sodium hydroxide and the amount of protein measured by the Lowry method[2], using a calibration curve prepared using bovine serum albumin. The method gave a reproducibility of ±0·008 mgm. protein.

The second test method involved a similar scheme with the use of 2·0 ml. of test material and one-half the amounts of bovine serum albumin and rabbit

Table 1

Mixture	Test material*	Bovine serum albumin	Rabbit anti-bovine serum albumin diluted 1/5	Rabbit normal serum diluted 1/5	Artificial sea water
	ml.		ml.	ml.	ml.
1		0 5 ml. (0·0155 mgm.)	0·5		4·0
2		0·5 ml. (0·0155 mgm.)			4 5
3			0 5		4·5
4				0·5	4·5
5	4·0			0·5	0 5
6	4 0				1·0
7	4·0	0·5 ml. (0 0031 mgm.)			0·5
8	4·0		0·5		0·5
9	4·0	0 5 ml. (0 0155 mgm.)	0·5		

* Sea anemone extract or ambient sea water from injected anemones.

anti-bovine serum albumin in a total volume of 3·0 ml. The reactants were placed in 10 mm. cuvettes in the Beckman *D.U.* spectrophotometer, and the turbidity was measured at intervals for 65 min. at a wave-length of 340 mμ using a slit-width of 0·218 mm. and a blank containing rabbit antiserum and artificial sea water. Temperature was maintained at 25° C. The method of measurement is essentially the same as that employed by Najjar *et al.*[8]. The optical density is observed to increase sharply during the first 30 min. of observation. By 60 min. the optical density becomes quite constant and there is only a small increase in the following 30 min.

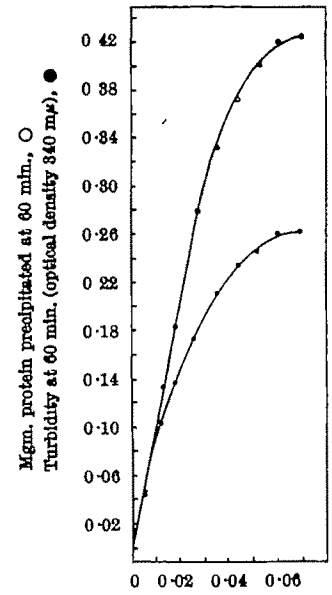
Extracts which tended to darken on standing could be cleared by treatment with 'Nuchar *C*–190–*N*' activated charcoal (Industrial Chemical Sales Division, West Virginia Pulp Paper Co.). The treatment with 'Nuchar' could not be used prior to the determination of residual bovine serum albumin as this protein is adsorbed during the removal of the interfering brown pigment. No detectable change in the antibody-like activity was produced by the use of the small amounts of 'Nuchar' employed.

In both test methods, the results were evaluated by comparison with a standard curve prepared using rabbit antiserum and bovine serum albumin diluted with artificial sea water. The relationship between the two methods of measurement is shown in Fig. 1.

The levels of bovine serum albumin and anti-bovine serum albumin used in all tests lie in the region of great excess of antibody. The reproducibility of the turbidimetric method was found to be within 0·004 optical density. It was observed that the values obtained by either method of measurement could be evaluated in terms of the other. The use of both methods of assay allows observation of the course of the reaction and a check of the final result.

Mixtures 1–4 acted as controls of the rabbit precipitating-system and were included in each group of tests. No significant difference in the blank values, mixtures 5 and 6, was observed in any experiment. These two mixtures acted as controls of the anemone extract. There was no indication of precipitation in mixture 7, demonstrating a lack of anemone antibody capable of precipitation under the conditions of the tests.

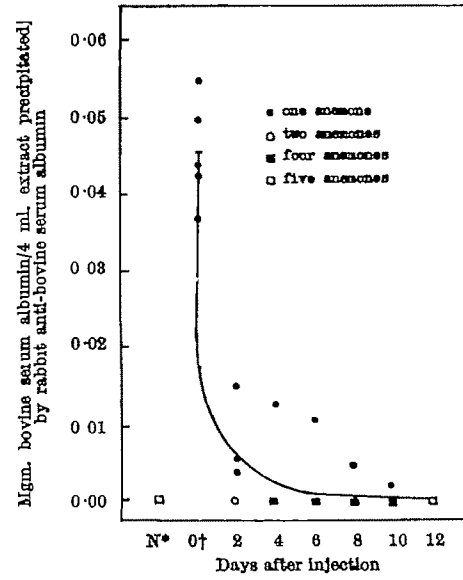
The precipitate in mixture 8 represented residual bovine serum albumin from the injection. The disappearance of injected bovine serum albumin from the animal, as indicated by the tests of the extracts,



Mgm. bovine serum albumin added to 0·5 ml. of rabbit anti-bovine serum albumin diluted 1/5

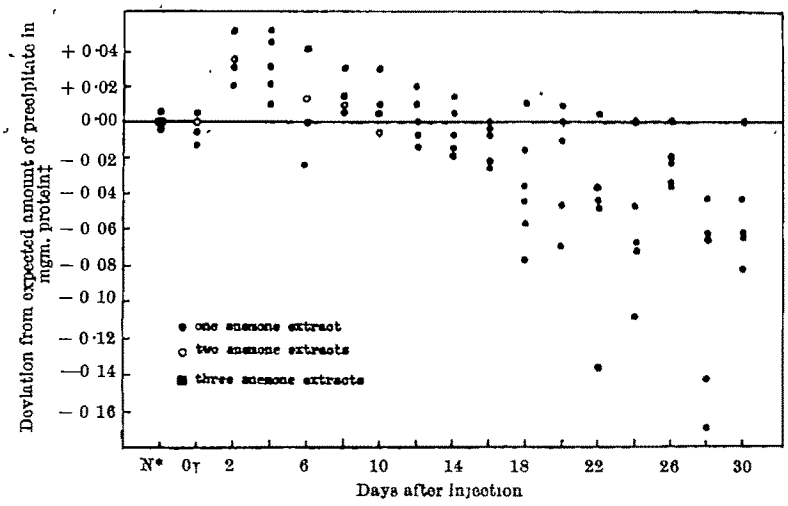
Fig. 1

follows the course indicated in Fig. 2, which includes a plot of the average amount of residual bovine serum albumin per 4 ml. of extract. From day 12 onwards, the amount of bovine serum albumin remaining was below the level of detection in all anemones. (The level of detection was 2 μgm. bovine serum albumin.) In no case was bovine serum albumin detected in the sea water surrounding injected anemones. If leakage of this antigen from the animals were responsible for the observed decrease, the albumin released would have been detected, because it would have been contained in half the volume used for preparation of the extracts. It may there-



* Normal anemones not injected with bovine serum albumin.
† Anemones immediately after injection of bovine serum albumin.

Fig. 2



* Normal anemones not injected with bovine serum albumin.
† Anemones immediately after injection of bovine serum albumin.
‡ All negative deviations have been corrected to deviation per 5 mgm. of extract protein.

Fig. 3

fore be concluded that the disappearance of the bulk of the injected antigen represents breakdown within the anemone rather than excretion. Examination of extracts over a period of time indicated that there was no destruction of bovine serum albumin due to proteolytic enzymes once the extract was prepared. Since observations on intracellular digestion in coelenterates indicate a distinctly acid condition in vacuoles containing materials undergoing hydrolysis, the observed absence of breakdown may be due to the somewhat alkaline reaction of the extracts due to the use of sea water as extractant[4].

Fig. 3 shows the deviations from the amount of precipitate expected in mixture 9 observed with extracts prepared from anemones. The expected amount of precipitate varied between 0·11 and 0·13 mgm. of protein, depending on the lot of rabbit antibody and bovine serum albumin used.

All deviations have been corrected for residual bovine serum albumin due to the injection. Since the anemones varied in volume from 2 to 20 ml., the negative deviations have been adjusted to give values per 5 mgm. of extract protein. The positive deviations could not be adjusted in a similar manner for reasons that will be discussed below. The maximum deviations actually measured were +0·05 and −0·128 mgm. protein.

Twenty-four hr. after the injection of bovine serum albumin, extracts appeared to add protein to the rabbit antibody-antigen precipitate. This additive effect gradually disappeared and was replaced by an inhibitory one. At about the eighteenth day after injection, strongly inhibitory extracts were found. Most of the extracts prepared from anemones throughout the remainder of the period of observation showed negative deviations. In an attempt to find a quantitative relationship between the kind of deviation produced and the concentration of anemone material, various dilutions of a strongly inhibitory extract were tested using a constant amount of bovine serum albumin and rabbit antibody. There was a decrease in the negative deviation by 0·0055 mgm. protein for each two-fold decrease in concentration of the anemone material, until the extract had been diluted to the point where the addition of protein could be observed. The additive effect disappeared on further dilution. Therefore, it appears that the inhibitory substance in anemone extracts is the same substance that is responsible for the positive deviations observed in anemones harvested soon after the injection of bovine serum albumin. The observed relationship between concentration of extract and magnitude of deviation was used in adjusting the negative deviations shown in Fig. 3.

The course of antibody synthesis as indicated by the examination of groups of anemones at intervals of time after the immunizing dose could be duplicated by testing one anemone repeatedly. Before injection, a small piece of tissue was cut from an anemone using a 5 mm. cork borer, and the antibody was extracted in the following manner. The tissue was ground in a chilled 12-ml. conical glass centrifuge tube using an etched glass stirring rod. Lipid and pigments were extracted, using a mixture of 3 parts of 95 per cent ethanol and 1 part of distilled water, previously chilled to −5° C. Two 12-ml. volumes of the ethanol solution were employed and the sediment collected by centrifugation at 2,000 r.p.m. for 5 min. after each extraction. The sediment was washed twice with chilled distilled water, allowed to drain thoroughly and finally extracted with 6 ml. of artificial sea water containing merthiolate. No activity could be observed when the extract from a non-immunized anemone was tested using the bovine serum albumin precipitating system. Bovine serum albumin was injected as described above. At daily intervals, pieces of tissue were removed and extracted. The consecutive extracts revealed again the additive and inhibitory effects described above; inhibitory extracts also showed the additive behaviour on dilution.

The specificity of the anemone material has been examined by the use of a precipitating system consisting of human serum albumin and rabbit anti-human serum albumin. Extracts from anemones immunized with bovine serum albumin did not affect the human serum albumin precipitating system. Extracts from anemones similarly immunized with human serum albumin produce no deviation of the bovine serum albumin precipitating system, but show additive and inhibitory effects when tested with the human serum albumin system.

In summary, there are indications that an inducible reactive substance may be elicited in anemones. This substance appears to have a degree of specificity comparable to rabbit antibody. The additive property of anemone antibody shows some interesting characteristics which are now being investigated.

This work has been supported by grants from the U.S. Public Health Service and the National Science Foundation.

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LETTERS TO THE EDITORS

RADIOPHYSICS

New Limits to the Diameters of Some Radio Sources

THE investigations at Jodrell Bank of the angular diameters of extra-terrestrial radio sources have now reached the stage where interferometric observations are being made with a base-line of 32,000 wave-lengths. The interferometer operates at a wave-length of 1·89 m., and uses the 250-ft. steerable paraboloid in conjunction with auxiliary aerials which are now placed about 40 miles to the west of Jodrell Bank near the Welsh coast. This is the longest base-line to be used so far for the observation of radio sources, and it is possible with this instrument to set new limits to the diameter of some radio sources which are significantly smaller than those previously reported[1].

A preliminary experiment is being carried out to investigate the fringe visibility of those sources which produced a measurable fringe when observed at the last base-line used, which was 9,700 wave-lengths. So far, 91 sources have been studied, and of these 38 have produced a measurable fringe. These sources lie in the area between right ascensions 16 hr. and 6 hr., and between declinations 58° and −21°; they have flux densities in the range $8{\cdot}5$–85×10^{-26} W.m.$^{-2}$ (c./s.)$^{-1}$. Each source has been observed at least twice and Fig. 1 is a facsimile of one of the records of the transit of source 3*C* 147 (*R.A.* 05h. 38m., Dec. 49° 51′, flux density 63×10^{-26} W.m.$^{-2}$ (c./s.)$^{-1}$).

As this is the longest base-line so far used there is no standard radio source of known diameter which can be used to calibrate the observations. The calibration must therefore rely on absolute measurements of fringe amplitude or comparisons with previous observations of the signal to noise ratio of the intense sources. Fig. 2 is a histogram of the results for the 38 sources which produced a measurable fringe. The abscissa is the ratio of the observed fringe amplitude on the recorder chart, corrected only for the polar diagram of the auxiliary aerial, to the flux density listed in the 3*C* catalogue[2]. This is an arbitrary scale dependent on the gain setting and sensitivity of the interferometer, but it is proportional to fringe visibility. A scale of absolute fringe visibility has been estimated from a comparison of the signal to noise ratio observed for three intense sources (3*C* 48, 147 and 459) with that observed at shorter base-lines, and this has been used to set limits to the diameters of the sources. The lower scale on Fig. 2 shows the estimated upper limits to the source diameters. It has been assumed that the sources are simple circular disks with a gaussian distribution of surface brightness; the scale shows the diameters between the points of half-brightness.

These observations will, of course, be affected by confusion and noise. However, the effective solid angle in which confusing sources can be observed is limited by various factors to less than half a square degree. It is estimated that, with this very small area, the error in fringe amplitude due to confusing sources (even if the confusing sources are unresolved) should not exceed 2×10^{-26} W.m.$^{-2}$ (c./s.)$^{-1}$ in 90 per cent of these observations.

These preliminary observations show that out of 91 sources at least seven have major features smaller than 3 seconds of arc, and that these sources have an extremely high surface brightness which is comparable with that of the intense radio source in Cygnus, I.A.U. 19*N*4*A*. The source I.A.U. 14*N*5*A* has recently been identified[3] with an object having a recessional velocity approaching half the speed of light. The

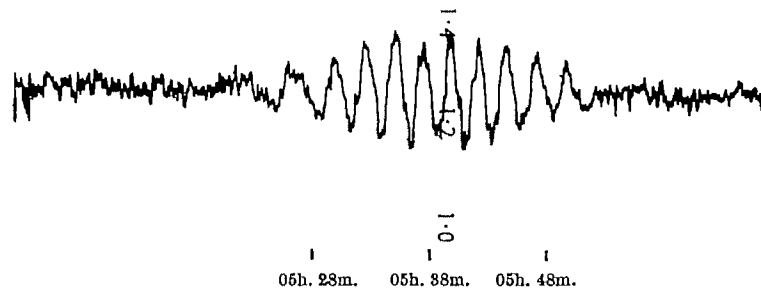

Fig. 1. Record of the transit of the source at *R.A.* 05h. 38m. obtained on September 19, 1960

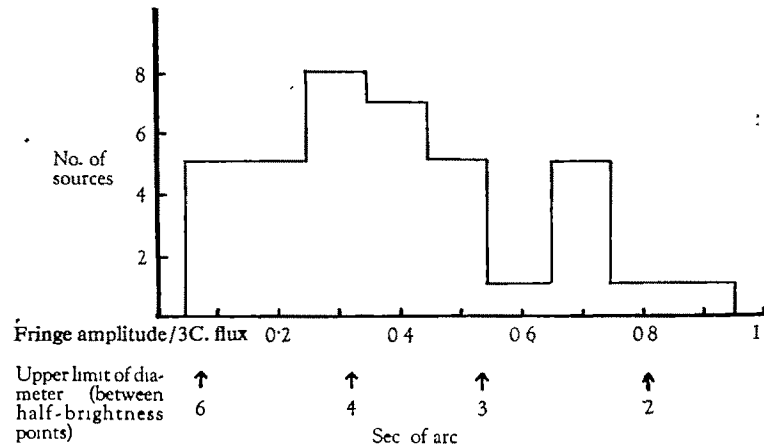

Fig. 2. Histogram of the normalized fringe amplitudes for the 38 sources which produced measurable fringes at 32,000 wave-lengths resolution. The scale of diameters has been estimated from a comparison of signal to noise ratio at this and shorter base-lines

diameter of this radio source has been estimated, from observations at 9,700 and 32,000 wave-lengths, as $4\frac{1}{2}$ sec. of arc in position angle 090°. This identification supports the view that these sources of small angular diameter and high surface temperature comparable to that of Cygnus *A* are objects at such great distances that cosmological effects should be significant.

It has been pointed out by Hoyle[4] and by Davidson[5] that there is a theoretical lower limit to the observable diameter of a radio source which is dependent on the particular cosmology considered. They have shown that, for sources similar to Cygnus *A*, this lower limit is 4 sec. of arc for a steady-state universe and 15 sec. of arc for an Einstein–de Sitter universe. The results in Fig. 2 show that a significant fraction of radio sources have an angular size less than the values predicted for either a steady state or an Einstein–de Sitter universe, but in making this comparison it must be remembered that the source Cygnus *A* is asymmetrical[6,7] with a ratio of major to minor axes greater than 4. All the measurements reported here refer to position angle 090°, and do not take account of any asymmetry in the sources.

We wish to thank Prof. A. C. B. Lovell for making available the facilities of Jodrell Bank, and both him and Prof. R. Hanbury Brown for their continued interest and advice during the course of this work. One of us (B. R.) is indebted to the Leverhulme Trust for a research fellowship.

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Propagation of Whistlers to Polar Latitudes

WITHIN the past three years, whistlers have been heard consistently at a number of stations located on the polar side of the auroral zones. Certain characteristics of polar whistlers have been reported by Martin[1] for Scott Base (geomagnetic latitude 79·3° S.), by Ungstrup[2] for Godhavn (79·8° N.) and by Helliwell *et al.*[3] for Byrd Station (70·6° S.). In each case similarities to whistlers received at lower latitudes are noted, which lend support to Martin's suggestion that polar whistlers originate in lower latitudes and are then propagated into the polar regions by reflexion between the Earth and the lower ionosphere. The purpose of this communication is to describe observations showing that lightning sources in middle latitudes can give rise to whistlers heard at polar latitudes.

Simultaneous observations of whistlers have been made regularly since June 1958 at Scott Base, Ross Dependency, Antarctica, and at Dunedin and Wellington, New Zealand, situated 3,600 km. and 4,100 km. north of Scott Base, respectively. The geomagnetic latitudes of Dunedin and Wellington are 50·8° S. and 45·4° S. respectively. The times of occurrence of whistlers at these stations are normally reported to the nearest second.

A statistically significant association has been found between the occurrence of whistlers at Scott Base and of those reported from the stations in New Zealand For example, for the first six months of 1960, during a total of 941 two-minute recording periods, 2,946 whistlers were heard at Wellington, while 1,548 were heard at Scott Base. Of these, 489 were found to be coincident. The number of coincidences expected to occur by chance is 48·5; thus there were 10·1 times more coincident whistlers than would be expected by chance. A similar analysis on a more limited series of results from Dunedin and Scott Base gave a ratio of actual coincidences to chance coincidences of similar magnitude (12·2). Statistical (chi-squared) tests applied to these results show that the correlation of occurrences of whistlers at these stations is highly significant.

Attempts have been made to examine the dispersion characteristics of coincident whistlers in order to determine whether these are identical at the three stations. A difficulty arises in obtaining readable spectrograms in that, when the field-strength of a whistler is strong at the New Zealand stations, it tends to be very weak at Scott Base, and vice versa. However, I have succeeded in obtaining readable spectrograms of long whistlers occurring at all three stations at 08h. 36m. 11s. U.T. on April 7, 1959. (The pattern of atmospherics occurring during a few seconds on either side of this time was used to obtain an accurate comparison of times.) At each station the whistler, which was swishy in character, was preceded by a loud atmospheric of the type classified as a 'bonk' by Morgan and Dinger[4]; on analysis, this bonk was identified as the initiating atmospheric. It had an unusually complex structure, indicating that multiple lightning discharges had taken place at 20–30 millisec. intervals during a total time of 0·19 sec.

The dispersion analysis was carried out using an 11-channel comb-filter analyser, the filter frequencies f being arranged to give equal increments of $f^{-1/2}$ between channels, so that dispersion curves obeying the Eckersley–Storey approximation[5] would be straight lines. The times of first and last observable response for each channel (starting and finishing times) are given in Fig. 1*a* and Fig. 1*b* respectively, time being measured from the commencement of the initiating bonk. The dispersion lines shown in Fig. 1*a* refer to the commencement of the bonk, and those in Fig. 1*b* refer to its end. Although the starting times at these three stations do not agree well, nevertheless, apart from the two exceptions, discussed below, the agreement of the finishing times is within the accuracy of determination of times from the spectrograms (normally about ± 0·02 sec.). These points closely describe a whistler component of dispersion 164 sec.$^{1/2}$, arising from the last component in the multiple lightning discharge.

An analysis of the wave-forms of the initiating bonk, as recorded at the three stations, suggested that the lightning-source was 1,100 ± 200 km. distant

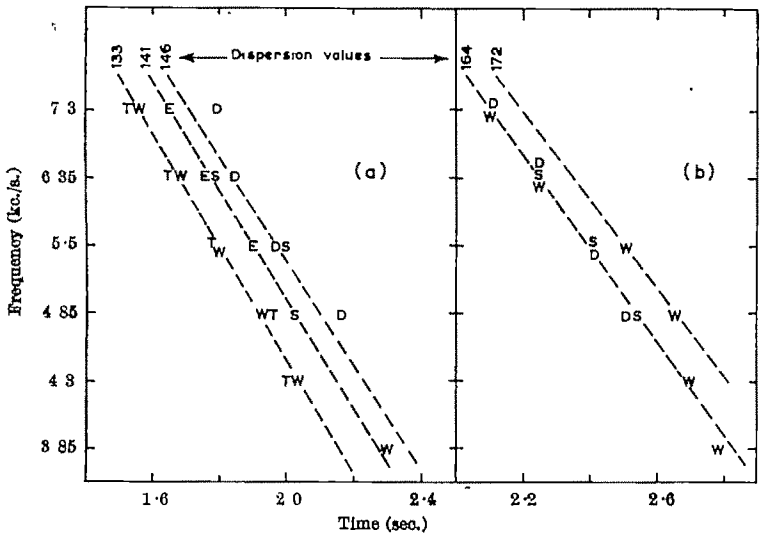

Fig. 1. Dispersion characteristics of whistlers apparently arising from the same source, as recorded at Scott Base (*S*), Dunedin (*D*), Wellington (*W*), Stanford (*T*) and Seattle (*E*). The northern hemisphere times have been adjusted as described in the text. (*a*) Starting times; (*b*) finishing times

from both Wellington and Dunedin, and 4,350 ± 300 km. from Scott Base, that is, in the vicinity of lat. 38° S., long. 163° E., in the middle of the Tasman Sea. The New Zealand Meteorological Service has kindly supplied the information that a vigorous depression had its centre at lat. 39° S., long. 163° E., at 0600 U.T. on the day in question. This centre had moved to lat. 40° S., long. 165° E., by 1200 U.T. Thunderstorms and cumulo-nimbus clouds reaching altitudes of 20,000 ft. were reported by ships and aircraft in the area at this time. The synoptic weather charts indicate that this was the only likely thunderstorm area for some thousands of miles around. Therefore it appears to be reasonably certain that this region, at a geomagnetic latitude of about 43° S., gave rise to the whistler heard at Scott Base.

Sonagrams of short whistlers recorded at Stanford and Seattle, U.S.A., which apparently arose from the same source, have been kindly supplied by Mr. L. H. Martin, of Stanford University. The geomagnetic latitudes of these stations are 43·7° N. and 53·6° N. respectively. Both sonagrams show multiple component structure. The first components are well defined, especially on the Stanford record, but in both cases there is no clearly distinguishable last component because of high noise-level from local atmospherics. The initiating atmospheric was readily identified with that found on the southern hemisphere spectrograms. A time correction of 0·04 sec. was made, to allow for the time of propagation of the atmospheric from its source to the west coast of the United States. The times thus corrected were then doubled to permit direct comparison with the southern hemisphere data. This is shown in Fig. 1*a*. It will be seen that the Stanford starting times agree well with the Wellington times for frequencies between 4·3 and 7·3 kc./s., and describe a whistler component of dispersion 133 sec.$^{1/2}$ arising from the initial lightning discharge. On the other hand, the Seattle starting times are consistent with two of the three Scott Base starting times and the 3·85 kc./s. response at Wellington, indicating a whistler component of dispersion 141 sec.$^{1/2}$. The lowest-latitude stations in each hemisphere (Stanford and Wellington) have thus recorded an earlier whistler component than the higher-latitude stations. The explanation of this may involve consideration of the terminal latitudes of the paths along which the various components were propagated through the outer ionosphere. The anomalous lateness of starting times at Dunedin is attributed to the exceptionally high noise-level there at that time.

In view of the way in which results from the various stations in both hemispheres correlate, and also in view of the multiple structure revealed by the Stanford and Seattle sonagrams, it seems reasonable to attribute the later finishing times at Wellington for frequencies of 4·85 and 5·5 kc./s. to the reception there of an additional component which was not recorded at Dunedin or Scott Base because of higher noise-levels at these two stations.

An extension of the dispersion analysis of the Wellington whistler showed no sign of a nose frequency up to 14·6 kc./s., the highest frequency at which there was a useful response. On the dipole representation of the geomagnetic field, this implies that the path of highest latitude for this whistler must have terminated below 60° geomagnetic latitude; if the nose frequency were one-half of the minimum gyrofrequency over the path, the maximum terminal latitude would be less than 55°. Since the nose frequency is likely to be at least 20 kc./s., the maximum terminal latitude is in fact likely to be less than 53°. Following an alternative line of reasoning, that of comparing the measured dispersion values with an empirical curve of the variation of dispersion with latitude given by Allcock[6], a maximum terminal latitude of about 51° is inferred. The general agreement between these two estimates of the maximum terminal latitude makes it reasonably certain that the whistler under consideration not only arose from a source in middle latitudes, but also was indeed a true middle-latitude whistler, being propagated through the outer ionosphere along paths which terminated in middle latitudes. Reception of this whistler at the polar station of Scott Base would therefore imply a final stage of propagation underneath the ionosphere for more than 2,800 km.

This work forms part of the radio research programme of the Dominion Physical Laboratory. I am grateful to Prof. R. A. Helliwell of Stanford University for his assistance in providing equipment, and to the Antarctic Division, Department of Scientific and Industrial Research, New Zealand, for operating the Scott Base whistler equipment.

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PHYSICS

Simultaneous Application of Townsend and Streamer Theory

RECENTLY conductivity current measurements up to the sparking potential have been carried out in hydrocarbon gases which can be interpreted if it is assumed that Townsend and streamer processes act simultaneously.

A sample measurement for *iso*pentane is shown in Fig. 1. At $E/p = 300$ V. cm.$^{-1}$/mm. mercury, $p = 3$ mm. mercury, the d.c. ionization current was measured, by successive reduction of i_0, over more than eight decades of amplification, without any sign of a deviation from the normal α slope, up to the sparking voltage of 990 V. which occurred at $d = 1 \cdot 1$ cm. The last slope was obtained with 10 electrons leaving the cathode per second and this type of measurement has often been repeated and confirmed.

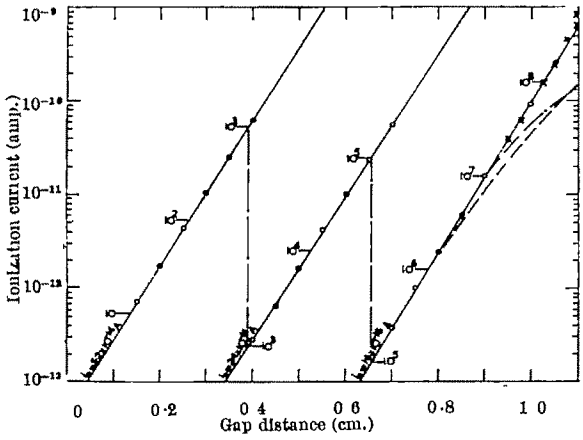

Fig. 1. Ionization current, i, as a function of gap distance, d, showing large multiplication possible in *iso*pentane without apparent deviation from a normal α slope. Spark occurred at 990 V., $d = 1 \cdot 1$ cm.; $E/p = 300$ V. cm.$^{-1}$ mm. Hg^{-1}, $p = 3$ mm. Hg, $\alpha = 17 \cdot 9$ cm.$^{-1}$. —O—O, Experimental curve; — — —, estimated α curve, Richter (ref. 1); - - -, estimated α curve, Heylen; ×—×—×, calculated values according to equation (3)

By monitoring the pulse shape of the ionic component of individual avalanches, it has been observed[1] that the number of charge carriers (n) increases less than $\exp(\alpha x)$ if n surpasses $N = 10^6$. The space charge field of the positive ions is held responsible for the reduction of the ionization of the advancing electrons and is comparable to the applied field; we are thus entering the streamer regime. It was found (for ether, a gas exhibiting an extremely low γ coefficient) that for $n \geqslant N$, Townsend's α coefficient could be expressed as:

$$\alpha(n) = \alpha\,(1 - B \ln n/N) \qquad (1)$$

in which $B = 0 \cdot 065$. From this, the charge multiplication factor was evaluated as:

$$x - x_N = \frac{1}{\alpha}\left\{\frac{1}{1 - B \ln n/N} - \frac{1}{B}\ln(1 - B \ln n/N) - 1\right\} \qquad (2)$$

in which $N = \exp(\alpha x_N)$. The reduction from the normal α slope, according to equation (2), is shown in Fig. 1 (dashed line), and does not agree with the observed data. The discrepancy can be cleared up if it is assumed that Townsend's secondary mechanism is operating simultaneously with the streamer inducing space charge reduction of Townsend's primary process. This can be taken into account by using the generalized Townsend equation:

$$i_x = i_0 \frac{\exp(\int_0^x \alpha dx)}{1 - \gamma\,(\exp(\int_0^x \alpha dx) - 1)} \qquad (3)$$

in which $\exp(\int_0^x \alpha x d)$ can be found from Fig. 1 (dashed line). An estimate of γ can be obtained by making equation (3) fit the experimental curve. Thus, for $\gamma = 4 \cdot 3 \times 10^{-8}$, a normal α slope would be recorded up to $d = 0 \cdot 9$; for longer gaps, an upcurving would occur and the Townsend criterion for breakdown would be reached at $d = 0 \cdot 98$, which is not in agreement with experiment.

From previous work[2] it has been surmized that for normal hydrocarbons, little space charge distortion occurs until $n \geqslant N = 10^7$, and from Richter's data[1] an equally good fit to $\alpha(n)$ can be obtained for $B = 0 \cdot 2$. Substitution of this value into equation (2) yields the curve as shown in Fig. 1 (dot-dashed line). Combining this with equation (3) yields $\gamma = 10^{-8}$; the calculated values are shown (×). It is observed that no apparent deviation from a normal α slope occurs to within 5 per cent of the sparking distance, at which a faster than usual Townsend upcurving takes place.

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The Nitrous Oxide Dosimeter

NITROUS oxide has been proposed[1] as a suitable material for the dosimetry of ionizing radiations over wide temperature- and pressure-ranges and with a wide variety of types of radiation. The basis for the yields quoted in ref. 1 was the measurement of radiation flux using ionization chambers or ferrous sulphate solutions. We have investigated the radiolysis of nitrous oxide and have compared the results of absolute measurements based on tritium as an internal source with measurements based on ferrous or ceric sulphate dosimetry, using cobalt-60 γ-rays or 4-MeV. X-rays as external sources.

It has been found that good agreement between the two methods is obtained provided the irradiations are done in vessels with internal diameters greater than about 15–20 mm. As the internal diameter decreases, the yields of all products, based on ferrous dosimetry, increase in a manner reminiscent of the increase in $G(Fe^{2+})$ from the ferrous sulphate dosimeter in vessels of a few millimetres diameter[2,3].

The products measured were nitrogen, oxygen and the oxides of nitrogen ($NO + NO_2$). Previous workers[1,4] have used liquid nitrogen to separate the volatile and non-volatile constituents of the irradiated gas, but since in this technique reactions occur in the traps which can cause serious errors in the yields of oxygen and oxides, in this work the constituents were not separated. Gas chromatography was used for nitrogen and oxygen analyses, and the oxides of nitrogen were determined spectrophotometrically as nitrite.

$G(N_2)$ was $11 \cdot 0 \pm 0 \cdot 4$ at ambient temperatures and is the average from all the types of radiation mentioned, weighted in favour of the tritium irradiations (for which $G(N_2)$ was $11 \cdot 2 \pm 0 \cdot 2$ and $11 \cdot 3 \pm 0 \cdot 5$ for two experiments).

The most reliable results are likely to be obtained if nitrogen alone is measured, since it is unaffected by trap reactions or other analytical complications, and its yield is also unaffected by foreign gases such as hydrogen or methane, both of which markedly reduce the yields of oxygen and oxides of nitrogen, or by traces of water, which affects the relative proportions of oxygen, nitric oxide and nitrogen dioxide.

A more detailed account of this work will appear elsewhere.

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The Wake of a Moving Drop

TWO-DIMENSIONAL flow behind bluff symmetrical obstacles has received the attention of fluid dynamicists for more than half a century. Considerations of the Kármán vortex-street afford an excellent example of the agreement between theoretical and experimental results. Three-dimensional wakes have been investigated intensively, but are less tractable as they do not exhibit the same uniformity or periodicity as the two-dimensional vortex-trails.

Practical considerations have been an important factor in confining most investigations to phenomena associated with the relative motion between a fluid and a rigid body. More recently, meteorological implications have prompted investigations into the mechanics of liquid drops falling through a quiescent gaseous medium such as air. Many engineering processes involving liquid–liquid phases secure contact through the dispersion of one phase as drops moving through a second liquid.

Telford, Thorndike and Bowen[1] described an experiment in which they determined the collision efficiency between equal-size drops about 150μ in diameter. Schotland[2] modelled the trajectories of cloud droplets of equal size by allowing steel spheres to fall through a sugar solution. The collision efficiencies obtained by these investigators support a wake collision process that may be important in the early stages of cloud drop growth studies. Studies of collisions between larger drops suggest a wake process is operative that may be of some importance in determining the drop-size distribution observed in natural rain. Collisions between equal size drops, moving at the same terminal velocities, suggest a pressure gradient behind the leading drop which accelerates the trailing drop into contact. The time displacement relationships of a drop moving through a medium are directly dependent on the drag force, which in turn depends on the nature of the wake.

Liquid–liquid systems were used in the experiments described in this communication. The wakes of single drops of various organic liquids, moving through water at terminal velocity, were observed and recorded photographically. The wake pattern was rendered visible as a water-soluble dye was scrubbed from the moving drop.

Fig. 1 shows the wake pattern behind a drop of carbon tetrachloride (equivalent diameter 0·24 cm.) moving through quiescent water at 25° C. with a Reynolds number of 360. Fig. 2 shows the wake of the same drop after its energy has been dissipated, but before its identity has been lost through diffusion processes. There is a time-interval of 10 sec. between the two exposures.

The wake behind a drop moving through a liquid phase with Reynolds numbers up to some value, limited by drop oscillations, is characterized by two rows of vortex rings. These rings all move at the same acute forward angle with the line of fall of the drop. The almost perfect symmetry is evident in the wakes of all drops, regardless of the deviation from sphericity, in which there are no local oscillations. Larger oscillating drops result in the production of more energetic rings, but lack the symmetry of the smaller

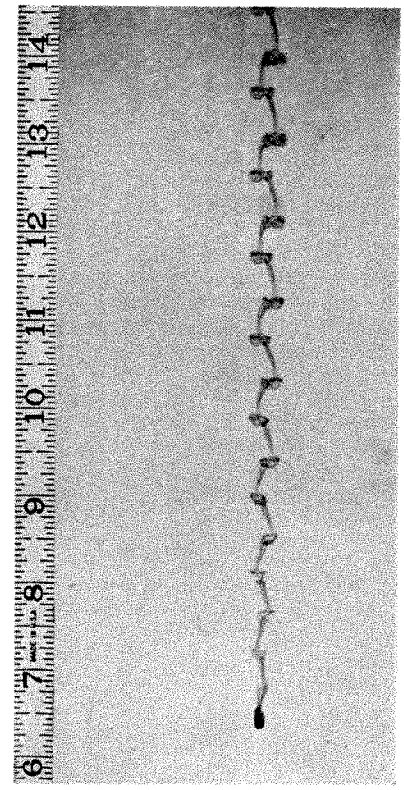

Fig. 1. The wake behind a carbon tetrachloride drop falling through water at terminal velocity. Reynolds number 360. Photograph taken at an angle of 45° with the plane of the wake

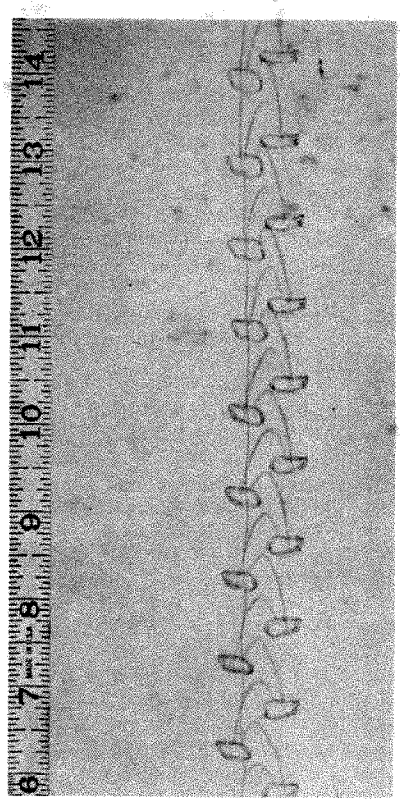

Fig. 2. The wake behind the same drop 10 sec. after the drop has passed

drops. Hu and Kinter[3], Johnson and Braida[4], and Licht and Narasimhamurty[5] report results on drop diameter–drop velocity relationships for carbon tetrachloride–water systems. These reports indicate that 0·32 cm. represents about the maximum size of a carbon tetrachloride drop that can fall through water without oscillation. This corresponds to a Reynolds number of about 900. In these experiments, the wake symmetry has been observed for drop-diameters and Reynolds numbers approaching these values.

Disturbances in the vortex sheet behind the drop are responsible for the shedding on alternate sides of the drop. The wake appears to be independent of gross oscillations of the drop. Any local oscillations or zig-zag motions of the drop as it passes through the disperse phase are not discernible. The work is being continued in liquid–liquid systems and extended to liquid–gaseous phases.

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CHEMISTRY

Organic Ion Flotation

IN an earlier communication[1], a procedure for concentrating inorganic ions is outlined. It has been found now that it is possible to concentrate organic ions from aqueous solution by adding a surfactant collector, of opposite charge, suitably prepared to ensure the absence of micelles, and then, by the introduction of fine bubbles, floating the insoluble product to the surface where it collects in the froth, or preferably as a scum. The principle is the same as for inorganic ion flotation, but there is one important distinction. In inorganic ion flotation, because the ions are often polyvalent, the product between the ion and the collector having more than one hydrophobic centre, is highly insoluble and usually forms a scum very quickly. But organic ions are often univalent, and therefore the product, though still insoluble, sheds water less readily, and there is more tendency to form a stable froth. This can, however, be broken by blowing hot air on to it, though it is not desirable to destroy it completely. A residual froth bed should be left, upon which the concentrate can float. This becomes necessary as the uni-univalent product, which is really a salt, can sometimes dissociate again, if allowed to come into contact with bulk water. If the precautions mentioned in the previous communication are observed, excellent recoveries from very dilute solutions are obtainable. Furthermore, the remarkable degree of selectivity shown by the method in the case of inorganic ions, when starvation amounts of collector are added incrementally, is shown as well in the case of organic ions.

In order to avoid laborious organic analyses, much of the exploratory work was done with dilute solutions of dyes or indicators, usually of a concentration of about 0·01 gm./l. Such solutions could be decolorized completely, sometimes in a matter of minutes, the colour being collected in the froth. Some dyes, having both anionic and cationic centres, could be floated by either cationic or anionic collectors, depending on the *p*H, but others could only be floated by one type of surfactant.

The following experiment will illustrate the selectivity. 3 mgm. each of potassium indigo sulphonate, congo red, methyl orange, bromphenol blue and phenolphthalein were freshly made up into a 400 ml. aqueous solution, and made slightly alkaline with ammonia to make the dyes anionic. This solution was put into a No. 4 sintered glass Buchner funnel. Solid lauryl pyridinium chloride was freshly dissolved in absolute alcohol (2·2 mgm./ml.) and was added in 1 ml. portions, followed by air blown gently through the sintered glass. The dyes were floated in the above order, the distinctive colour of each being clearly perceptible in the froth at each stage. After addition of about 7 ml. of collector, the solution was completely colourless. In a similar experiment, to which Lauth's violet, a cationic dye, had been added, the blue colour of it remained and could not be removed by a cationic collector. If, however, the solution was made slightly acid, *p*H 5, and α-sulpholauric acid added as a collector, the dye was removed by bubbling, leaving the solution colourless.

In working with dyes, it is advisable to use fresh solutions, as dyes have a tendency to form micelles, and old solutions may give misleading results. As it is

only ions which are collected, and as organic substances are usually weakly dissociated, the control of *p*H is very critical. As cationic collectors, the alkyl quaternary ammonium soaps, or the long-chain amines proved most suitable, and as anionic collectors, α-sulpholauric acid or its potassium salt proved most convenient. It is possible to recover the floated organic ion by a double decomposition reaction in a non-aqueous solvent, either benzene or alcohol, each procedure being determined by a knowledge of the chemistry of the species involved.

A number of organic ions, chosen at random, have been floated, establishing the generality of the method. These included picrate, gallate, tetraphenyl boron, and the alkaloids strychnine and brucine. This indicates that the method might be useful in collecting organic ions from natural products, especially as the carbohydrates are not likely to float. It has potential application in concentrating antibiotics and other valuable biological products which are ionizable.

Another possible use is in clarifying solutions. For example, a sugar solution that had been charred to a black molasses residue was dissolved in water to give a dirty brown solution. Using trimethyldodecylammonium chloride as a collector, the colouring matter was floated into the froth, leaving the solution almost colourless.

One of the difficulties in taking the fullest advantage of the selectivity shown by ion flotation in respect of organic ions is that the products are usually colourless, so that it becomes difficult to ascertain when one species is fully collected and the next is about to concentrate. It may become possible to overcome this problem by taking advantage of the large variety of dyestuffs. If these were to be placed in a series of relative floatability, it may be possible to find a dye just intermediate between the two species to be separated. On the introduction of a small amount of such a 'marker dye' into the solution, it would be possible to see when the collection of the first species is finished, by the first appearance of the dye colour in the froth.

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Dipole Moments of Fluorine Monoxide and Sulphur Tetrafluoride

IN setting up a teaching experiment on the dipole moments of gases, we recently took the opportunity to measure the temperature dependence of the polarization of fluorine monoxide (F_2O) and sulphur tetrafluoride (SF_4). The condenser comprised two concentric stainless steel cylinders similar to that described by Groves and Sugden[1]. The capacity of the condenser was about 80 *p*F. and was measured with an accuracy of 1 part in 16,000 by a ratio-transformer bridge. The condenser was mounted in a cylindrical glass vessel which was immersed in the thermostat bath. Capacities were measured with the gases at atmospheric pressure over the temperature-ranges −78° to +80° C. for fluorine monoxide and −30° to +80° C. for sulphur tetrafluoride. The apparatus was calibrated with dry air free of carbon dioxide to eliminate the effect of stray capacity. Fluorine monoxide was made by bubbling fluorine, diluted with nitrogen, through 2 per cent caustic soda solution[2]: sulphur tetrafluoride was obtained through the courtesy of Imperial Chemical Industries, Ltd. (Alkali Division).

The plot of total polarization against reciprocal temperature was not sufficiently accurate to permit extrapolation to infinite temperature. Values of the induced polarization were therefore estimated independently: 5 c.c./mole for fluorine monoxide and 12·5 c.c./mole for sulphur tetrafluoride. Straight lines drawn through these and the experimental points gave the following values of the dipole moments; the errors indicate maximum and minimum slopes of lines drawn through the estimated point at infinite temperature.

Fluorine monoxide $\mu = 0{\cdot}4 \pm 0{\cdot}1\ D$ using $P_0 = 5$ c.c./mole; sulphur tetrafluoride $\mu = 1{\cdot}0 \pm 0{\cdot}1\ D$ using $P_0 = 12{\cdot}5$ c.c./mole.

The value for fluorine monoxide is much smaller than that of OH_2 (1·84 *D*) and is thus similar to NF_3 (0·2 *D*) the dipole moment of which is much smaller than that of NH_3 (1·5 *D*). Coulson[3] suggests that the true bond moment of OH in water is 1·08 *D* in the sense $\overset{+}{O}\overset{\longrightarrow}{—}H$. The lone pair moment in water must then be 3·19 *D*. If the same lone pair moment is assumed in fluorine monoxide on the grounds that the same angle indicates the same hybridization, then the true O—F bond moment is 2·9 or 2·3 *D* depending on the sense of the overall moment, 0·4 *D*.

Little can be said about sulphur tetrafluoride except that the dipole moment is consistent with the C_{2v} structure which has been proposed[4], and which arises from a trigonal bipyramid (dsp^3 hybridization) when one of the three equatorial positions is occupied by the lone pair. It would, however, be equally consistent with the C_{3v} symmetry which would obtain if the lone pair occupied a polar position.

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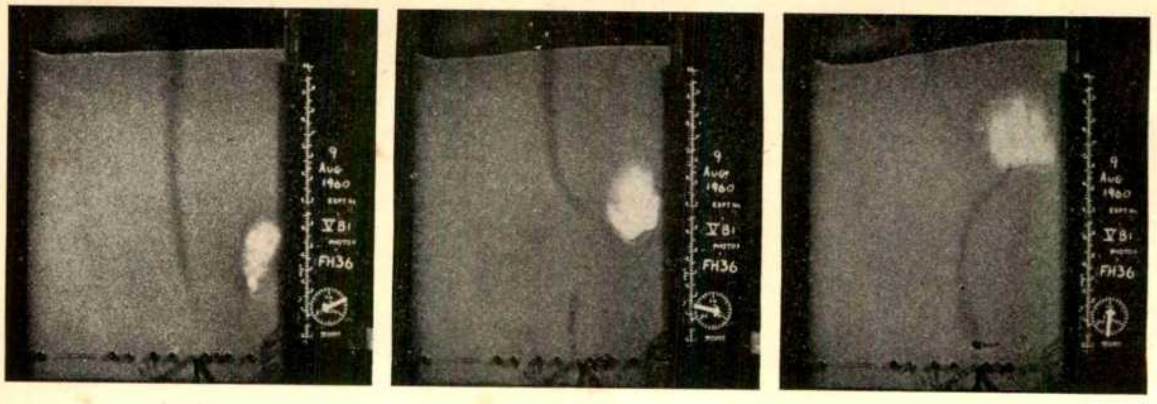
Gas-Flow Patterns in Fluidized Beds

A FLUIDIZED bed is sometimes used as a means of carrying out a chemical reaction between a gas and solid particles. In gas-fluidized beds, 'bubbles' form and there is considerable interest in the part played by these in gas/solids in contact. It has been suggested, for example, that some of the gas rises through the bed in the form of bubbles and effectively by-passes the solid particles[2]. Several investigators[1-7] have made various indirect measurements and have concluded that back-mixing of the gas occurs. These processes are important in estimating reaction-rates. So far as we are aware, no one has hitherto observed directly gas-flow patterns within the bed.

We have recently measured directly local gas velocities in a fluidized bed under special conditions.



$t = 0$ $t = 0{\cdot}19$ sec. $t = 0{\cdot}40$ sec.

Fig. 1

The bed was 12 in. wide and 15 in. deep, but only 1 in. from back to front so that it was effectively two-dimensional. The containing walls were made of 'Perspex', and within them 0·46-mm. diameter glass spheres were fluidized by air. Typical 'bubbles' formed and with rear illumination they could be seen in some detail. Near the bottom of the bed a number of small holes were drilled through the wall and into any of these a fine stream of nitrogen peroxide could be injected. With suitable illumination the progress of this coloured tracer stream could be followed through the bed, and by interrupting it periodically, velocities could be measured. The tracer flow-rate was less than 0·5 per cent of the fluidizing gas-rate so that its overall effect was negligible.

The accompanying photographs (Fig. 1) were selected from a film taken at 100 frames/sec. They show events at approximately 0·2-sec. intervals. The air velocity based on the empty cross-section was 0·9 ft./sec. (about 10 per cent above the minimum fluidization velocity) and the 'bubble' velocity is seen to be about 1·3 ft./sec. but it is increasing up the bed. The tracer stream velocity was about 1·6 ft./sec. and gas is seen to be continuously flowing into the void. Other photographs show the tracer flowing into the void as a jet, but it quickly loses its identity and becomes mixed with air. From a 'bubble' filled with this diluted nitrogen peroxide, we have seen the gas diffuse through the surrounding particles, mostly through the top of the void. Thus, gas in the 'bubble' is by no means isolated from the bulk of the bed. Back mixing of the gas by reverse flow does not generally occur, at least during gentle fluidization, but occasionally, when the solids are very violently mixed, they carry tracer gas with them against the general direction of flow; but this is a rare event.

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Evidence for a Nitric Oxide Complex with Cupric Fluoride

ALTHOUGH it has been recognized for some time that nitric oxide and cupric chloride or bromide combine in non-aqueous solvents to form nitrosyl complexes[1], the composition of these has only recently been determined[2]. The deep blue colour is due to the covalent $CuX_2.NO$ (possibly solvated): this compound dissociates into colourless ions:

$$CuX_2.NO + ROH \rightleftarrows CuX_2 + H^+ + RONO \qquad (ROH = \text{alcohol})$$

and this has been responsible for erroneous structures suggested for the complexes. Unsuccessful attempts have been made to prepare nitrosyl complexes in alcoholic solution from other cupric salts, including the fluoride[3]. Recently, a study of the variation of dissociation constant of the cupric chloride nitrosyls as a function of the dielectric constant of the alcohol has been made[4]: some results are shown in Table 1.

Table 1. DISSOCIATION CONSTANTS FOR $CuCl_2.NO$ IN ALCOHOLS

Solvent	K (23° C.)
Methanol	$4{\cdot}2 \times 10^{-2}$
Ethanol	$5{\cdot}4 \times 10^{-3}$
n-Propanol	$5{\cdot}3 \times 10^{-4}$
n-Butanol	$2{\cdot}0 \times 10^{-5}$

The decrease in dissociation is much greater than would be predicted by the Born equation if dielectric constant were the only factor involved. Thus it appeared that if a nitrosyl could be prepared from cupric fluoride it would only be stable in an alcohol such as n-butanol. Using anhydrous cupric fluoride, a violet colour is indeed obtained when nitric oxide is bubbled into the butanol solution, and the absorption of the gas is greater than it is in the absence of cupric salt. The colour fades rapidly, and a white precipitate containing copper and fluoride forms. A similar result is obtained with hydrated cupric fluoride. If the solvent used is t-butanol, the violet colour is quite stable, and no precipitate forms for at least 10 min. Addition of hydrofluoric acid has no effect on the optical spectrum of the t-butanol complex; but when a trace of the acid is added to any other alcohols containing either anhydrous or hydrated cupric fluoride, and nitric oxide bubbled through, the deep blue nitrosyl colour forms immediately and is quite stable. Fig. 1 shows the close resemblance of the absorption spectra of some of the fluoride nitrosyls to the cupric bromide nitrosyl formed in n-butanol.

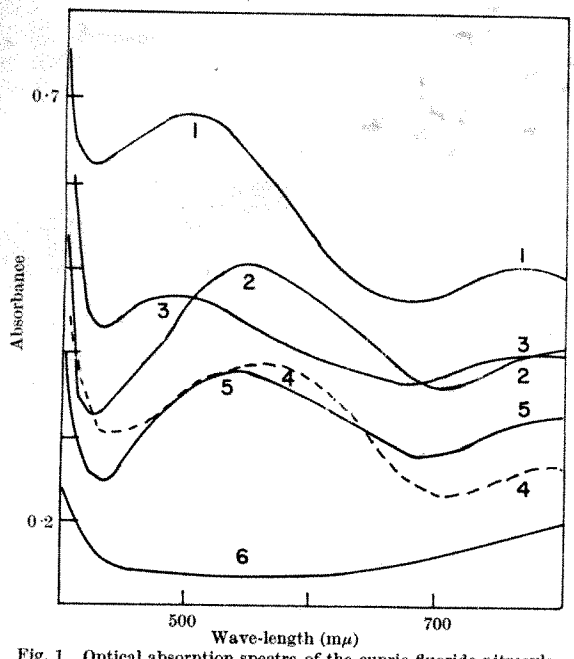

Fig. 1. Optical absorption spectra of the cupric fluoride nitrosyls in alcohols
1, Ethanol; 2, *n*-butanol; 3, *t*-butanol; 4 (dotted line), $CuBr_2.NO$ in *n*-butanol, shown for comparison; 5, *n*-propanol; 6, CuF_2 hydrate in *n*-propanol

There is a gradual shift in the position of the absorption maximum of the complex as the solvent is changed. Table 2 shows wave-lengths of maximum absorption for the three nitrosyl complexes in alcohols[4].

Table 2. Position of Absorption Maxima

Solvent	$CuF_2.NO$	Max. λ(mμ) $CuCl_2.NO$	$CuBr_2.NO$
Ethanol	499	550	570
n-Propanol	551	550	570
n-Butanol	551	550	565
t-Butanol	475	—	530

Methanol is the only alcohol examined so far in which the nitric oxide–cupric fluoride cannot be formed in the presence of hydrofluoric acid: only a transient yellow coloration is obtained. The nitrosyl solutions are not stabilized by lithium or sodium fluorides as they are by hydrofluoric acid. The role of the acid is merely to depress the ionization of the covalent nitrosyl.

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Separation of Amino-acid Mixtures on Sulphonated Polystyrene Resin-loaded Papers

The high resolving powers of columns of cross-linked sulphonated polystyrene resins when applied to the separation of mixtures of amino-acids has been demonstrated by the classic work of Moore and Stein[1] and afterwards by other workers[2,3].

For rapid qualitative separations a paper chromatographic technique offers definite advantages. In addition to its simplicity of operation is the ability to: (*a*) detect the separated zones on the paper, thus rendering elution unnecessary; (*b*) develop several chromatograms side by side; (*c*) record simply the rate of movement of a zone relative to that of the solvent front; and (*d*) combine two separate developments on the same sheet of paper as a two-dimensional chromatogram.

The advent of the ion-exchange papers has made it possible to realize the advantages of both ion-exchange method and paper chromatographic technique. The object of the work presented here is to compare in a purely qualitative manner the resolving powers of ion-exchange resin in column and paper form.

Separations of the amino-acids on ion-exchange cellulose papers have previously been described[4], as also have some limited separations on ion-exchange resin-loaded papers, but so far the resolution on the latter materials has not approached that possible on resin columns[5,6].

The most satisfactory results were obtained on a paper (patent applied for), made specially in these Laboratories, containing 'Zeokarb 225 (*WR* 1·5–2·0)' resin in a form particularly suited to the requirements of chromatographic separations.

A number of other sulphonated polystyrene resin-loaded papers were also investigated, including some commercially available papers, but were found to be of limited use for critical separations.

1 μgm. of each of sixteen amino-acids was applied as separate spots to a sheet of the resin-loaded paper which had previously been equilibrated with 0·2 *M* *p*H 3·1 buffer[1]. The equilibrated paper was carefully blotted to remove excess liquid and the amino-acids were applied to the wet paper. The chromatogram was developed in the 0·2 *M* *p*H 3·1 buffer by a descending technique for a period of 90 min., after which the dried paper was sprayed with a 0·2 per cent solution of ninhydrin in acetone containing 0·1 per cent collidine[7]. The pattern of amino-acids which resulted is illustrated in Fig. 1.

A separation of amino-acids on a column of 'Zeokarb 225 (*WR* 1·5–2·0)' through 200-mesh resin, developed according to the Moore and Stein technique, is illustrated in Fig. 2.

10 mgm. of amino-acid mixture was applied to the column, and the complete run took 50 hr.

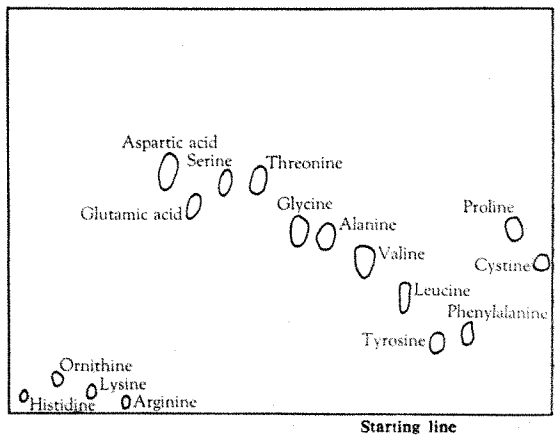

Fig. 1

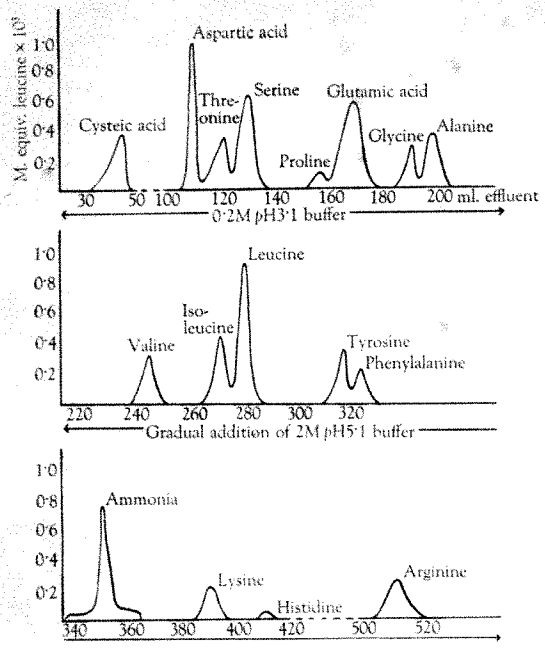

Fig. 2

Although the gradient elution of the column technique has been replaced on the paper by a simple elution with a single buffer, the sequences on the two forms of the resin, with the possible exception of the basic group of amino-acids, are comparable, and such a comparison is made in Table 1.

Table 1. A COMPARISON OF THE SEQUENCE OF AMINO-ACIDS ON COLUMN AND PAPERS CONTAINING 'ZEOKARB 225' RESIN

Sequence of decreasing rate of movement	
Sulphonated polystyrene resin column (4·5 per cent cross-linked). Developed according to Moore and Stein (ref. 1)	Sulphonated polystyrene resin-loaded paper. Developed in 0·2 *M* *p*H 3·1 buffer
Asp	Asp
Thr	Thr
Ser	Ser
Pro	Glu
Glu	Pro
Gly	Gly
Ala	Ala
Val	Val
Leu	Cys
Tyr	Leu
Phe	Phe
Orn	Tyr
Lys	Orn
His	Lys
Arg	His
	Arg

It may be seen that some differences in sequence on the two forms of the resin occur and that these are mainly associated with a reversal of the tyrosine–phenylalanine and the proline–glutamic acid groups. These differences can probably be attributed to the influence of the cellulose matrix on separations on the resin-loaded papers.

With the exception of the above differences the high resolution of the column technique is matched by that of the paper, and because the latter can be achieved without elution the time required for such a separation is considerably reduced.

A property of the ion-exchange paper which has not been used in the above separation is that associated with the cellulose matrix itself when the ion-exchange characteristics are suppressed. Separations describing the use of a new two-dimensional technique in which ion-exchange and 'partition' techniques are combined on the ion-exchange cellulose papers have been described[4,8].

In the case of the sulphonated polystyrene resin-loaded paper the separation of the amino-acids achieved under ion-exchange conditions ideally combines with that achieved under 'partition' conditions. This is because the sequences of amino-acids produced by the two sets of conditions are very different. This is a point of difference from the ion-exchange cellulose papers and is due to the different matrixes associated with the two types of exchanger. A separation illustrating the new two-dimensional method is shown in Fig. 3.

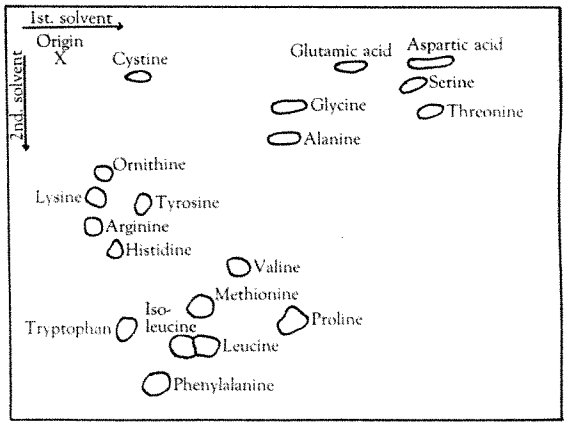

Fig. 3

In this the first development was carried out with 0·2 *M* *p*H 3·1 buffer on the dry sodium form of the paper and the second development in *m*-cresol – 0·3 per cent ammonia. The ammonia solution, present in the bottom of the chromatography tank, assured a suppression of the effect of ion-exchange characteristics by producing an anionic form of the amino-acids. The paper was equilibrated over the ammonia for 1 hr. before introduction of the second solvent. The complete separation was achieved in a single day.

The most striking feature of the separation illustrated in Fig. 3 is the absence of amino-acid spots along the diagonal of the paper through the origin. A diagonal distribution of spots and consequently a lack of high resolution are common features of many conventional two-dimensional chromatograms. By completely breaking up such a distribution and by adding to the high resolving power of the resin itself the new two-dimensional technique on sulphonated polystyrene resin-loaded paper probably provides the highest degree of resolution of amino-acids yet obtained in a single chromatographic analysis.

A fuller account of the analysis of amino-acid mixtures on different types of ion-exchange papers is being prepared and will be published elsewhere.

I wish to thank the directors of W. and R. Balston, Ltd., for permission to publish this communication.

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BIOCHEMISTRY

Hexosamine Synthesis by Cell-free Extracts of Various Bacteria

An enzyme system catalysing the synthesis of glucosamine-6-phosphate from glutamine and fructose-6-phosphate or glucose-6-phosphate has been demonstrated in *Neurospora crassa*[1,3], rat liver[2,3] and *Escherichia coli*[3]. Ghosh *et al.*[3], who purified the enzyme from these various sources and studied its properties, have called it L-glutamine-D-fructose-6-phosphate transamidase. We have determined transamidase activity in fresh, cell-free extracts of *Bacillus cereus*, *Micrococcus lysodeikticus*, *Aerobacter aerogenes* and *Escherichia coli*. Results indicate that, for a given weight of cells, activity is higher in Gram-positive than in Gram-negative bacteria, and for a given organism, activity increases markedly during the lag and early exponential phases of growth, but decreases during the stationary phase. The high transamidase activity associated with dividing cells is probably related to the synthesis of cell-wall basal structure[4], which contains amino-sugars. During these investigations, using a system with standard conditions of *p*H, substrate concentrations and reaction time at 37°, it was found that the amount of glucosamine-6-phosphate synthesized rarely exceeded 25 per cent theoretical, and frequently was not proportional to enzyme concentration when different volumes of the same cell extract were tested in parallel. An attempt was made to explain these findings.

Cell-free extracts were prepared from *Bacillus cereus* vegetative cells suspended in water (20–50 mgm. dry weight/ml.) by disintegration with ballotini beads in a Mickle disintegrator[5] and centrifugation of the homogenates. The activity of an extract prepared in this way was equivalent to that obtained from the same weight of cells disintegrated in a Hughes press[6]. The rates of formation of hexosamine in the presence of extract and various amounts of glucose-6-phosphate (extract contained phosphoglucoisomerase[3]) and glutamine at *p*H 6·5 are shown in Fig. 1. Control tubes containing heat-inactivated extract and substrates were included, and hexosamine was determined in tests and controls by the method of Rondle and Morgan[7] modified by the use of carbonate–bicarbonate buffer[8]. In all cases hexosamine increased to a maximum not exceeding 25 per cent theoretical (based on amount of glucose-6-phosphate present) and then decreased. Similar results were obtained when reaction mixtures were buffered at *p*H 7·5. Apparently the low maximum yield of product was not due to enzyme inactivation during incubation since hexosamine was synthesized when glutamine was added to glucose-6-phosphate + extract + buffer preincubated for 1 hr. at 37°. Nor was destruction of substrates by glutaminase and phosphatase activities in the extract sufficient to explain the results. Loss of hexosamine-reacting material after the maximum had been reached was not due to formation of *N*-acetylhexosamine derivatives or incorporation into a larger molecule since no increase in hexosamine was found after hydrolysis with 6 *N* hydrochloric acid. Comb and Roseman[9] purified and studied the properties of an enzyme in *Escherichia coli* which deaminated glucosamine-6-phosphate releasing fructose-6-phosphate and ammonia; the reaction was reversible. An enzyme with similar properties was present in extracts of the bacteria mentioned

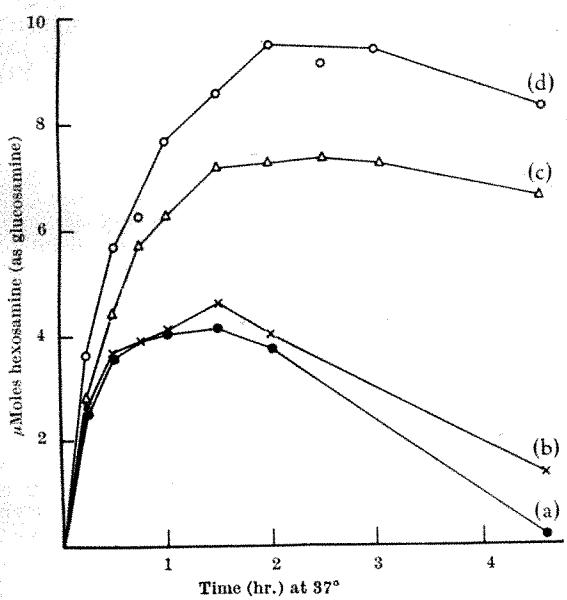

Fig. 1. Synthesis of hexosamine by an extract of disintegrated *Bacillus cereus* cells. Reaction mixtures (1 ml.) contained 0·3 *M* phosphate buffer, *p*H 6·5 (0·2 ml.), extract (from 18 mgm. dry weight cells) and substrates as follows (μmoles):

	(*a*)	(*b*)	(*c*)	(*d*)
Glucose-6-phosphate	20	20	40	40
Glutamine	20	50	40	100

Samples (0·1 ml.) removed immediately and at intervals during incubation at 37° were acidified with acetic acid, heated at 100° for 2 min. and diluted to 3 ml. Hexosamine was determined in the supernatant fluids (1 ml.)

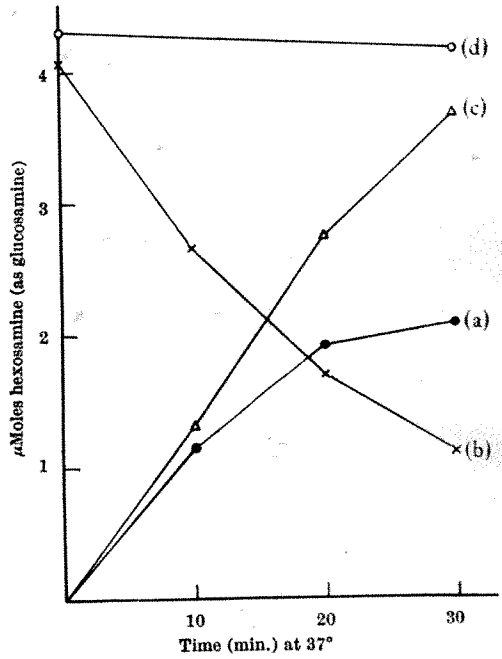

Fig. 2. Comparison of transamidase and deaminase activities in an extract of *Bacillus cereus* cells. Reaction mixtures (0·5 ml.) contained 0·4 *M* phosphate buffer (0·2 ml.), extract (from 6 mgm. dry weight cells) and other additions as follows (μmoles):

	(*a*)	(*b*)	(*c*)	(*d*)
Glucose-6-phosphate	15	—	15	15
Glutamine	25	—	25	—
Glucosamine-6-phosphate	—	4·3	—	4·3
Ammonium chloride	—	—	375	375
Versene	—	—	15	15

Samples (0·1 ml.) removed and treated as in Fig. 1

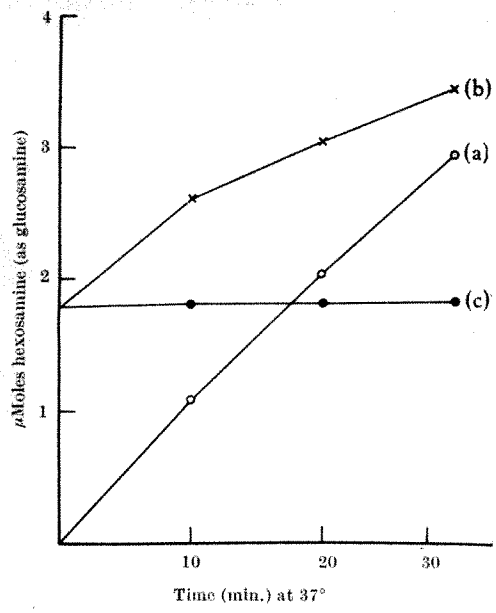

Fig. 3. Effect of added glucosamine-6-phosphate on hexosamine synthesis in the presence of excess ammonium salt. Reaction mixtures (0·5 ml.) contained 0·4 *M* phosphate buffer, *p*H 7·5 (0·12 ml.), extract (from 14 mgm. dry weight *Bacillus cereus* cells), versene (15 μmoles), ammonium chloride (250 μmoles), glucose-6-phosphate (10 μmoles) and other additions as follows (μmoles):

	(*a*)	(*b*)	(*c*)
Glucosamine-6-phosphate	—	1·8	1·8
Glutamine	20	20	—

Samples (0·1 ml.) removed and treated as in Fig. 1

above and its activity was maximal near *p*H 8·5 but appreciable at *p*H 6·5–7·5. Using the same amount of *B. cereus* cell extract at *p*H 7·5, the rate of disappearance of hexosamine from a reaction mixture containing glucosamine-6-phosphate was compared with the rate of hexosamine synthesis in the presence of glucose-6-phosphate and glutamine (Fig. 2). Results indicated that the apparently restricted synthesis of hexosamine was due to destruction of the product by deaminase activity. Attempts were made to inhibit the degradation reaction. Deaminase activity was markedly reduced by a mixture of disodium ethylenediamine tetraacetic acid (versene) ammonium salt in excess and glucose-6-phosphate, whereas transamidase activity increased in the presence of ammonium salt + versene (Fig. 2) and was proportional to the volume of extract added when reaction mixtures were incubated for 15–30 min. at 37°. A small synthesis of hexosamine occurred when extract was incubated with glucose-6-phosphate and excess ammonium salt at *p*H 7·5, but this did not account for the increased transamidase activity. However, it was shown that deaminase activity was not completely inhibited under these conditions, by measuring transamidase activity in the presence and absence of added glucosamine-6-phosphate; inhibition was less when the concentration of hexosamine in reaction mixtures increased (Fig. 3).

Under the conditions described, the direct, accurate measurement of L-glutamine-D-fructose-6-phosphate transamidase activity in crude bacterial extracts is not possible owing to the presence of glucosamine-6-phosphate deaminase. Methods for the purification of the two enzymes have been described by other workers[3,9], and it is possible that quantitative separation of the transamidase could be achieved. However, the instability of the enzyme[1–3] makes this a difficult problem.

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Heterogeneity of Liver Lecithin isolated by Chromatography on Silicic Acid Columns

THE recent report by Collins[1] of the heterogeneity of lecithin labelled with phosphorus-32 is supported by results obtained by us as part of an investigation of the effect of ethionine on the incorporation of phosphorus-32 into the liver phosphatides of rats. This will be reported in full elsewhere but an experiment on normal rats, which is relevant to the work of Collins, is described here.

Three rats were each injected intraperitoneally with 4 μc. of labelled orthophosphate. Three hr. later, the rats were killed and their livers were removed. The lipids from the combined livers were extracted and freed from water-soluble components containing radioactive phosphorus by a procedure similar to that described by Fishler and Chaikoff[2], except that the ether extract of the liver lipids was washed with 0·1 *N* hydrochloric acid and 0·01 *N* sodium chloride[3], rather than with a solution of unlabelled sodium phosphate.

The total phosphatides were first separated from the other lipids in the extract on a silicic acid column[4] and were then fractionated on a second column of silicic acid using mixtures of chloroform and methanol as the eluting solutions[5,6]. The silicic acid columns were 'aged' before use as described by Gray and Macfarlane[7] to minimize breakdown of acetal phosphatides. The fractions from the column were analysed for choline, amino-nitrogen and inositol, as well as for total phosphorus and esterified fatty acids. The fractionation, on the basis of the phosphorus analyses, is shown by the elution curve in Fig. 1. The main component eluted by the 4 : 1 chloroform/methanol mixture is a mixture of serine and ethanolamine phosphatides, and the main component eluted by the 1 : 1 chloroform/methanol mixture is lecithin. Inositol phosphatide is eluted immediately before the lecithin and, in this particular fractionation, is incompletely separated from it. This pattern of elution of rat liver phosphatides is the same as that described by Hanahan *et al.*[6].

The specific activities of the successive fractions collected from the column during the elution of the lecithin component are also shown in Fig. 1. There is a continuous rise in the specific activity as the lecithin is eluted. This increase in specific activity could be caused by contamination of the lecithin with the components which either preceded or followed

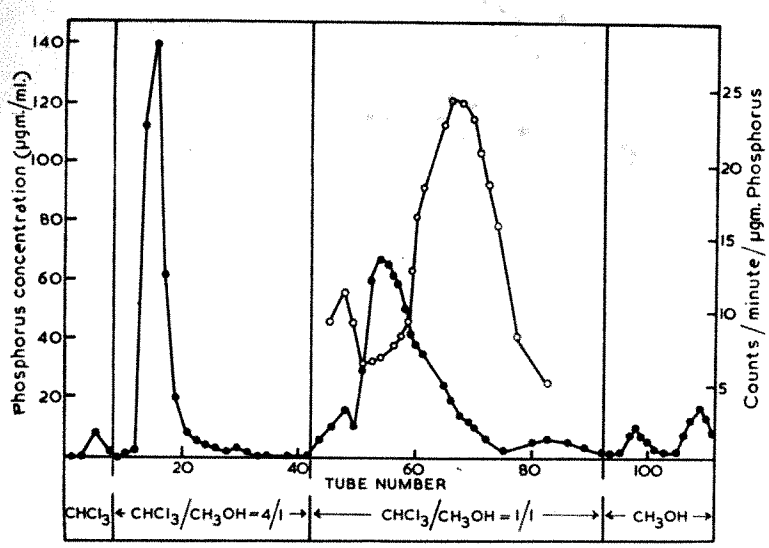

Fig. 1. Separation of liver phosphatides on a column of silicic acid (Mallinckrodt's analytical reagent, 100 mesh). Load, 25 mgm. per gm. silicic acid. Flow-rate, 0·5–1 ml. per min. The eluting solvents were mixtures of chloroform and methanol in the ratios shown in the figure. 10 ml. or 20 ml. samples of eluate were collected. —●—, phosphorus concentration in µgm./ml.; —O—, counts/min./µgm. phosphorus

it from the column. However, the specific activity of the inositol phosphatide fraction, measured in tube 48, was 12·0 and that of the uncharacterized component eluted immediately after the lecithin, measured in tubes 80–85, was 6·3. Such an explanation is therefore unlikely. A similar rise in specific activity, not shown here, was observed as the mixed serine and ethanolamine phosphatides were eluted.

The combined fractions in the tubes 50–55 (fraction *A*) and in tubes 60–72 (fraction *B*) from the lecithin peak were examined further. Acetal phosphatides, measured by the method of Gray and Macfarlane[7], formed 3 per cent of the total phosphatides in fraction *A* and were absent from fraction *B*. The phosphorus/choline/esterified fatty acid ratio in fraction *A* was 1/0·97/1·90 and that in faction *B* was 1/0·92/1·94. After methanolysis of the fractions, the methyl esters of the fatty acids were analysed by gas-liquid chromatography (Table 1).

Table 1. PERCENTAGE FATTY ACID COMPOSITION OF LECITHIN SUB-FRACTIONS *A* AND *B*

Fatty acid (trivial names)	No. of carbon atoms and double bonds	Retention time relative to stearate	Fraction *A*	Fraction *B*
Myristic	14–0	0·204–0·215	—	0·46
—	15–0	0·310–0·314	—	0·42
Palmitic	16–0	0·456–0·461	23	33·2
Palmitoleic	16–1	0·515–0·520	0·72	1·98
—	17–0 (?)	0·665–0·690	0·72	0·68
—	17–? un.	0·830–0·833	0·50	—
Stearic	18–0	1·000	44·4	16·3
Oleic	18–1	1·10–1·11	4·53	15·4
Linoleic	18–2	1·34–1·35	5·81	21·2
Arachidonic (?)	20–4 (?)	3·52–3·56	20·2	10·3

The fatty acids in fractions *A* (tubes 50–55) and *B* (tubes 60–72) were converted to the methyl esters by refluxing the fractions with 1·3 *N* hydrochloric acid in a dry methanol/benzene mixture for 2 hr. The methyl esters were separated on the Pye argon gas chromatograph at 175° C. and with an argon flow-rate of 50–60 ml./min. The stationary phase was the adipate ester of polyethylene glycol (10 per cent on acid-washed, 100–120 mesh, 'Celite'). The relative retention time for the methyl ester of arachidonic acid on this column is normally 3·22. The identification of the C20–4 component as arachidonic acid is probably correct, however, since its relative retention time on a second column with 'Apiezon *L*' as stationary phase was 1·48, the usual value for the methyl ester of arachidonic acid. Under the above experimental conditions the determination of unsaturated acids with C22 and upwards is unsatisfactory and values for these acids are not included in Table 1. They were present in both fractions as minor components, the amounts in fraction *A* being greater than those in fraction *B*.

The results show marked differences in the fatty acid composition of the two fractions. For example, stearic and arachidonic acids are the main saturated and unsaturated acids in fraction *A*, whereas in fraction *B* the main saturated acid is palmitic acid and the main unsaturated acid is linoleic acid. The combined percentage of mono- and poly-saturated fatty acids is greater in fraction *B* than in fraction *A*. This pattern has been confirmed in further work.

As prepared by silicic acid chromatography, rat liver 'lecithin' therefore appears to be heterogeneous. Its heterogeneity can be expressed both in terms of differences in fatty-acid composition and in the rate of turnover of the 'lecithin' phosphorus.

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Transforming Activity of Deoxyribonucleic Acid labelled with 5-Bromouracil

Ephrati-Elizur and Zamenhof[1] demonstrated that deoxyribonucleic acid from *Bacillus subtilis* grown in 5-bromouracil-supplemented media contained this analogue and retained its transforming activity. It thus became important to determine the specific transforming activity for purified fractions of each of the three molecular variants of deoxyribonucleic acid which can be extracted from organisms treated with 5-bromouracil: (1) unlabelled deoxyribonucleic acid

molecules, and those in which 5-bromouracil has been substituted for thymine in (2) one strand ('unifilar' labelling) or in (3) both strands ('bifilar' labelling) of the double helix. Two strains of *Bacillus subtilis*, wild type[2] and uracil-requiring strain 265 (kindly supplied by Dr. R. Guthrie), served as the donors of deoxyribonucleic acid. These were first grown with aeration at 37° C. for 4 hr. in nutrient broth supplemented with thymidine (10 μgm. per ml.), and afterwards incubated for 2–3 generations in minimal broth[2] containing 2–5 μgm. 5-fluorodeoxyuridine (serving as the thymidylic acid synthetase inhibitor[3]), 25 μgm. uridine (to suppress the conversion of 5-fluorodeoxyuridine to 5-fluorouracil and 5-fluorouridine) and 50–250 μgm. 5-bromodeoxyuridine per ml. Under these conditions, similar to those first employed for *Escherichia coli* by Lorkiewicz and Szybalski[4], the molar ratio of 5-bromouracil to 5-bromouracil + thymine (5-bromouracil substitution) in non-fractionated deoxyribonucleic acid varied from 35 to 61 per cent as assessed by chromatographic determination[5].

Employing another procedure, with aminopterin as inhibitor of thymidylic acid synthesis, the wild-type strain was reported to incorporate essentially no 5-bromouracil, while analogue substitution in strain 265 was 12 per cent[1]. Highly polymerized deoxyribonucleic acid was isolated from cells lysed by lysozyme (100 μgm./ml.) and sodium laureate (5 per cent), deproteinized by the chloroform–butanol or phenol[5] procedures and freed of ribonucleic acid by

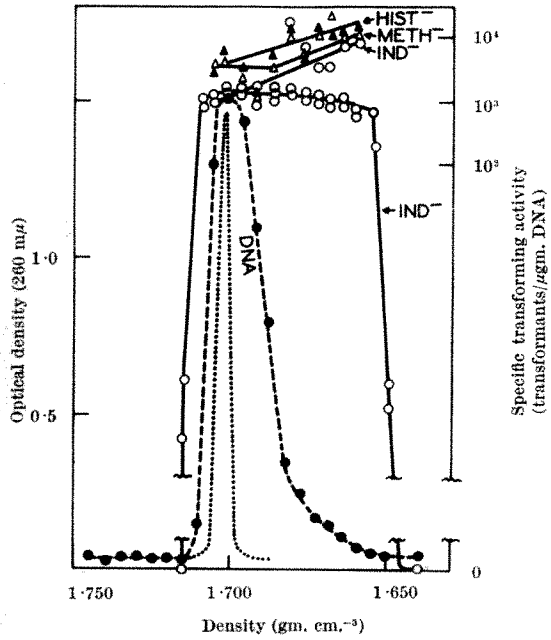

Fig. 1. Buoyant density distribution of deoxyribonucleic acid (*B. subtilis* transforming principle) centrifuged for 72 hr. at 35,000 r.p.m. in the *SW*-39*L* rotor (broken line) or for 20 hr. at 44,770 r.p.m. in the analytical centrifuge, 'Spinco' model *E* equipped with ultra-violet optics (ref. 6) (dotted line), and the specific transforming activities of the same fractions, all adjusted to similar optical density, and tested with indole- (⊙) (two experiments), methionine- (△) and histidine-16- (▲) requiring recipient strains of *B. subtilis* (0·1 μgm. deoxyribonucleic acid, 10^8 cells per ml. medium). Each point corresponds to a 3- or 9-drop fraction (30–90 μl.), out of the total 3 ml. used for centrifugation. We are indebted to Mr. Carl Schildkraut of the Department of Chemistry, Harvard University, for the analytical centrifuge runs and to Drs. J. Marmur and J. Eigner and Prof. P. Doty for the help and hospitality extended to one of us (W. S.) during the performance of these determinations

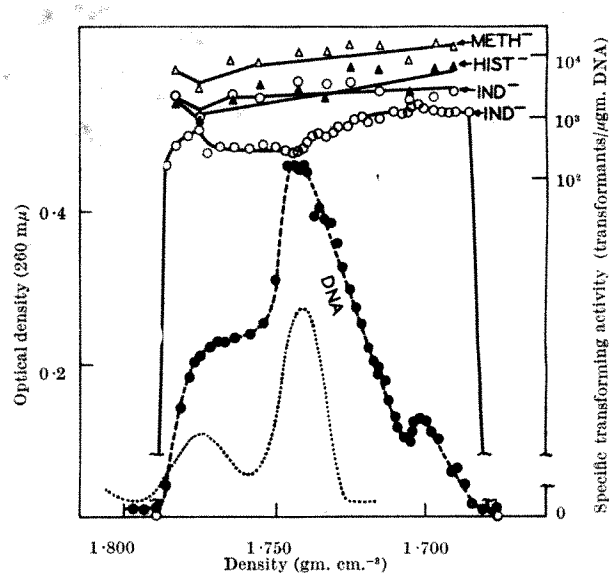

Fig. 2. Buoyant density distribution of deoxyribonucleic acid labelled with 5-bromodeoxyuridine, extracted from *B. subtilis* grown for approximately two generations on 5-bromodeoxyuridine, 5-fluorodeoxyuridine, uracil-supplemented minimal medium. For explanation of curves, see Fig. 1. The left peak (1·776 gm. × cm.⁻³) corresponds to 70·5 per cent 'bifilar' 5-bromodeoxyuridine labelling while the centre peak (1·742 gm. × cm.⁻³) represents the 'hybrid' molecule (70·5 per cent 'unifilar' labelling). Since guanine + cytosine comprise 42 moles per cent of *B. subtilis* deoxyribonucleic acid bases (ref. 11), overall incorporation of bromouracil into the deoxyribonucleic acid represented by these density peaks was calculated to amount to 46·7 per cent, which figure agrees with the results of chromatographic 5-bromouracil determinations (ref. 5) on non-fractionated deoxyribonucleic acid. The small peak on the right (1·702) probably corresponds to deoxyribonucleic acid free of 5-bromodeoxyuridine extracted from the small proportion of cells which were non-viable or died at the time of transfer to 5-bromodeoxyuridine-supplemented medium

ribonuclease treatment (37°, 2 hr.) and overnight dialysis. The density gradient centrifugation procedure[6] was employed for the fractionation of deoxyribonucleic acid labelled with 5-bromodeoxyuridine. When centrifuged for 72 hr. at 35,000 r.p.m. in a 'Spinco' swinging-bucket rotor, the normal, deoxyribonucleic acid molecules free from 5-bromodeoxyuridine converged to a position in the cæsium chloride gradient corresponding to a density of approximately 1·703 gm. cm.⁻³ (Fig. 1). This was determined either by analytical cæsium chloride centrifugation[6] or by measuring the density and deoxyribonucleic acid content (optimal density at 260 mμ) of all the fractions, 30–90 μl. each, collected by the method described by Szybalski[7]. Specific transforming activity for 3 genetic markers was determined for each fraction, employing indole, methionine, and histidine-deficient receptor strains of *B. subtilis*. The methods for preparation and treatment of recipient cells were essentially the same as described by Spizizen[2]. As can be inferred from Fig. 1, the specific transforming activity, expressed as the number of transformant colonies per μgm. deoxyribonucleic acid (using a standard number of 10^3 recipient cells per ml., under standard conditions), was practically identical for all the fractions of normal, deoxyribonucleic acid free from 5-bromodeoxyuridine.

Similar determinations were performed on 5-bromodeoxyuridine-labelled, cæsium-chloride centrifuged and fractionated transforming deoxyribonucleic acid. The fact that this labelled deoxyribonucleic acid formed bands at only three density-levels, corresponding to the parental, and hypothetical

'unifilarly' ('hybrid'), and 'bifilarly' labelled molecules, is consistent with the hypothesis of semi-conservative replication of *B. subtilis* deoxyribonucleic acid, by analogy with the data of Meselson and Stahl[6]. As briefly reported earlier (indole marker)[8], and as can be seen in Fig. 2, heavy labelling with 5-bromodeoxyuridine of the transforming deoxyribonucleic acid in one (1·742 gm. cm.$^{-3}$ peak) or both (1·776 gm. cm.$^{-3}$ peak) strands did not significantly affect the specific transforming activity for the three markers tested. The labelled deoxyribonucleic acid used in this experiment was highly polymerized with sedimentation constant $S_{20,w} = 44s$ (corrected for deoxyribonucleic acid concentration equal to 0), and essentially free of any denatured material, as inferred from the shape of the 'melting' profile[9,10].

In summary, it might be concluded that transforming *B. subtilis* deoxyribonucleic acid molecules retain their biological activity even after extensive 'unifilar' or 'bifilar' labelling with 5-bromodeoxyuridine, as assessed with three genetic markers.

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Crystallization of the Complex of D-Amino-Acid Oxidase and Benzoate

WE have been investigating D-amino-acid oxidase apo-protein, flavin adenine dinucleotide and the substrate with reference to complex formation[1,2]. In the previous communication[1], it was reported that the addition of the apo-protein to flavin adenine dinucleotide causes a shift and decrease of the absorption peak at 450 mμ of the latter. It was also found that the co-existence of benzoate, a substrate-substitute, and the apo-protein causes further marked

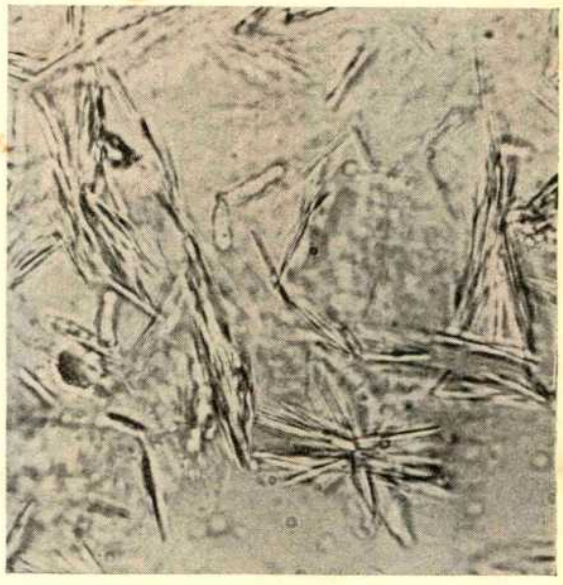

Fig. 1. Crystal of the complex of D-amino-acid oxidase holoenzyme and benzoate. (× 1,000)

changes in the absorption spectrum of the flavin adenine dinucleotide. Two important changes were especially noted: (1) the intensity of the absorption at 450 mμ is further decreased and that at 485 mμ is increased to form a shoulder, and (2) a new absorption peak appears at 465 mμ. These results indicate that both the apo-protein and the benzoate combine with two different binding sites of the *iso*alloxazine nucleus of flavin adenine dinucleotide. On the other hand, the fact that benzoate competes with the substrate, D-amino-acid[3,4], indicates combination between benzoate and the apo-protein. Hence it may be considered that the apo-protein, flavin adenine dinucleotide and benzoate combine to form a tight complex[5].

We have now isolated the complex of D-amino-acid oxidase apo-protein, flavin adenine dinucleotide and benzoate. Excess of both flavin adenine dinucleotide and benzoate was mixed with the apo-protein dissolved in pyrophosphate buffer ($M/60$, pH 8·3) at 0°. Then, ammonium sulphate to 0·2 saturation was added to this mixture, bringing the pH to 5·1. A yellow precipitate was obtained by centrifugation. This precipitate was dissolved in pyrophosphate buffer ($M/60$, pH 8·3) and precipitated by ammonium sulphate at pH 5·1. The precipitate was dissolved in its own volume of pyrophosphate buffer ($M/60$, pH 8·3), and allowed to stand at room temperature. Needle-shaped crystals then appeared (Fig. 1).

The absorption spectrum of the crystallized preparation is shown in Fig. 2, curve I. The shape of this absorption spectrum is identical with that of flavin adenine dinucleotide co-existing with both the apo-protein and benzoate[1].

The presence of benzoate in this crystal was assumed, and the benzoate was determined. The solution of the crystal was acidified with dilute hydrochloric acid, and benzoic acid was extracted with ether, from which it was re-extracted with 0·01 N aqueous potassium hydroxide. For the estimation of benzoate, its absorption at 225 mμ was measured. The presence of benzoic acid in the solution was shown by Folin's reagent after oxidation by hydrogen peroxide. The results showed that the

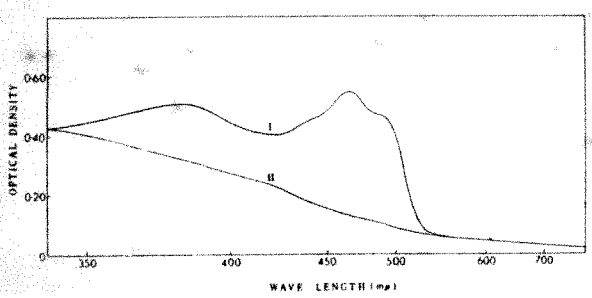

Fig. 2. Spectrum of the complex of D-amino-acid oxidase holoenzyme and benzoate. Curve I, spectrum of the solution of the crystal; the crystal was dissolved in 0·05 *M* potassium phosphate buffer, *p*H 6·3; curve II, spectrum of the same solution 5 min. after the addition of an excess of D-alanine. The spectra were obtained with a Hitachi recording spectrophotometer at room temperature

crystal contained equimoles of the apo-protein, flavin adenine dinucleotide and benzoate.

The enzyme activity of this crystallized sample was also examined. Complete decolorization was demonstrated by the addition of excess D-alanine, as shown in Fig. 2, curve II. With excess D-alanine, this sample showed the same turn-over as that of the apo-protein reported previously[6].

It was also found that when an excess of D-alanine was added to the sample, and the enzyme was precipitated by ammonium sulphate, benzoate was found in the supernatant.

From these results, it may be concluded that the crystal we obtained is the complex of reconstructed D-amino-acid oxidase holoenzyme and benzoate, and that benzoate acts as a hinge to form a tight complex of the apo-protein and flavin adenine dinucleotide without any denaturation of the active core of the apo-protein, and benzoate, a substrate-substitute, can easily be exchanged by the real substrate, D-amino-acid. Hence it is considered that the apo-protein, coenzyme and the substrate combine with each other like three corners of a triangle.

In this connexion, we have compared our crystal with 'holoenzyme of D-amino-acid oxidase' obtained by Kubo *et al.*[7] and Massey and Palmer[8]. Kubo *et al.*[7] reported that they obtained the holoenzyme crystal without splitting off its prosthetic group. We have examined the absorption spectrum of the solution of the crystal obtained by Kubo's method and we find a shoulder at 485 mμ. This result, together with the fact that benzoate was used during the preparation procedure of their enzyme, suggested that the benzoate may still be present in the enzyme sample. Analysis showed indeed that this sample also contains equimoles of the apo-protein, flavin adenine dinucleotide and benzoate.

Recently, Massey and Palmer[8] reported that they obtained a crystal by further purification of Kubo's sample using a calcium phosphate gel-cellulose column and that they removed iron-containing impurities from the sample. This purification was repeated in our laboratory, and it was also found that the treatment by calcium phosphate gel-cellulose chromatography could be simplified by the following treatment: the mixture of calcium phosphate gel and cellulose powder (1 : 30, w/w) was added to the enzyme sample prepared by the method of Kubo *et al.*[7], and stirred at *p*H 7·1. Then the *p*H was brought to 5·1 and the mixture centrifuged at 0°. The reddish-brown precipitate was removed. Repeating this procedure twice, a clear yellow supernatant was obtained. A crop of needle-shaped crystals was obtained from the supernatant.

The absorption spectrum of the crystallized sample obtained by the method of Massey and Palmer[8] and that obtained by the simplified method were identical with that of our crystal synthesized from the apo-protein, flavin adenine dinucleotide and benzoate (Fig. 1, curve I).

The quantity of benzoate in this crystallized sample was also estimated, and it was found that equimoles of the apo-protein, coenzyme and benzoate were present in the sample.

From these results, it is considered that the crystal of 'D-amino-acid oxidase' obtained by Kubo *et al.* and also that by Massey and Palmer are not the enzyme itself, but a complex of D-amino-acid oxidase holoenzyme and benzoate.

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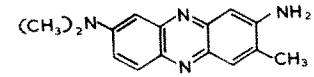
The Phenazinimines: a Possible Explanation of Anomalies associated with Neutral Red

D. L. Vivian and Morris Belkin in 1956 reported[1] that they had synthesized a compound which from the 'unambiguous' method used[2] should be 2-amino-8-dimethylamino-3-methylphenazine:



I

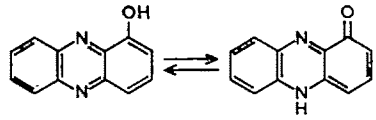
This is the accepted structure for the colour base of neutral red, and a compound having this configuration, when converted to its hydrochloride, should show the normal neutral red behaviour of acting as a vital stain, that is, should stain living cells without killing them. As stated by Vivian and Belkin, however, the compound actually obtained, although giving an analysis agreeing with I, when converted to its hydrochloride, did not show the characteristic vital staining behaviour of neutral red. It also differed from the colour base obtained by removing the hydrogen chloride from a sample of commercial neutral red through chromatographic adsorption on basic alumina, in that it had a very different melting point, as well as in giving a brown colour with concentrated sulphuric acid, instead of the deep green colour which the commercial base forms. Still another point of difference is that the free base from the commercial neutral red fluoresces very slightly if at all in ether

solution, while the more soluble synthetic fluoresces a very strong green under ultra-violet illumination.

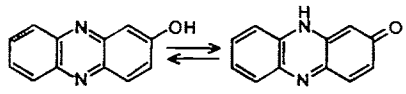
It was found possible by solution in sulphuric acid to convert the new base into one which did behave as the base obtained from commercial neutral red, and also gave the characteristic vital staining of cells from two varieties of *Amoeba* and from sarcoma 37 ascites tumour when it was converted to its hydrochloride, but no attempt was made in this first report to arrive at an explanation of the true nature of the new compound.

Now, however, as a result of further consideration of the problem, together with that of some experimental facts already known, but with which the authors were unacquainted at the time, I have formulated the following possible explanation:

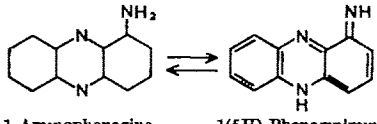
By analogy with 1- and 2-phenazinol, which have been shown to be tautomeric, respectively, with 1(5H)-phenazinone, and 2(10H)-phenazinone[3], it seems highly probable that equivalent systems exist with 1- and 2-aminophenazine:



1-Phenazinol — 1(5H)-Phenazinone or 1,5-dihydro-1-ketophenazine

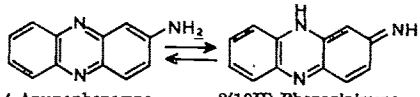


2-Phenazinol — 2(10H)-Phenazinone or 2,10-dihydro-2-ketophenazine



1-Aminophenazine — 1(5H)-Phenazinimine or 1,5-dihydro-1-iminophenazine

II



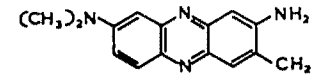
4-Aminophenazine — 2(10H)-Phenazinimine or 2,10-dihydro-2-iminophenazine

III

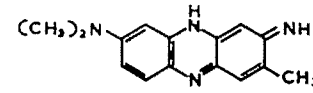
Following the nomenclature of the corresponding keto compounds: it is suggested here that II might be called 1(5H)-phenazinimine, and III, 2(10H)-phenazinimine, as shown above.

Just as Badger, Pearce, and Pettit have stated[3] that the system 1-phenazinol–1(5H)-phenazinone must exist primarily, if not entirely, in the hydroxy form, due to hydrogen bonding with the nitrogen atom in the 10-position, so, too, it is probable that the amino form predominates in the system 1-aminophenazine–2(5H)-phenazinone, even though the predominance would not be expected to be as great. For the sake of academic completeness, however, both the 1-aminophenazine and the 2-aminophenazine systems are illustrated here.

The tautomers of the unsubstituted phenazinol–phenazinone systems apparently are incapable of independent existence, as by analogy are probably those of the unsubstituted aminophenazine–phenazinimine systems also. However, appropriate substitution has made it possible to isolate both forms in one system, at least, that of 1,3,4-trimethyl-2-phenazinol–1,3,4-trimethyl-2(10H)-phenazinone[4]. Hence, in view of the demonstrated fact that separable isomers of 2-aminophenazine do exist when the compound is further substituted by an amino or hydroxyl group in the 8-position[1], it seems a reasonable hypothesis that their structures are wholly analogous to those of the phenazinol–phenazinone systems. If this be true, the two forms of the colour base of neutral red must be as shown below:



2-Amino-8-dimethylamino-3-methylphenazine



8-Dimethylamino-3-methyl-2(10H)-phenazinimine or 2,10-dihydro-8-dimethylamino-2-imino-3-methylphenazine

Existence of a third compound, arising from the higher-temperature neutralization of the sulphuric acid solution of the non-staining form of the base, as is likewise mentioned in the paper by Vivian and Belkin[1], may possibly be due to polymerization under these conditions, but no definite conclusions can be drawn without further work.

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Constraints in the Determination of Active-Centre Topography

THE inactivation of succinic semialdehyde dehydrogenase by trypsin has recently been found to be accelerated by a factor of greater than 100 when triphosphopyridine nucleotide, a substrate of the dehydrogenase, is included in the reaction mixture[1]. Evidence was presented that the site at which triphosphopyridine nucleotide is effective is the same for both dehydrogenase activity and for acceleration of inactivation by trypsin. It was concluded that the binding of a pyridine nucleotide substrate to succinic semialdehyde dehydrogenase produces a configurational change in the enzyme, and, in so doing, results in the exposure of a linkage labile to trypsin. Indirect evidence of such configurational changes has been noted by others[2-4] and suggests that the phenomenon may be of widespread occurrence.

These considerations lead to pertinent deductions concerning the relationship of enzyme topography and enzyme activity. Consider the above-noted case of succinic semialdehyde dehydrogenase[1]. Clearly, the enzyme can exist in at least two different geometric shapes which may be designated as form *A* (the structure of the enzyme in the absence of triphosphopyridine nucleotide) and form *B* (the enzyme in the presence of triphosphopyridine nucleotide), respec-

tively. It is understood that additional forms of the enzyme are not precluded. Since the active centre of an enzyme may be deformed by interaction with the substrate, simultaneous determination of the reaction-rate and the original geometry of the enzyme molecule (form *A*) are not possible. It should be noted that in actual practice estimations of the dimensions of enzyme active centres are arrived at by measuring relative reaction-rates of substrates and structurally related inhibitors. In view of the foregoing argument, these data cannot logically be used to approximate the molecular configuration of the initial state of the enzyme, that is, form *A*.

A possible extension of this concept is that the active centre may not be deformed by each substrate in precisely the same manner, but may be shaped within limits by the particular substrate[3,4].

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World-wide Distribution of Iodine-131 in Animal Thyroids following Announcements of Isolated Nuclear Weapons Tests in North Africa

MOST nuclear weapons tests have been associated with repeated releases of fission products within a few weeks, and the iodine-131 in animal thyroids increased progressively with succeeding tests[1]. In February and April 1960, individual nuclear weapons tests were announced to have occurred in the Sahara Desert. The results on which this report is based were obtained by analysis of preserved thyroid glands sent to the University of Tennessee by volunteer correspondents.

The gamma-radioactivity of the thyroid glands was measured as described in 1956 (ref. 1) and the radioactivity was corrected to the date of slaughter of the animals.

The graphs in Fig. 1 show that iodine-131 of the animal population had reached very low levels before February 10, 1960, except for animals raised near Nashville, Tennessee. The first increases in thyroid iodine-131 content following the test of February 13, 1960, were found in sheep from Haifa, Israel, on February 21, and Portugal on February 23, 1960. On February 24, the cattle from Formosa contained one hundred times more iodine-131 than they previously had in January and February of 1960. There is a strong suggestion that pigs from Memphis, Tennessee, had increased amounts by February 24, 1960. In March 1960, there were increases in thyroid radioiodine in all the animal populations which I sampled. The highest concentrations of radioiodine were found in the thyroids of sheep from Portugal; otherwise the concentrations of radioiodine in animal thyroids reached quantitatively similar maxima in sheep from Germany, London and Nashville and in cattle from Memphis and Formosa. The sheep thyroids generally contained more radioiodine than those from cattle.

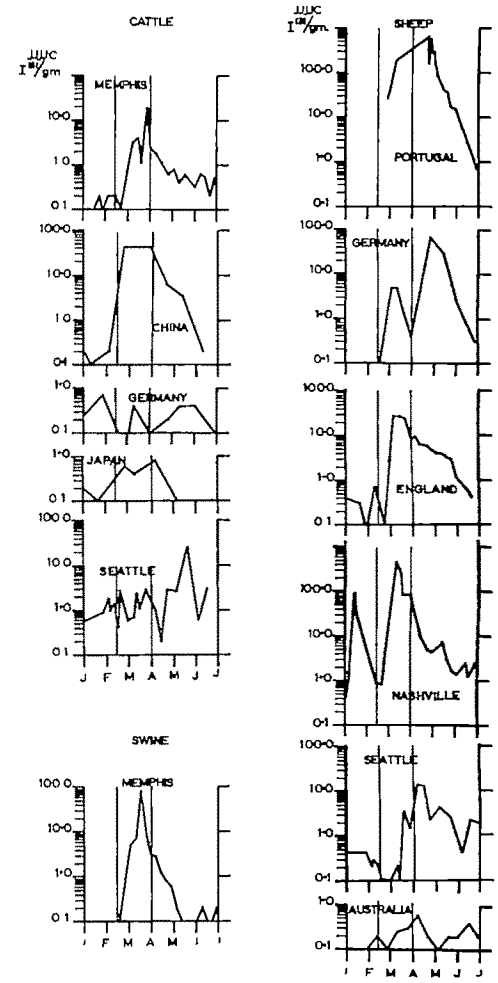

Fig. 1. Micromicrocuries of iodine-131 per gm. of thyroid corrected to date of slaughter of unselected slaughterhouse animals from January to July 1960. 788 thyroids from Memphis cattle, 302 Memphis pigs and 394 Nashville sheep were tested. 83 thyroids from the Republic of China, sent by Dr. Yu-hsi M. Wang, University of Taiwan. 35 cattle and 61 sheep thyroids from Munich, Germany, sent by Karl Schury of Max Muhlpointner A.G. Glands from 464 sheep were sent by E. F. McCleery from London. 35 cattle thyroids were sent from Japan by R. Tanaka, Ibaraki University. 111 cattle and 176 sheep glands were sent by Mr. A. Cirolini, Seattle, Washington. 247 sheep thyroids were sent by Dr. Roger Melick, of the University of Melbourne. 161 sheep thyroids were sent by Dr. J. Amaral Mendes, of the Laboratorio Nacional de Investigacao Veterinaria, Lisbon. Dr. Kurt Steinitz, of Haifa, Israel, sent sheep thyroids slaughtered in Haifa on February 21 and 24, 1960

The relatively large concentration of thyroid iodine-131 in pigs from Memphis was unexpected.

There is a definite tendency towards biphasic iodine-131 concentration curves in Fig. 1 during the period February–April, even though it is thought that only one nuclear test was conducted during that time. This biphasic character is similar to curves obtained from Australian sheep in December of 1957 (ref. 2) and may be characteristic of iodine-131 accumulation after nuclear tests. Another explanation of two maxima between February and April would be the presence, that I cannot explain, of new iodine-131 in the atmosphere, similar to the increased iodine-131 observed in sheep at Nashville in January 1960. After April 1, 1960, in most animal populations the radioactive iodine disappeared with a half-life which was greater than eight days, probably because of the

addition of new fission products after April 1. The sheep population around Munich, Germany, and in Portugal received the most iodine-131 after the test of April 1, but the sheep in London and Nashville received the greatest amounts of iodine-131 before the April 1 nuclear test. The observations available are not sufficient to explain these differences. Cattle in Japan and sheep in Australia showed very small amounts of iodine-131 from the weapons test in North Africa. The amount of fall-out in Australia was probably reduced by the great distance of Melbourne from the latitude of origin of the fission products. Japanese cattle have usually had less iodine-131 than other populations during the past five years.

The maximum concentration of iodine-131 in the sheep at Nashville was observed in March and quantitatively it was similar to that observed 38 months previously, when the iodine-131 in sheep thyroids (in December 1956) was believed to have had its origin in northern Siberia in November 1956.

These observations show again that the monitoring of radioiodine in thyroid glands of grazing animals is a sensitive and informative method for evaluating the biological exposure of animal populations to fission products.

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PHYSIOLOGY

Auto-Antibodies against Antigen derived from Colon in the Microsomes of Regional Colonic Lymph Glands in Human Ulcerative Colitis

THE sera of children with ulcerative colitis have been shown to contain a γ-globulin which reacts with an antigen prepared by phenol–water extraction of human colon. The serum factor may be termed an auto-antibody[1]. This communication presents evidence that antibody against the same antigen also occurs in the regional colonic lymph glands but not in the ileal glands of the patients and that it is bound to the microsomes of the colonic glands.

About 10 gm. of regional colonic lymph glands were obtained during colectomy from each of two children (*A* and *B*) with severe ulcerative colitis. In patient *B* regional ileal lymph glands (5 gm.) were obtained from the mesentery at a distance of 40 cm. from the ileocæcal valve. Serum from these two patients and from others was also available.

Immediately after surgery the glands were homogenized with a Potter–Elvehjem homogenizer in ice-cold 0·25 *M* sucrose with 0·001 *M* Mg^{2+}. Twice-washed microsomes (sediment after centrifugation at 105,000*g*) and cell sap (final supernatant) were prepared following Kern *et al.*[2]. The microsomal sediments were finally homogenized again and suspended in the sucrose medium to the original concentration. Protein was determined according to ref 3.

Table 1. HÆMAGGLUTINATION OF SHEEP RED BLOOD CELLS COATED WITH PHENOL–WATER EXTRACTED ANTIGEN FROM HUMAN COLON

Test solutions	Patient *A*		Patient *B*	
	Protein (mgm./ml.)	Titre*	Protein (mgm./ml.)	Titre*
Microsomes from colonic glands	3 75	0	4 00	0
Cell sap from colonic glands	10 50	16	18 50	64
Microsomes from ileal glands			4·50	0
Cell sap from ileal glands			16 00	0
Serum of patient		128		32
Norman human serum		0		0
Physiological saline		0		0

* The titres are the reciprocal of the highest dilutions giving macroscopically visible hæmagglutination when 1 ml. aliquots of serial dilutions of the fractions or the sera were mixed with equal volumes of a 0 5 per cent suspension of coated red cells. The antigen solution used for coating contained 100 μgm./ml. of the lyophilized material. The two experiments (patients *A* and *B*, respectively) were made on different days, using different samples of red blood cells and different antigen solutions for coating. Controls with uncoated red blood cells were negative in all cases.

In the immunological tests, sheep red blood cells were coated by the Middlebrook–Dubos method[4] with antigen extracted from fœtal colon[1]. Cell sap and sera were inactivated (56° C., 20 min.) before use and absorbed with sheep red cells to remove heterophile antibodies.

Table 1 shows the results of two typical experiments. As can be seen, the hæmagglutinating activity was confined, in both patients, to the serum and cell sap of the colonic lymph glands. The cell sap of the ileal lymph glands was inactive. No hæmagglutination was obtained with any of the three microsomal fractions. However, there is some evidence that antibody bound to microsomes is non-hæmagglutinating[5]. On the other hand, Kern *et al.*[2] have demonstrated antibody in microsomes of lymph nodes from immunized animals by its antigen-combining capacity. Therefore, in a second series of experiments, the antigen-binding capacity of serum and of the various fractions from the colonic lymph

Table 2. HÆMAGGLUTINATION OF SHEEP RED BLOOD CELLS, COATED WITH ANTIGEN INCUBATED WITH VARIOUS PREPARATIONS FROM PATIENT *A**

Incubations	1 antigen + microsomes	2 antigen + cell sap	3 antigen + antiserum *A*	4 antigen + normal serum	5 antigen + saline
Incubation† Coating‡ of red blood cells Hæmagglutination§					
Titres	0	0	0	64	64

* See Table 1 for analytical data.

† 1 ml. aliquots of antigen in saline (150 μgm./ml.) were incubated for 4 hr. at 20° C., with 2 ml. of either one of the samples indicated in columns 1–5. Columns 4 and 5: controls. No precipitate appeared in the incubation mixtures.

‡ 1 ml. of a red blood cell suspension was added to each of the incubation mixtures.

§ After washing, hæmagglutination was performed with a known hæmagglutinating serum from another patient. Titres are the reciprocals of the highest dilution of antiserum giving macroscopically visible hæmagglutination with equal volumes of a 0·5 per cent suspension of coated red cells.

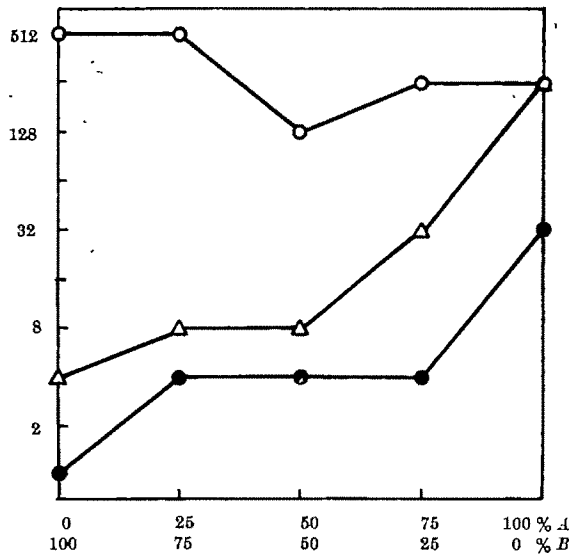

Fig. 1. Hæmagglutination of sheep red blood cells, coated with antigen incubated with various preparations from patient *B*. 1 ml. aliquots of the antigen (150 μgm./ml.) were incubated with 2 ml. of either undiluted microsomes or cell sap (see Table 1 for analytical data), serum from the patient, or normal serum. In addition, aliquots of the antigen were also incubated with 2 ml. samples of microsomes, diluted with their homologous cell sap in three different proportions, or with similar mixtures of patient serum and normal serum. For details of incubation, see Table 2. The hæmagglutinations were performed with a known positive serum from another patient. Abscissa, proportions (per cent) in which the various fractions (*A* and *B*) were mixed before they were added to the antigen for incubation. Ordinate, reciprocal of highest dilution of antiserum giving macroscopically visible hæmagglutination. In the control where antigen had been diluted with 2 ml. of physiological saline, the hæmagglutination end-point was 512.

●, Colonic glands; *A*, cell sap; *B*, microsomes. ○, Ileal glands; *A*, cell sap; *B*, microsomes. △, Serum; *A*, normal serum; *B*, antiserum

glands was measured. The procedure is outlined in Table 2, which shows the results of a typical experiment with the specimens from patient *A*. It will be seen that incubation of the antigen with normal human serum did not abolish its ability to sensitize the red cells. In contrast, incubation of the antigen with microsomes, cell sap or serum of the patient prevented hæmagglutination completely. Similar results were obtained with the specimens from the second patient. Fig 1 shows the typical results of an experiment made with all the samples obtained from patient *B*. The figure reveals that the inhibiting capacity of the cell sap from the colonic glands was appreciably lower than that of an equally diluted sample of the microsomes. The inhibitory capacity of undiluted serum from this patient was also lower than that of the colonic microsomes. However, since the chemical nature of the antibodies is unknown, no conclusions can be drawn regarding their concentration in the different preparations. Microsomes and cell sap from the ileal glands, as well as normal human serum, were inactive.

The mechanism of hæmagglutination inhibition by immune microsomes is unknown. It could be assumed that both antibody-active particles and antigen are bound to the red cells. In this case the molecular structures responsible for adsorption of the antigen to the red cells would be different from the structures combining with antibody. This has actually been shown for the α-hæmosensitisin of *Mycobacterium tuberculosis*[6]; this substance can be adsorbed directly to the red blood cells by the Middlebrook–Dubos procedure[4]. Although the immunological activity resides in the polysaccharides constituting the bulk of the material, a small lipid fraction seems to be necessary for sensitization[6].

The finding of antibodies in colonic gland microsomes is in agreement with that of other workers who found antibodies in splenic or lymphatic microsomes of immunized animals[2,5,7]. In contrast, microsomes (and cell sap) of more distant lymph glands were devoid of antibody activity. This would appear to rule out the possibility that the antibodies in the regional colonic glands were adsorbed serum antibodies. In this connexion, it should be mentioned that Kern *et al.*[8] could not find any adsorption of antibodies when antiserum was added to isolated microsomal fractions from non-immunized animals. Rather, then, the presence of antibodies in our samples would reflect a synthetic activity occurring in the microsomes of certain cells in the regional colonic glands. There is considerable evidence that proteins which are secreted are synthesized by the ribonucleoprotein particles, constituting a part of the microsomal fraction[8,9]. Before being released into the cell sap or the medium, the products of the synthetic activities of the particles often remain temporarily attached to the membranous elements which also are obtained in the microsomal fraction upon ultracentrifugation[8]. In order to study the mode of intracellular binding, attempts were made to solubilize antibodies from the microsomes by means of phospholipases and various detergents which are known to liberate proteins from the membranous parts of the microsomal fraction[8,10,11]. In a number of preliminary experiments, positive precipitin reactions were obtained in agar diffusion tests, using extracts of microsomes treated with phospholipase *A* from bee venom. Preliminary attempts to liberate precipitating or hæmagglutinating antibodies from isolated ribonucleoprotein particles by increasing the *p*H, treatment with chelating agents or with ribonuclease[5,7] have been unsuccessful.

In the homograft reaction, immunologically competent cells have been shown to be localized in the regional lymph nodes[12]. If immune reactions play any part in the pathogenesis of ulcerative colitis, it is likely that the lesions are the expression of a hypersensitive state, mediated by cell-bound antibodies of the same type as those participating in the homograft reaction, or in delayed hypersensitivity[13]. It is therefore of interest that, in the present case, isolated subcellular structures of regional colonic lymph glands exhibit an antigen-binding activity without foregoing extraction. Thus tissue lesions might be initiated by the binding of antigen on cells of the colon to antibody-bearing membranes of the immunologically competent cells. It is possible that in the latter cells antibody-active protein is transported from its site of formation, perhaps on the ribonucleoprotein particles, to the surface of the cell. The cell membrane is supposed to be chemically and morphologically related to the endoplasmic reticulum and its fragments will probably appear in the microsomal fraction[14]. A surface antibody of this nature could be of some importance in delayed hypersensitivity[15].

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Diurnal Changes in the Topographical Distribution of Glycogen in the Brain of *Iguana iguana*

RECENTLY I investigated the topographical distribution of glycogen in the brain of *Iguana iguana* in relation to the environmental temperature, and in animals with glycogen-accumulation disease[1]. It appeared that a decrease in environmental temperature results sometimes in a decrease in concentration of the glycogen in the brain tissue, and in some cases an increase, for in animals with heptomegalia glycogenica the glycogen concentration in the tissue of the cortex cerebri, the diencephalon, the mesencephalon, the cerebellum and the medulla oblongata increases significantly.

In continuation of these experiments the diurnal changes in the brain glycogen of *Iguana* were investigated. For this purpose the concentration of the brain glycogen was determined in 60 males and 60 females at 6-hr. intervals in the five topographical regions of the brain mentioned. The environmental temperature at which the animals were kept was 36·8 ± 0·3° C. For the glycogen determination I used Kerr's method[2], the reduction compounds being determined by Nelson's method[3] (see also in this connexion the paper of Jakoubek and Svorad[4]). The glycogen values are given in mgm./100 gm. fresh brain tissue in Table 1. For the determination of each value 15 animals were used.

As can be seen from Table 1, there are no significant periodic changes in the cortex cerebri, the mesencephalon, the cerebellum and the medulla oblongata. However, in the diencephalon a significant difference in the glycogen concentration can be seen.

Thus, the changes in concentration of the brain glycogen not only run parallel to several altered states of behaviour in the individual[6,7], but are also related to the autonomic functions, which are regulated at the highest level.

These results correspond with those of Svorad[5] obtained in the rat.

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Table 1. DIURNAL CHANGES IN GLYCOGEN CONCENTRATION IN THE BRAIN OF *Iguana iguana*. THE GLYCOGEN VALUES ARE GIVEN IN MGM./100 GM. FRESH BRAIN TISSUE. FOR THE DETERMINATION OF EACH VALUE 15 ANIMALS WERE USED. M, MALE; F, FEMALE

Parts of the brain	Sex	Astronomical time 1 hr.	7 hr.	13 hr.	19 hr.
Cortex cerebri	m	88·1 ± 3·9	84·6 ± 6·0	86·3 ± 4·6	87·2 ± 4·7
	f	86·9 ± 5·4	83·9 ± 4·1	85·8 ± 5·1	85·9 ± 3·9
Diencephalon	m	104·9 ± 5·7	121·9 ± 4·9	124·7 ± 6·0	114·9 ± 5·8
	f	107·2 ± 4·0	123·6 ± 5·7	126·1 ± 4·8	117·2 ± 4·9
Mesencephalon	m	117·1 ± 5·1	111·8 ± 4·7	114·2 ± 7·1	115·3 ± 6·0
	f	116·3 ± 4·3	110·7 ± 4·3	113·1 ± 6·0	114·8 ± 5·5
Cerebellum	m	80·9 ± 5·9	78·1 ± 6·0	80·7 ± 5·1	81·4 ± 5·9
	f	82·3 ± 5·6	79·8 ± 4·5	82·5 ± 4·2	83·1 ± 5·3
Medulla oblongata	m	112·0 ± 4·7	107·5 ± 5·6	109·3 ± 4·7	109·0 ± 4·2
	f	113·4 ± 5·7	110·1 ± 3·8	111·6 ± 5·3	110·2 ± 5·8

Muscular Dystrophy in the Siamese Fighting Fish as an Aberration of the Connective Tissue

RECENTLY I carried out a histochemical study of the ability of connective tissue in normal muscles and atrophied muscles of *Iguana iguana* to dephosphorylate various high-energy phosphates derived from adenosine monophosphate and some other compounds[1].

In continuation of this work I carried out a corresponding investigation in a fish, namely, the Siamese fighting fish *Betta splendens* Regan, belonging

to the family Anabantidae. In this species a distinct senile period occurs, in which the animals are seen to move slowly near the surface of the water. For this investigation very old specimens were used, in which a progressive muscular dystrophy had occurred.

For the determination of the 5-nucleotidase activity of the material, the histochemical methods of Beckett and Bourne[2] were used.

Since adenosine monophosphate is dephosphorylated by 5-nucleotidase, the ability of the connective tissue to bring about dephosphorylation of various high-energy phosphates derived from adenosine monophosphate in the normal and atrophied muscles of *Betta* was investigated. In addition, some other phosphate compounds of a certain physiological importance and some other esters were investigated. These substances were adenosine diphosphate, adenosine triphosphate, creatine phosphate, acetyl phosphate, cytidine, inosine, guanosine, pyridoxal phosphate, thiamine pyrophosphate, riboflavin-5-phosphate, diphosphopyridine nucleotide, triphosphopyridine nucleotide, phosphoglyceraldehyde, hexosediphosphate, fructose-1- and 6-phosphates and glucose-1- and glucose-6-phosphates. The histochemical reactions of all these compounds were compared with that of β-glycerophosphate.

In the 81 cases of muscular dystrophy in *Betta*, with the exception of creatine phosphate, dephosphorylation of the above-mentioned high-energy phosphate compounds by the elements of the connective tissue and by a number of the muscle fibres was observed. However, the intermediate glycolytic compounds showed no hydrolysation.

By the dephosphorylation experiments in fourteen of the 81 cases I was able to establish a dephosphorylation of thiamine pyrophosphate. The co-enzymes pyridoxal phosphate and riboflavin-5-phosphate could not be demonstrated to be affected.

In all cases of progressive muscular dystrophy in *Betta* the elements of the connective tissue were found to dephosphorylate the diphosphopyridine nucleotide and the triphosphopyridine nucleotide. Just as in the muscular dystrophy of man[3] and of *Iguana*[1], in the case of the diphosphopyridine nucleotide a stronger dephosphorylation was observed than in that of the triphosphopyridine nucleotide.

Summarizing, we may conclude that in the elements of the connective tissue surrounding the muscle fibres, enzymes destructive of compounds vital to muscular metabolic processes have been identified with certainty. These enzymes must no doubt play a certain part in the genesis of the progressive muscular dystrophy.

Just as is the case in man[3] and in *Iguana*[1], the pathological changes in the muscles of *Betta* in progressive muscular dystrophy consist of an increase in number of the sarcolemmal nuclei, an atrophy of the muscle fibres, a great diversity of the size of the muscle fibres, a proliferation of the elements of the connective tissue and storage of varying amounts of fat. The sarcolemmal nuclei may assume the form of chains localized centrally in the muscle fibres. Between these changes and those in progressive muscular dystrophy in man there is a good correspondence.

Adams, Denny-Brown and Pearson[4] arrived at the conclusion that phagocytosis of degenerating muscle fibres is rare. Bourne and Golarz[3], however, found evidence in a number of cases for what appears to be an invasion and a destruction of muscle fibres by the neighbouring connective tissue.

Bourne and Golarz[3], who by their study of ten cases of progressive muscular dystrophy in man obtained corresponding results, have given three possible interpretations, namely: (1) The primary defect may still be in the muscle-fibre membrane. In this connexion, the diffusion of the phosphate esters from the muscle fibres into the neighbouring medium may result in the adaptive synthesis of certain enzymes to hydrolyse them in the elements of the connective tissue. (2) The synthesis of the metabolically very important phosphate compounds occurs in the muscle fibres, but nevertheless there may be some leakage in the normal metabolism, much in the same way as the vitamin A leaks away from the retina in the retinene-cycle. The replacement of this leakage by transport from the lymphatic and the vascular system, if there is inadequate synthesis by the muscle fibres themselves, would be prevented by the connective tissue elements, which contain the appropriate phosphorolytic enzymes. (3) The production of the hydrolytic enzymes by the elements of the connective tissue may lead to diffusion of these enzymes into, as well as adsorption on to, the membrane of the muscle fibres, and possibly penetration of this membrane, resulting in a complete blockage of the normal metabolic processes of these fibres.

Comparing these possible interpretations, Bourne and Golarz[3] came to the conclusion that the fundamental defect in progressive muscular dystrophy in man may be in the elements of the connective tissue supporting the muscle fibres, and not in these fibres themselves (possibility 1).

On the other hand, possibility 2 is not sufficiently in agreement with current views on the metabolic processes in the muscle fibre. Possibility 3 is not so probable either, because the penetration of the sarcolemma by the hydrolytic enzymes has still to be established. It is not improbable that the accumulation of such a range of phosphatases at this site might break down its structural integrity as well as its selective permeability.

My results obtained in the muscular dystrophy of *Betta* and of *Iguana*[1] point in exactly the same direction, and may therefore be an argument for the concept that an aberration of the neighbouring connective tissue is the primary cause of the muscular dystrophy in fishes as well as reptiles.

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Initiation of Mammary Secretion in Rats by Electrical Stimulation of Nervous System

DURING recent years the interaction of neural and endocrine factors in the initiation of mammary secretion in different species of animals is being increasingly recognized, and it has been shown that electrical stimulation of the uterine cervix of œstrogen-primed virgin female rats can initiate mammary

secretion[1]. In the present experiments, attempts were made to determine whether electrical stimulation of other areas would similarly result in mammary secretion.

Virgin female rats were injected subcutaneously daily with 10 μgm. œstradiol for 10 days to develop their mammary glands. For the following 5 days, groups of rats were electrically stimulated for 30 sec. twice daily in the regions of the head, lumbar vertebræ, nasal mucosa and nipples. Control rats were injected twice daily with saline for 5 days. On the sixteenth day, the rats were killed, and the right inguinal mammary glands were removed for histological preparations. The mammary glands of the controls regressed to a bare duct system, whereas almost all the electrically stimulated rats showed maintenance of the mammary lobule-alveolar system and initiation of lactation. These results suggest that electrical stimulation of the central nervous system induces release of prolactin and adrenocorticotrophic hormone from the anterior pituitary, since both hormones are required to induce mammary secretion in the œstrogen-primed rats.

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HÆMATOLOGY

Anti-i : a New Cold Antibody

IN 1956 Wiener and his colleagues[1] described an antibody occurring in a case of cold antibody hæmolytic anæmia which they called anti-I. The I antigen has an almost universal distribution, but five examples of i cells were found in testing 22,000 donors. It was considered that the Ii phenotypes arose by the action of two allelomorphic genes *I* and *i*, individuals of the phenotype i being *ii*.

More recently, Jenkins *et al.*[2] have described an English donor whose cells are i and whose serum contains a naturally occurring anti-I that is not auto. Using these cells, the antibodies in a number of other cases of cold antibody hæmolytic anæmia were also found to have I specificity. At the same time Tippett *et al.*[3] have reported a number of blood samples that are extremely weak in I although not as weak as the i donor of Jenkins *et al.* The serum of these people also contains anti-I that is not auto.

The results of the above workers show clearly that i cells also contain some I, but an enormous gulf separates them from the I of normal adults. Cord-blood cells were also found to be extremely weak in I.

Recently, we encountered a remarkable antibody that appears to clarify the Ii relationship in human red cells. This antibody was found in the serum of a patient not yet diagnosed but probably suffering from a reticulosis.

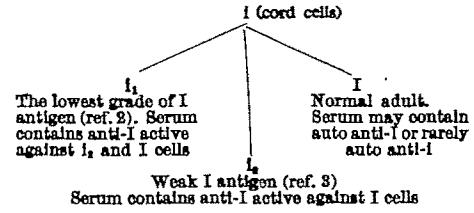
The serum of this patient weakly agglutinated his own and 500 normal adult red cell samples at low temperature (average titre at 12° C. about 1 in 16). Tests with three examples of i cells and five examples of the slightly stronger variant described by Tippett *et al.* all gave strongly positive results with titres ranging from 1 in 32,000 up to 1 in 250,000, the three i samples all giving maximum titres. More than 40 cord blood samples were tested and all gave strong reactions similar to adult cells of the i phenotype.

Repeated absorptions of the serum with various cells showed that a single antibody was present reacting powerfully with i and cord cells and weakly with adult I cells. Clearly this antibody has anti-i specificity. Electrophoretic studies have shown that the antibody is present in the β-globulin fraction of the serum.

Tests on a number of infants of various ages show that within 18 months of birth the i reaction becomes steadily weaker while the I reaction becomes stronger until the normal adult relationship of strong I and weak i is established. It appears that all normal adult and infant samples have some I and some i, and cells that are strong in I are weak in i and vice versa.

It is clear that the abnormality found in the cells of the rare adults of the i phenotype is not that they are i, for everyone is probably i for a few weeks of life, but that the I has failed to develop. This type of reaction surely cannot reflect the action of *I* and *i* as allelomorphic genes. We think that the abnormality found in these i adults is caused by the absence of a genetically controlled factor that is essential for the proper development of I.

Our results have shown that the anti-i serum is able to place people very precisely on the I scale in an indirect way by measuring the amount of i that they possess. In view of this the following terminology in the I group system is suggested:



Details of these results will be submitted for publication elsewhere.

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Ageing of Hæmoglobin

THE problem of ageing of protein molecules has been considered by several authors. Kunkel[1] in man, Ranney[2] in the rabbit, have attempted to demonstrate the ageing of hæmoglobin, taking advantage of the metabolic heterogeneity of hæmoglobins described by us in 1950[3]. They observe, indeed, during the life of the red cells, an equalization of the specific activities of hæmoglobin fractions which were unequal initially. These authors were using iron-59, and it is known that iron is re-utilized after the death of the red cells: this prevents observation of an eventual crossing of the specific activity curves of different fractions in the course of the ageing of the

red cells. Therefore they cannot decide between the two following hypotheses: (1) there are metabolic exchanges between the fractions, contrary to the theory of the metabolic inertness of hæmoglobin; (2) there is ageing of part of the hæmoglobin, which during this process changes its electric charge and becomes concentrated in one of the fractions.

In an attempt to overcome this difficulty, we used valine labelled with carbon-14, which we injected intraperitoneally into rabbits weighing 2–3 kgm. at a dosage of 8 μc./kgm. Blood was removed at various intervals from 1 to 80 days after injection.

Hæmoglobin was prepared as the carbon monoxy derivative and purified by salting out[4]. Checks of purity were made by starch-gel electrophoresis in phosphate buffer *p*H 6·5, μ 0·033 (ref. 5). The hæmoglobin samples were then submitted to electrophoresis on starch blocks in veronal buffer *p*H 8·6, 0·05 *M* for 16 hr. under 5 V./cm.

Under such conditions we obtained two fractions: a major one (R_1) and a minor one which migrated more towards the anode (R_3). No fraction corresponding to hæmoglobin A_2 was observed in the rabbit. The respective amounts of main and minor fractions were 90 and 10 per cent. These percentages were relatively constant from one rabbit to the other and did not vary for the same rabbit.

Each fraction was eluted with water and centrifuged at 15,000*g* for 1 hr. The eluates were precipitated with trichloracetic acid, washed several times with water, acetone and ether, and dried *in vacuo*. The powders so obtained were prepared as pellets (compression, 5,000 lb. per sq. in.). Their activity was then determined with a flow counter and the specific activity computed after correction for thickness.

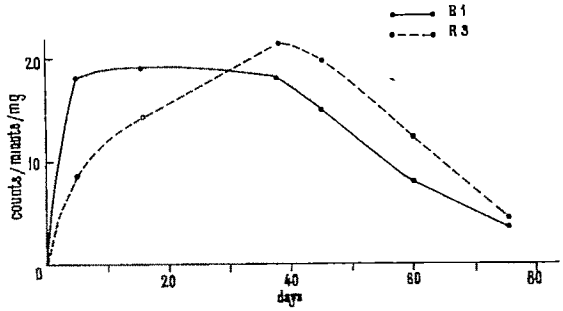

Fig. 1. Variations of specific activity of the two fractions of rabbit hæmoglobin at different times

Fig. 1 shows how the specific activity of the two fractions varies; the results from one rabbit only was used for this graph. The experiment was repeated on six different rabbits, and results are given in Table 1.

The specific activity of R_1 increases up to a plateau, which is reached after 5 days and is maintained for about 40 days, after which it declines. That of R_3 is initially lower; it reaches and passes that of R_1 near the thirty-fifth day and then begins to decrease without showing a plateau, but it remains higher than R_1.

These observations confirm once more the metabolic heterogeneity of rabbit hæmoglobin. On the other hand, the inversion of the ratio of the specific activity of the hæmoglobin fractions according to time is a completely new fact. It involves a progressive enrichment in ^{14}C valine of the R_3 fraction with time.

Table 1. RATIO OF SPECIFIC ACTIVITY, R_3/R_1

	Days after the injection	Ratio
Rabbit No. 1	5	0·60
	16	0·75
	37	1·18
	45	1·30
	60	1·30
	80	1·20
Rabbit No. 2	6	0·70
	23	0 70
	50	1·20
	72	1 00
Rabbit No. 3	5	0 67
	39	1·00
	55	1·40
Rabbit No. 4	1	0·32
	4	0·52
	46	1·25
	60	1 20
Rabbit No. 5	27	0 75
	46	1 30
Rabbit No. 6	21	0·75
	23	0·82
	52	1·28
	59	1 18

This fact cannot be explained only by metabolic exchanges between the two hæmoglobin fractions, which could at most give rise to an equalization of the specific activities. The most likely explanation is that, during the ageing of the red cell, part of the hæmoglobin itself undergoes modification. It becomes more electronegative, which changes its motility. So after the fortieth day the anodic fraction contains a high proportion of the labelled hæmoglobin. Its specific activity becomes greater than that of the main cathodic fraction, the radioactivity of which has been diluted by a large amount of newly synthesized, and therefore non-labelled, hæmoglobin. These modifications must be distinguished from those observed on blood aged *in vitro*[6], but their nature may be the same. Electrophoretic modifications of hæmoglobin have been described[7] in red cells aged *in vivo*; but these modifications may be due to difference in the molecular environment in the red cell with ageing. Our observations lead to the assumption of a change of hæmoglobin configuration, involving exteriorization of negative polar groups or, on the other hand, dissimulation of positive polar groups.

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PATHOLOGY

An Effect of Early Dilution on the Establishment of Lysogeny in *Salmonella typhimurium*

It is known that the frequency of lysogenic response in a culture of *Salmonella typhimurium* strain *LT*2, infected with the temperate bacteriophage *P*22, can be influenced by the ratio of phage to bacterium (multiplicity of infection)[1-3], and by modifying the metabolism of the infected cells soon after infection, for example, by the addition of chloramphenicol[4]. With a high multiplicity of infection a high frequency of lysogenic response is obtained. Using a low multiplicity of infection a low lysogenic response results. If these infected cells are exposed to chloramphenicol (25 μgm./ml.) 5 min. after infection and the chloramphenicol removed by dilution 15 min. later, then practically every cell infected becomes lysogenic.

We have been examining the effect of lower concentrations of chloramphenicol in contact with cells infected with a low multiplicity of infection (2·8) for a shorter period of time. Fig. 1 shows that a concentration of 5 μgm./ml. in contact with the cells for 7 min. is sufficient to reverse the 'decision' of the majority of the cells to lyse. What is more interesting is that the infected control culture shows a high frequency of survivors when sampled and diluted into buffer 5 min after infection. This high frequency of survivors decreases with time until it reaches a minimum at 12 min. In all our previous experiments the control value for lysogenic response was measured at the end of the experiment and thus gave this minimum value.

In view of these results, measurements were made of the frequency of lysogenic and lytic responses of a similarly infected culture when samples were removed and diluted into buffer at room temperature during the first 15 min. after infection. The results are shown in Fig. 2. There is an evolution of the lysogenic response during this period rising to a maximum 6 min. after infection, decreasing to a minimum at 12 min. The lytic response complements the lysogenic response. These results were later found to be true, even when dilutions were made into broth or buffer at room temperature (26·5° C.) or 37° C.

Under the conditions of the experiments above, 80 per cent of the cells would have been infected with at least one phage particle by 2 min. At 6 min., 95 per cent would be infected. This may account for the rise in lysogenic response between 2 and 6 min. after infection.

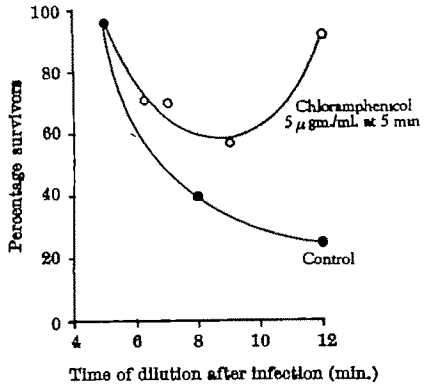

Fig. 1. Effect of dilution on survival of *LT*2 cells infected with phage *P*22, with and without chloramphenicol

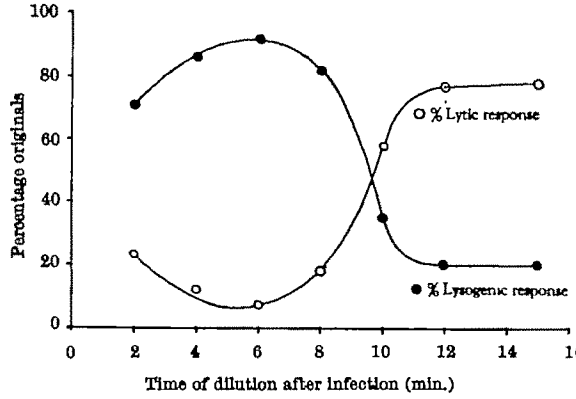

Fig. 2. Effect of dilution on lysogenic and lytic responses in *LT*2 cells infected with phage *P*22

Chloramphenicol is said to reverse the 'decision' of a cell to lyse by virtue of its ability to inhibit protein synthesis[4]. The results reported in this communication indicate that dilution into fresh medium is equally effective if carried out before the 'decision' period is reached. This 'decision' period was shown by Lwoff to be 6–10 min. after infection in *S. typhimurium* infected with an *A*1 phage[2]. The importance of dilution in a lytic phage system has been reported by Lanni[5], who showed that in the *T*5-*E. coli F*' system dilution of high bacterial concentrations is necessary to stabilize the phage–host complex.

It would be interesting to know whether the effect of early dilution reported here has been found in other lysogenic systems or is restricted to *S. typhimurium*.

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A Filterable Hæmolysin from *Escherichia coli*

Some strains of *Escherichia coli* are hæmolytic when grown on blood-agar, and attempts made to demonstrate a soluble hæmolysin in culture filtrates are usually unsuccessful. We have been able to obtain hæmolytic filtrates with four such strains when grown in a culture medium prepared as follows.

A pound of lean beef is cut into small pieces and boiled in 500 ml. of *N*/20 aqueous sodium hydroxide. After simmering for 15 min. it is strained through a muslin cloth, and excess fluid removed. The meat is dried by pressing between filter paper and placed in a flask to which 500 ml. of infusion broth is added; the *p*H is adjusted to 7·6. The medium is sterilized by steaming for 24 hr. and autoclaving for 20 min. at 120° C.

Three of the strains used (0138 : *K*81*B*, 0139 : *K*82*B*, and 0141 : *K*85*B*) were recovered from diseased

pigs[1] and the fourth (*RVC*58—the antigens of which are not yet determined) from diseased calves[2]. The cultures were incubated at 37° C. for 2, 4, 6, 8, 10, 12, 18, 24, 48 and 96 hr., and filtered through 'Ford *SD* Sterimats' at a negative pressure of about 150 mm. of mercury. The filtrates were collected and diluted with physiological saline; they were tested against 1 per cent (final concentration) washed rabbit red cells at 37° C. Examinations were made at half-hourly intervals.

Hæmolytic activity occurred with filtrates from cultures 4–24 hr. old, the maximum activity being with cultures of 6–10 hr. The titre rarely exceeded 1 : 32, and no filtrate prepared from cultures grown for 48 or 96 hr. was hæmolytic. There was little variation in the *p*H of these filtrates (about 7·4–7·6) and all were sterile. The first portion of the fractions passing the filter was always non-hæmolytic, due probably to some absorption by the filter pad.

The hæmolysin is thermo-labile. Filtrates from 6-hr. cultures lost about half their activity when stored at 4° C. for six days, and when left overnight on the bench. Activity was reduced after 18 hr. at 37° C., while it was destroyed after 15 min. at 56° C.

Cultures were incubated in atmospheres of carbon dioxide and of hydrogen, and filtrates from these were also hæmolytic but less active. There was no evidence of a hæmolysin in filtrates from cultures grown in 1 per cent peptone water, infusion broth, 2 per cent, 6 per cent and 10 per cent serum broth.

The hæmolytic activity could be removed by treatment of the filtrate with 30 per cent aqueous ammonium sulphate. The precipitate, when redissolved, dialysed and made isotonic, was less active than the original filtrate and this decrease may be associated with the labile nature of the hæmolysin. Similar precipitates prepared from uninoculated media and a filtrate from a 6-hr. culture of a non-hæmolytic strain were non-hæmolytic.

According to Kunicki-Goldfinger *et al.*[3], hæmolysis induced by strains of *E. coli* is due to the products of autolysis. Our findings are not in accord with this, since hæmolytic activity appears to be confined to young cultures. After 10 hr. incubation this activity declines.

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Development of a Leukæmia resistant to Cyclophosphamide ('Cytoxan')

THE alkylating agent, N,N-bis-(β-chlorethyl)-N′, O-propylenephosphoric acid ester diamide[1] (*B*-518, *cyclo*phosphamide, 'Endoxan', 'Cytoxan'), has been markedly effective in suppressing the growth of a variety of transplanted tumours in rats[2,3] and mice[3]. The mechanism of activation of this agent has not been determined. It is known that the drug is not cytotoxic *in vitro*, but is activated *in vivo*[4]. Nicotinamide has been reported to prevent the toxic and antitumour effects of 'Cytoxan'[5]. However, the relationship of nicotinamide or diphosphopyridine nucleotide to either the activation or the action of this alkylating agent is unknown. Resistant tumours have proved valuable for the study of the mechanism of action of chemotherapeutic compounds. Sublines resistant to alkylating agents and derived from previously sensitive tumours are uncommon and have not been investigated extensively. It was thought that if a tumour resistant to 'Cytoxan' could be developed, it might provide a useful model for the study of the action of this alkylating agent.

The *L*-1210 leukæmia was selected for study because it was sensitive to 'Cytoxan'[6], it could be carried in the ascites form, and it has been employed by others in studies of resistance to various antitumour agents. It has been reported that the effectiveness of 'Cytoxan' in increasing the median survival of mice with advanced *L*-1210 leukæmia was markedly enhanced by a schedule of once-weekly drug administration compared to more frequent treatment[7]. This finding suggested that the isolation of a resistant variant might be facilitated by the use of large single doses of 'Cytoxan'.

Sensitive *L*-1210 leukæmia was originally obtained from Dr. Lloyd Law. Four groups of *CDBA* mice were given intraperitoneal injections of 1–5 million leukæmic cells. Three groups of 7 mice each were treated 24 hr. later with a single intraperitoneal injection of 'Cytoxan' of 150, 180, or 200 mgm./kgm. An untreated group served as a survival control. The first mouse to develop extensive ascites in the 200 mgm./kgm. treatment group was considered most likely to harbour resistant leukæmic cells. Ascites was transferred from this animal into mice for the succeeding experiment. These animals were similarly grouped and treated. This procedure was repeated serially. The median survival for untreated mice was 7–10 days. The median survivals of mice treated with 200 mgm./kgm. exceeded those of untreated mice by 88–143 per cent. Resistance was recognized in the seventh transfer generation by a decrease in median survival of treated mice to 30 per cent beyond controls. This resistant tumour was carried in the absence of drug for 12 generations, and maintained its resistance, as shown in Fig. 1. The percentage increase in median survival beyond controls for the

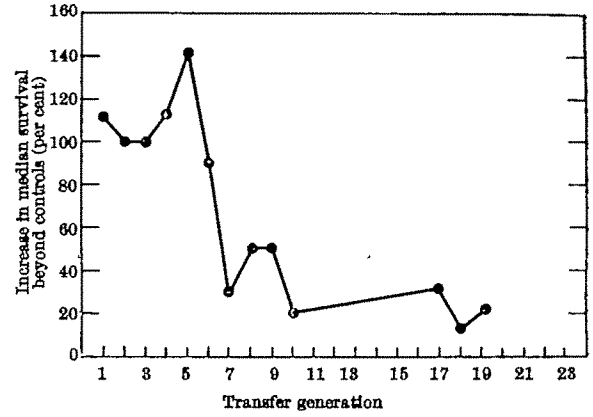

Fig. 1. A group of 7 mice in each transfer generation received 'Cytoxan' intraperitoneally, 200 mgm./kgm., one day after tumour implantation. The percentage increase in median survival beyond controls is shown. *CDBA* male mice were used

200 mgm./kgm. group is plotted for each transfer generation. Grossly and microscopically, the characteristics of this resistant variant, designated *L*-1210/*Cy-R*, and the parent leukæmia are similar, as are the courses of the disease produced by each.

Resistance was also demonstrated by the following experiments. A single intraperitoneal injection of 'Cytoxan' of 250 mgm./kgm. was given to mice 1 hr. after subcutaneous implantation of 10^5 tumour cells of the sensitive leukæmia. The drug prevented these cells from becoming established, and treated mice survived. Mice similarly treated after implantation with *L*-1210/*Cy-R* tumour cells, however, died of leukæmia. Fig. 2 shows the effects of repeated weekly intraperitoneal treatment on the survival of mice bearing 5-day implants of the sensitive and resistant leukæmias. A 275 per cent increase in survival beyond controls was obtained with mice bearing the sensitive leukæmia, compared with only 30 per cent for those with the resistant subline.

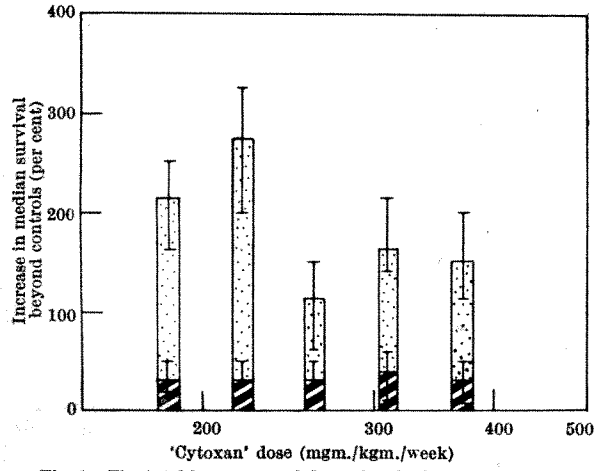

Fig. 2. The total bar measured from the abscissa represents the percentage increase in median survival beyond controls for 10 mice with the sensitive leukæmia (stippled areas), and for 10 mice with the resistant leukæmia (hatched areas). Fifteen untreated controls were used for each leukæmia. *CDBA* male mice were used. Intraperitoneal implant. Treatment: intraperitoneal weekly from the fifth day

L-1210/*Cy-R* is now in the forty-second transfer generation in the absence of drug exposure and has remained resistant. Preliminary experiments indicate that *L*-1210/*Cy-R* is sensitive to treatment with the antimetabolites, 6-mercaptopurine and 'Methotrexate', but cross-resistant to the alkylating agents uracil mustard, triethylene melamine, and triethylene thiophosphoramide.

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RADIOBIOLOGY

Localization of Radioactivity in Tumours of Mice injected intravenously with Killed, Radioiodinated *Brucella abortus*

WORKERS studying the phagocytic activity of tumour cells seem to prefer *in vitro* systems[1,2]. Little work appears to have been done on the ability of tumour cells to take up colloidal or particulate substances *in vivo*. Because of the possible practical importance of the subject, it was decided to study the reticulo-endothelial activity of mouse tumours. Acetone-killed, radioiodinated *Brucella abortus* (^{131}IBr) were chosen as the test particle, since previous work[3] had shown that these bacteria are a very sensitive indicator of phagocytic activity.

Mice bearing 14–16 day old Krebs's carcinoma or 8–12 day old sarcoma-37 were used. The carcinoma was implanted into the femoral muscles of the left hind leg. The sarcoma was implanted under the skin in the region of the dorsal or lumbar vertebræ. Transplantation was performed with either trocar or syringe. In the latter case, 0·1–0·5 ml. of a dense suspension of tumour cells in phosphate buffer saline, *p*H 7·2, were injected. Details on preparation of bacteria, iodination and counting techniques, etc., have already been described[4].

Groups of 5–6 mice bearing sarcoma-37, as well as untreated controls, were given intravenously (into the tail vein) 0·1 mgm. labelled *Brucella* in 0·2 ml. saline. The mice were killed after 1 hr. and the organs removed for radioactivity determinations. Blood samples were obtained by bleeding the mice from the cut neck blood vessels, while under ether anæsthesia. The blood was collected in tubes containing citrate or heparin as anticoagulants. In several experiments, the radioactivity in tumours of mice injected with ^{131}IBr was compared with that in tumours of mice injected with radioactive iodide. In these experiments the procedure was somewhat modified: immediately before injecting the labelled material, 5 mgm. sodium iodide were administered intra-abdominally to all mice. An additional 0·8 mgm. sodium iodide was included in the intravenous inoculum. The mice were killed 5 hr. after injection. This procedure was adopted in order to reduce the uptake of labelled iodide by the tumours.

The results are summarized in Table 1; they show that in both types of experiments a significant amount of radioactivity was found in the tumours. The distribution of the label injected as iodide was completely different from that of the label injected as iodinated bacteria.

The amount of radioactivity in Krebs's carcinoma was smaller than in sarcoma. At 1 hr. after inoculation, carcinoma-bearing legs contained about 3 per cent of the injected radioactivity, as compared to 1 per cent in the normal leg.

The radioactivity in the tumours was, in general, proportional to the weight of the tissue, although this relationship did not always hold for the individual animals. Approximately 2·4 per cent of the injected radioactivity could be found in 1 gm. of tumour at 1 hr. after inoculation.

These experiments, while demonstrating the localization of radioactivity in the neoplasms, did not provide any clues as to the mechanism involved. Attempts to detect intracellular *Brucella* in tumour

Table 1. MEAN RADIOACTIVITY IN ORGANS OF MICE INJECTED WITH RADIOIODINATED *Br. abortus* OR RADIOACTIVE IODINE (PER CENT OF INJECTED RADIOACTIVITY)

Exp. No.	Description of mice	Material injected	Radioactivity in organs				Remarks
			Tumour	Spleen	Liver	Blood (1 ml.)	
1	Normal	Iodine-131 *Brucella*	—	9·7	23·9	9·5	Organs removed 1 hr. after injection of label
	Tumour-bearing*	Iodine-131 *Brucella*	6·1	6·1	27·7	6·9	
2	Tumour-bearing	Iodine-131 as iodide	1·1	0·06	0·5	1·0	Organs removed 5 hr. after injection of label
	Tumour-bearing	Iodine-131 *Brucella*	3·1	9·7	21·0	1·3	

* This group contained six animals. All others contained five animals. The radioactivity bound to *Brucella* was 96,000 c.p.m. That injected as iodide was 121,000 c.p.m.

smears stained with May–Grünwald–Giemsa were inconclusive, apparently because of the small size of this organism. When, however, a dense suspension of heat-killed group *A Streptococci* were injected, unmistakable proof of phagocytosis by both neoplastic and stroma cells was obtained (Fig. 1). It should be added that much less radioactivity was localized in the tumour with labelled *Streptococci* than that with labelled *Brucella*.

It appears, therefore, that phagocytosis is at least one of the mechanisms leading to concentration of radioactivity in the tumour tissue. It will be interesting to see whether these results can be reproduced in man, since they might form the basis of an additional diagnostic tool for the detection of cancer. Full details of this work will be published elsewhere.

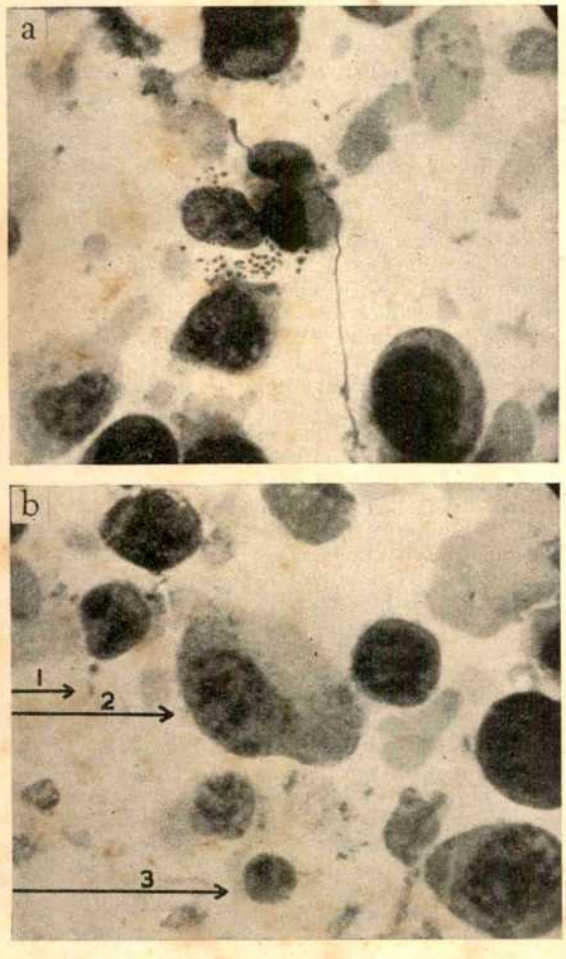

Fig. 1. *a*, *Streptococci* phagocytosed by tumour stroma cell: *b*, 1, extracellular cocci, 2, two pairs of cocci engulfed in nuclear vacuoles of malignant cell, 3, one pair of cocci in the process of being phagocytosed

I am grateful to Prof. J. Gross, of the Department of Experimental Medicine and Cancer Research, for discussions and suggestions during the course of this work, to Mr. G. Rasooly and Miss N. Grünwald for technical assistance, and to Dr. M. Pikovski for the supply of tumours.

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Rate of Formation of Atropine in *Atropa belladonna* Plants

WE have studied the biogenesis of atropine-^{14}C in *Atropa belladonna* plants by a method which we believe to be novel in this field, but which is comparable with that applied so successfully by Calvin[1] to the elucidation of the path of carbon in photosynthesis.

A number of complete plants 2–3 months old were allowed to assimilate a single dose of carbon-14 dioxide by photosynthesis in the leaves, and were then left to continue growth under normal greenhouse conditions. At various intervals plants were killed and extracted to determine the soluble and insoluble activity remaining in the shoots and roots, and the activity in the form of atropine.

In a typical experiment, a 2–3 month old *Atropa belladonna* plant was placed in a photosynthesis chamber and fed with carbon-14 dioxide (1 mc.). It was found that more than 90 per cent of the activity was taken up by the plant during 4 hr. photosynthesis. The plant was removed from the photosynthesis chamber and grown under hydroponic conditions with the roots immersed in nutrient solution[2], in a greenhouse. After a suitable time of 'active' growth, the shoots and roots separately were continuously extracted for three days with boiling 80 per cent aqueous ethanol (about 250 ml.) and the activity of the extracts measured. Most of the solvent was removed under reduced pressure, and 0·2 *N* sulphuric acid (200 ml.) added. This acid solution was extracted with chloroform/ether (20 : 80) until the extracts were colourless, and after basifying the aqueous solution with ammonia, the alkaloids were extracted with the same solvent mixture. The alkaloid extract was dried with sodium sulphate, the solvents removed

Table 1

Plant No.	Active growth (time in days)	Soluble shoot activity (μc.)	Soluble root activity (μc.)	Total soluble activity (μc./gm. dry weight)	Insoluble shoot activity (μc.)	Insoluble root activity (μc.)	Total insoluble activity (μc./gm. dry weight)	Dry weight of plant	Ratio of atropine activity in μc./gm. dry weight to activity remaining in plant in μc.	Ratio of atropine activity in μc./gm. dry weight to soluble activity in μc.
1	0·2	465	4	260	148	1	83	1·82	$0·071 \times 10^{-6}$	$0·094 \times 10^{-6}$
2	4	216	39	333	201	8	270	0·77	35×10^{-6}	64×10^{-6}
3	5	*	*	91	*	*	200	2·0	39×10^{-6}	237×10^{-6}
4	6	199	61	230	301	30	290	1·15	83×10^{-6}	190×10^{-6}
5	7	190	39	153	333	43	295	1·53	21×10^{-6}	56×10^{-6}
6	10	*	*	200	*	*	350	0·81	115×10^{-6}	248×10^{-6}
7	13	*	*	140	*	*	85	2·16	21×10^{-6}	33×10^{-6}
8	16	*	*	62	*	*	110	2·17	60×10^{-6}	160×10^{-6}
9	20	94	13	80	275	67	300	1·13	136×10^{-6}	571×10^{-6}
10	21	102	2	70	247	35	230	1·24	83×10^{-6}	308×10^{-6}
11	22	44	10	50	150	41	170	1·11	120×10^{-6}	540×10^{-6}
12	23	42	5	55	94	50	160	0·86	164×10^{-6}	666×10^{-6}
13	25	*	*	90	*	*	200	1·43	118×10^{-6}	380×10^{-6}
14	30	*	*	35	*	*	90	2·67	27×10^{-6}	103×10^{-6}
15	31	61	44	50	133	92	100	2·21	220×10^{-6}	71×10^{-6}

* Not determined.

under reduced pressure, and the alkaloids purified by chromatography on paper in butanol/water/acetic acid[3]. The atropine was washed from the paper, and carrier atropine (100 mgm.) was added and then converted into the picrate, which was crystallized several times from hot water and had melting point 176° C. Dilution analysis of the atropine-^{14}C picrate indicated a radiochemical purity greater than 98 per cent.

The picrate was burnt in a stream of dry oxygen and the carbon-14 dioxide absorbed in hot barium hydroxide. The precipitated barium carbonate-^{14}C was counted in a calibrated 2π-flow counter using argon/methane (90 : 10) as the flow gas. The insoluble plant residues were ground to a fine powder and also converted into barium carbonate-^{14}C by combustion in oxygen as above. The activity of the barium carbonate in this case was measured with an end-window counter.

The results of a typical series are presented in Table 1.

The figures are erratic, and we consider that experimentation on a larger scale than we were able to undertake is called for to achieve results which will be statistically more than roughly quantitative. We wish, however, to direct particular attention to the figures in the last column, which show the atropine activity by comparison with the soluble activity, both derived solely from the single initial dose of carbon-14 dioxide. A pronounced maximum is shown at 20–25 days, and a less pronounced maximum at 5–10 days. The total soluble activity, however, reaches a maximum within a few hours and thereafter decays, roughly exponentially, to about 40 per cent at 7–10 days and 20 per cent at 21 days, of the initial value. The total insoluble activity at first increases rather slowly and then falls off.

We think that these results of a preliminary investigation are relevant to the question of whether the biogenesis of atropine (or indeed of alkaloids generally) is an 'upgrade' process from small molecules or a 'downgrade' process from larger molecules[4]. In conjunction with published results from precursor studies[5], they lead us to suggest that both processes are involved but that a 'downgrade' process plays the greater part, since the maximum atropine labelling appears so long after the activity and specific activity of the soluble carbon-14 have passed their maximum values.

These experiments arose from what was originally planned to be a series of experiments with labelled precursors to obtain evidence on the theories put forward by Robinson[6,7]. Some biosynthetic atropine-^{14}C was desired in the first place to investigate the rate of turnover in the plant, and we were surprised to find that a fairly long period was required to produce appreciable labelling from a dose of carbon-14 dioxide. Evidence on this rate of turnover is still lacking. We have, however, fed methylamine-^{14}C hydrochloride (1 mc., 3·6 mgm. in 180 ml.) via the roots of *Atropa belladonna* plants and extracted the atropine after nine days. Although the amine was readily taken up by the plant, the atropine activity (in μc./gm. dry weight/μc. of activity remaining in the plant) was only 37×10^{-6}. This comparatively low figure suggests that methylamine as such is not in fact directly incorporated in the biogenesis of atropine.

We believe that the method of a single dose of carbon-14 dioxide followed by normal growth and periodic analysis might profitably be more widely used in problems of this kind, since it offers the closest possible approach to normal physiological conditions in tracer experiments. It is susceptible of refinement in that the relative labelling in different carbon atoms might be determined after various growth periods. It is a complicating feature of atropine that the tropine and tropic acid moieties doubtless arise by different biogenetic paths and no doubt become labelled at different rates, although as yet we have not investigated this point.

We thank Dr. W. P. Grove for his interest in this work and one of us (E. A. E.) thanks the United Kingdom Atomic Energy Authority for the award of a Harwell fellowship (1955–58).

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BIOLOGY

Prolonged Survival of Human Sperm in chemically defined Media at Room Temperatures

It has been pointed out that mammalian sperm represents an ideal tissue for exploring, under well-defined conditions *in vitro*, the intricate biochemical and physiological mechanisms underlying the viability and senescence of living cells[1]. Efforts to move in this direction have been restricted by the necessity of having to maintain mammalian sperm in complex, undefined media and at temperatures which suppress metabolic activity.

Our success with the maintenance of functionally and metabolically active bovine spermatozoa at room temperatures[2] prompted us to investigate the possibilities of sustaining human sperm at close to physiological temperatures in various chemically defined maintenance media. Of all the media tested, medium 199 (Morgan, Morton and Parker[3]), a product of Hyland Laboratories in California, provided human sperm with the most satisfactory and compatible environment, which was capable of supporting their survival and activity for several days at room temperatures (25 ± 2° C.).

The procedures employed were as follows: Semen collected from human donors was pooled immediately after liquefaction. The spermatozoa were washed free of seminal plasma by centrifugation (700*g* for 15 min.). After washing twice in the medium under investigation, the final volume was adjusted to give a concentration of 5–10 million cells/ml. of sterile medium. All media tested contained the following additives in final concentration: 31 mgm./100 ml. penicillin (sodium), 68 mgm./100 ml. dihydrostreptomycin sulphate, 300 mgm./100 ml. sulphanilamide, 4 units mycostatin per ml. and 150 units aqueous solution of sterile catalase (Worthington Biochemical Corporation) per ml. The suspension of human sperm was poured into small, sterile plastic vials, filled as completely as possible and stored in the dark[4] at room temperatures. Initially and daily afterwards, separate unopened vials were removed, inverted several times to provide a uniform suspension of cells and measurements taken to assess motility and viability. The concentration of live sperm was determined by means of the eosin–nigrosin differential staining technique[5]. The vigour of the progressive motility was rated by means of an arbitrary scale graduated from 0 (no motility) to 5 (excellent progressive motility). The number of motile cells was calculated by killing and counting all the dead, non-motile cells in one hæmocytometer and counting the non-motile cells in a second hæmocytometer. The difference between these two counts represented the concentration of motile sperm in the population. *p*H measurements were taken at various intervals during the experiment.

Table 1 summarizes the results of three replicate experiments. The number of live and progressively motile cells suspended in medium 199, buffered with 0·02 *M tris*, remained relatively constant for five days. It should be noted that medium 199 buffered with bicarbonate and carbon dioxide did not sustain cell viability as well as media buffered with *tris* or phosphate.

The *p*H of the *tris*-buffered 199 sperm suspension, initially 7·1, was usually lowered 0·1–0·2 of a *p*H unit on the fifth day of storage. Changing the medium on the third or fifth day of storage did not appreciably affect the time of survival of the sperm. However, the slight increase in alkalinity of the fresh medium noticeably increased the vigour of their translatory motion. The introduction of a small amount of egg yolk (0·5–1·0 per cent) into the medium significantly enhanced both the progressive motility and the survival time of these cells.

Table 1. Effect of *Tris*-Buffered Maintenance Medium 199 on Motility and Survival of Human Spermatozoa kept at Room Temperatures for Six Days

Age of sperm (days)	Live (per cent)	Motile (per cent)	Quality of motility*
0	60	67	3·5
1	58	64	4·0
2	52	51	3·5
3	55	54	3·5
4	49	55	3·5
5	45	50	3·5
6	34	37	3·0

* 0 (non-motile), 1 (vibratory), 2 (poor progressive), 3 (fair progressive), 4 (good progressive), 5 (excellent progressive).

This technique makes possible a more comprehensive investigation into the metabolic and functional behaviour of young and aged post-mitotic human cell populations, under well-defined and rigidly controlled conditions.

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Development of the Electric Organ of Mormyridae

The existence of striated myofibril structures persisting in the electroplaques of adult fish had led several authors[1–3] to consider muscle as the tissue of origin of the electric organs of Mormyridae, but no data have been published to justify this assumption. Recently I have presented circumstantial evidence showing indirectly that the electric organ of the Mormyridae does in fact arise from the deep lateral muscle[4]; however, direct experimental evidence was still lacking.

Through the courtesy of M. J. Daget, head of the Hydrobiological Laboratory of the Institut Français d'Afrique Noire, Diafarabé, Sudan, I had the opportunity of examining a batch of young Mormyridae and am now able to provide direct evidence on the origin and ontogenetic development of the electric organ of these fish.

As is well known, all species of the family Mormyridae possess two pairs of organs situated symmetrically on each side of the vertebral column between the caudal, dorsal and anal fins[5]. In the adult fish each organ is composed of a single series of electroplaques,

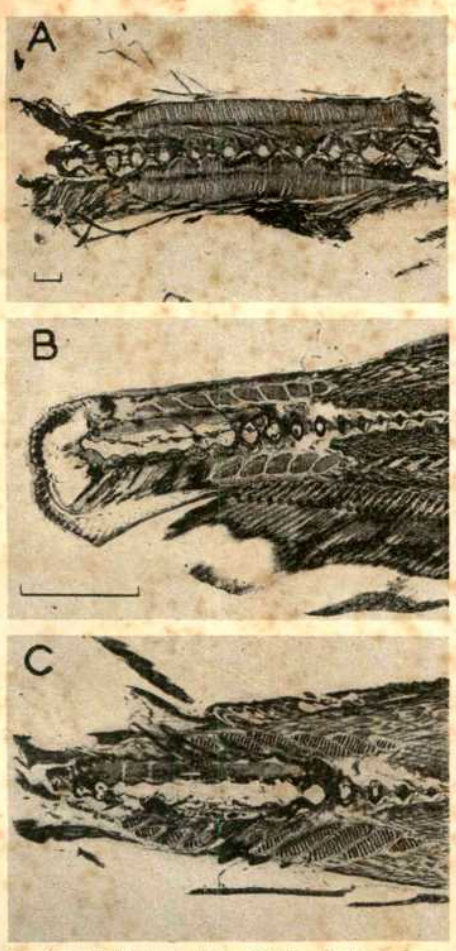

Fig. 1. Longitudinal sections of tails of three Mormyridae. *A*, *Mormyrops deliciosus* (120 mm.) adult; *B*, *Hyperopisus occ.* (24·5 mm.); *C*, *Mormyrus rume* (24·5 mm.); both young. Hæmatoxylin – eosin stain. Scale, 1 mm.

which are juxtaposed and are variable in number, 40–200 according to the species. The electroplaques are of the same size and are situated perpendicularly to the longitudinal axis of the fish. The very regular disposition of the electroplaques (Fig. 1*A*) seems to indicate that the organ arises from a special centre.

However, longitudinal histological sections of the tail of a very young *Mormyrus rume* (Figs. 1*C* and 2*A*) show that the electric organ, which is of uniform structure in the adult, is here composed of about ten groups of electroplaques. Each group is situated within a single myomere and occupies only the portion adjacent to the vertebral column. The plaques are arranged perpendicularly to the myoseptal wall in the same way as the muscle fibres. The nerve trunk is situated in the myosept and the nerve fibres penetrate only between those electroplaques which are situated in the myomere anterior to the myosept; only the caudal surfaces of the electroplaques receive nerve endings.

Although the organ is not fully developed, the majority of the electroplaques have their final aspect: double electroplasmic wall in the form of an envelope, enclosing a non-electroplasmic striated structure; the surface of the posterior wall has cylindrical prolongations (pedicles) of which only the extremity is surrounded by nerve endings.

However, in the neighbourhood of the intact fibres of the myomeres which form part of the organ, electroplaques in different evolutionary stages may be seen: for example, in one case, the electroplasm is fully formed, but does not yet possess any pedicles; the plaque is still oval and the interior is often markedly striated. In other cases, the electroplasm is only partially formed; it is rich in nuclei and surrounds the caudal part of a bundle of muscle fibres of which the cranial extremity is still attached to the myosept. The striation of these muscle fibres is clearly visible, although it is less-strongly coloured than that of the neighbouring muscle tissue.

The following preliminary conclusions can be drawn from these observations: (1) The electric organ of *Mormyrus rume* arises from several myomeres; (2) the electroplaques of these organs develop from striated muscle fibre already formed; (3) in contrast to the electroplaques of *Gymnarchus niloticus* (family Mormyridae), those of *Mormyrus rume* are formed from the muscle tissue of a single myomere; (4) the pedicle is probably formed during a later stage of the development of the electroplaque; (5) the innervation is of monoseptal origin.

We have also shown the plurimyomeric origin of electric organs in other species of Mormyridae; thus in the organ of a *Hyperopisus occidentalis* (24·5 mm. in length) (Figs. 1*B* and 2*B*) and a *Mormyrops deliciosus* (38 mm. in length), the myomeric segmentation is still evident. These two fishes were older than the *Mormyrus rume* previously described, and all their electroplaques are at the same stage of development; they still show, however, a marked difference in comparison with electroplaques of the adult fish, which in these two species present a peculiarity. In contrast to *Mormyrus rume*, in which the anastomizing pedicles are fused on to the surface of the electroplaque nearest to the pedicle, the pedicles of the adult *Hyperopisus occidentalis* and *Mormyrops deliciosus* pierce and traverse the electroplaque and fuse on to the surface which is opposite to the pedicle[6]. We also know that excitation arriving from the extreme point of the pedicle is propagated towards the electroplaque and is distributed in the first place over the surface of the electroplaque opposite to the pedicle (Szabo, Th., unpublished observations).

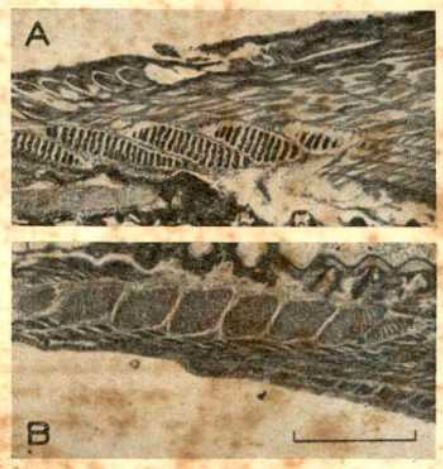

Fig. 2. *A*, Higher magnification of Fig. 1 *C*. *B*, longitudinal section of the electric organ of *Hyperopisus occ.* In both cases the myomeric segmentation is still evident. Hæmatoxylin – eosin stain. Scale 0·5 mm.

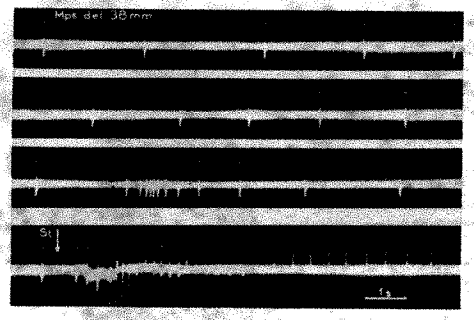

Fig. 3. Oscillographic recording of the electric activity of a *Mormyrops deliciosus* (38 mm.): electric activity of the resting animal (first three recordings) interrupted (arrow *St*) by cutaneous stimulation, provoking an acceleration of the spontaneous emission

In the very young fish, although the electroplaques already possess their long pedicles and these their nervous endings, the pedicles are attached to the surface of the electroplaque nearest to the pedicle and do not traverse the electroplaque. Accordingly, microscopic examination reveals no discontinuity in the electroplaque. Oscillographic recordings also prove that in these young electroplaques, which already function (Fig. 3), it is the surface nearest to the pedicle which is initially active and not the opposite surface, as in the adult.

In summary, there seem to exist three stages in the development of the pedicled electroplaques of Mormyridae: (1) formation of the electroplasmic tissue; (2) consecutive rapid appearance of the pedicle and its innervation; (3) piercing of the electroplaque, occurring in certain species at a later stage of development.

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The Manatee: Ecology and Use for Weed Control

SINCE 1885 the Botanic Gardens in Georgetown, British Guiana, has had in some ornamental pools manatees (*Trichechus manatus*, order Sirenia), which have been always fed with grass by visitors. These pools have been kept clear by the manatees and it seemed always necessary to get additional food in the form of grass. It was therefore felt that experiments should be proceeded with using these animals for weed control, and some have been maintained in the reservoirs of the water purification plant and have effectively kept these clear of aquatic plants, particularly *Cabomba aquatica*, *Anacharis*, *Leersia*, *Utricularia*.

We have since found that the manatee is not merely an occasional but also a very voracious and determined grass feeder, which can in fact clear trenches which are covered with grass or *Nymphaea*, *Nelumbo*, *Eichornia*, as well as submerged aquatics, and they have been doing a very commendable job in confined areas. During 1959–60 several experiments were carried out, and it has been found that two manatees $7\frac{1}{2}$ ft. long were capable of clearing a canal 22 ft. wide and 1,600 yd. long in 17 weeks. They will also keep it clear of weeds to allow the free passage of water and will break any wood barrier fixed across the canal in order to get at grass beyond the barrier. These animals are not numerous, they are perfectly docile, easily bruised and seemingly very slow in reproduction. I have collected 46 of them to date, and they have been distributed in several canals of drainage and irrigation schemes throughout the country. They are found in the rivers of British Guiana and are caught by fishermen in seines, but can easily be drowned.

Much information has been collected on their anatomy through the University of Florida and much more information is desired on their ecology and reproductive habits. I would like to have any further information available. I have already had inquiries from Ceylon, Thailand and Malaya as to the prospects of the use of these animals in those countries for weed control of the water hyacinth and other aquatic plants which are a costly nuisance.

As a means of water-weed control, the use of these animals is far more effective and lasting than the usual chemical weedicides. They are harmless to fishes and other water animals, and are seemingly unaffected even by electric eels which are normal inhabitants of some of the irrigation canals into which these manatees were introduced. The only risk in their wide use is that they may be slaughtered for their meat; legislation is now being enacted to ensure their complete protection.

A full account of ecological work on these mammals will shortly be published.

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Equivalent Pore Radius in the Axolemma of the Giant Axon of the Squid

PREVIOUS work[1,2] on the fine structure of the giant nerve fibre of the squid has revealed the existence of slit-like channels ~60 Å. wide by ~5·3μ long traversing the Schwann cell along a tortuous path the total length of which is ~4·3μ. The axolemma itself is surrounded by a space ~83 Å. wide. It has been demonstrated that no effective osmotic pressure can be developed across the Schwann cell layer. Hence the axolemma appears to be the barrier for osmotically induced flow into the axoplasm.

The present communication deals with the determination of the reflexion coefficient σ of the axolemma for a set of non-electrolytic molecules of small radii. The σ values were then used (based on the principles developed by Durbin, Frank and Solomon[3], Durbin[4] and Solomon[5]) to calculate an equivalent pore radius for the axolemma in resting condition.

The giant nerve fibre from the first stellar nerve of the squid *Doryteuthis plei* was used. The technique and equipment were the same as those previously described[2]. The experiments were carried out at 23° C.; they consisted in measuring the volume changes of the axon, initially in artificial sea water (1,010 mOsm./l.)[6], and at various time-intervals after

this medium had been removed and replaced by a test solution. Test solutions were prepared by adding a known amount of non-electrolyte, usually 60, 230, and 480 mOsm./l., to artificial sea water made hypotonic (780 mOsm./l.) by the subtraction of 230 mOsm. of sodium chloride per litre. The cryoscopic point of a solution that has a concentration of 1 Osmol. per kgm. of water is $-1{\cdot}858°$ C. The probing solutes were methanol, formamide, ethanol, urea, ethylene glycol and glycerol. Their molecular radii were obtained from Fisher–Hirschfelder–Taylor models (Table 1).

Table 1. REFLEXION COEFFICIENT OF THE AXOLEMMA FOR THE TEST SOLUTES

Solute	Molecular radius (Å.)	No. of experiments	σ Mean ± S.E.
Methanol	1·83	7	0·35 ± 0·03
Formamide	1·96	5	0·44 ± 0·02
Ethanol	2·13	5	0·63 ± 0·03
Urea	2·17	4	0·70 ± 0·03
Ethylene glycol	2·24	3	0·72 ± 0·03
Glycerol	2·77	4	0·96 ± 0·02

The rate of volume change per unit area may be described by the following equation:

$$dV/A\ dt = L_p\ \Delta\pi_i - \sigma L_p\ RT\Delta c_s \qquad (1)$$

in which L_p is a phenomenological coefficient[7], $\Delta\pi_i$ the osmotic pressure difference of non-penetrating solutes, R the gas constant, T the absolute temperature, Δc_s the concentration difference of the penetrating solute, and σ the reflexion coefficient[8,9]. σ measures the ability of the membrane to discriminate between the particular permeable solute used, and the solvent. It is considered that osmotic balance exists across the membrane when the rate of volume change at zero time is zero. From equation 1, it can be shown that:

$$\sigma = (\Delta\pi_i/RT)/\Delta c_s, \text{ when } dV/A\ dt = 0 \text{ at } t = 0 \qquad (2)$$

The osmolar concentration difference of the penetrating solutes which equilibrate a $\Delta\pi_i/RT$ of 230 mOsm./l. for the six different test solutes was determined by graphic interpolation, and afterwards σ by using equation 2 (Table 1). As expected, σ is found to depend on the radius of the solute molecule.

Durbin, Frank and Solomon[3] have suggested, and later Durbin[4] has demonstrated, that $\sigma = 1 - A_{sf}/A_{wf}$, where A_{sf} and A_{wf} are the effective pore areas available for filtration of the solute and solvent molecules respectively. Renkin's[10] equation 19 shows that A_{xf}, the effective pore area for the passage of a molecule x, is equal to:

$$A_{xf} = A_p\{2[1-(r_x/r_p)]^2 - [1-(r_x/r_p)]^4\}$$
$$[1-2{\cdot}104\,(r_x/r_p)+2{\cdot}09\,(r_x/r_p)^3-0{\cdot}95\,(r_x/r_p)^5] \qquad (3)$$

n which A_p is the geometrical pore area, and r_x and r_p are the radii of the molecule and the pore respectively. Dividing equation 3 for a given solute (s) of known radius (r_s) by the same equation for the water molecule (the radius for water, r_w, was taken as 1·5 Å.[11]), the ratio A_{sf}/A_{wf} may be determined for any r_p value.

Our experimental values for $(1-\sigma) \pm$ one standard error plotted as a function of the molecular radius can be fitted by a curve which corresponds to an equivalent pore radius of 4·25 Å., as is shown in Fig. 1. The uncertainty in fitting the curve is ±0·25 Å. The present result is independent of the nature of the path of the ions across the axolemma.

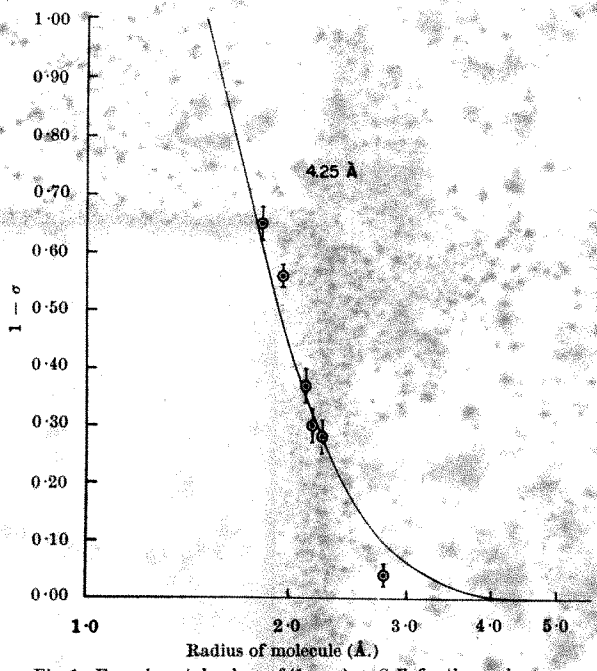

Fig. 1. Experimental values of $(1-\sigma) \pm$ S.E. for the axolemma, plotted as a function of the molecular radius. These values are fitted by a curve corresponding to an equivalent pore radius of 4·25 Å. The uncertainty in fitting the curve is ± 0·25 Å.

The presence of pores with a 4·25 Å. radius indicates that the axolemma is the membrane across which the ionic gradient necessary for nerve activity is maintained.

We are indebted to Prof. A. K. Solomon for helpful discussions during his stay at the Institute; and to Dr. Guillermo Whittembury, Dr. Richard P. Durbin, and Dr. Leopoldo Villegas for critical comments regarding this work.

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Transport of Phosphorus by Fungal Mycelium

TRANSLOCATION of nutrients by fungal mycelium has been reported by Schütte[1] and by Grossbard and Stranks[2]. Attempts in this Department to determine the rate of transport of phosphorus using a tracer technique have, however, indicated that the mycelium of *Phycomyces nitens*, *Absidia glauca* and *Chaetomium*

spp. is only able to transport phosphorus-32 under certain limited conditions.

The experimental procedure is to pour a synthetic agar medium plus 2 per cent glucose into Petri dishes and then to remove, aseptically, a 5-mm. wide channel along a diameter of the Petri dish. The organism is inoculated in the centre of one of the halves of the medium and grows over the channel to form a hyphal bridge between the two halves. Potassium dihydrogen phosphate, labelled with phosphorus-32, can be added to either the inoculated or the uninoculated half of the agar culture by removing a disk of agar with a cork borer and dropping the labelled solution into the well so formed. To sample, 5 mm. square portions of the agar bearing the mycelium were removed, dried on planchettes under an infra-red lamp, and counted.

The results showed that there was no translocation of phosphorus through established mycelium either from the inoculated side to the colonized side of the culture or in the reverse direction, that is, from the younger to the older part of the mycelium. The only condition under which it was possible to show transport of phosphorus in appreciable amounts was where the solution containing labelled potassium dihydrogen phosphate was added to the inoculated side of the Petri dish before growth of the mycelium over the channel had ceased. In these circumstances the mycelium takes up phosphorus which is carried by the extending hyphæ.

It seems clear, therefore, that a distinction needs to be made between translocation through established mycelium independently of the growth of the hyphæ, as in the case of movement of dyes reported in *Armillaria mellea*, *Collybia velutipes* and other agarics by Schütte[1], and transport by the uptake of material at one site and its transference in the mycelium to another site due to hyphal extension, as in the case of phosphorus reported here, and cobalt and cæsium transport referred to by Grossbard and Stranks[2]. That transport of phosphorus is via the extending mycelium itself has been confirmed in the case of *Chaetomium* sp. by transferring mycelium which had been grown on phosphorus-32 labelled medium to potato dextrose agar containing no phosphorus-32. The resultant colony consisted of mycelium which was shown both by auto-radiographs and by counting to contain phosphorus-32 up to its margin. No activity was apparent beyond the edge of the colony, indicating that phosphorus so absorbed into the mycelium does not exchange appreciably with the phosphorus present in the medium nor diffuse out into it.

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GENETICS

White Band, a New Spotting Mutation in the Syrian Hamster

THE first mutation reported in the Syrian hamster, *Mesocricetus auratus*, was a recessive type of white spotting which has been designated as piebald[1]. The new mutation to be described here differs from piebald in two respects: (1) the mutation is inherited as a dominant to normal pigmentation; and (2) the characteristic spotting pattern produced by the mutation is phenotypically distinguishable. The new mutant gene has been termed 'white band' and has been given the symbol *Ba*. The gene was discovered in the United States in 1957, and stock carrying the gene was imported into Britain during 1959.

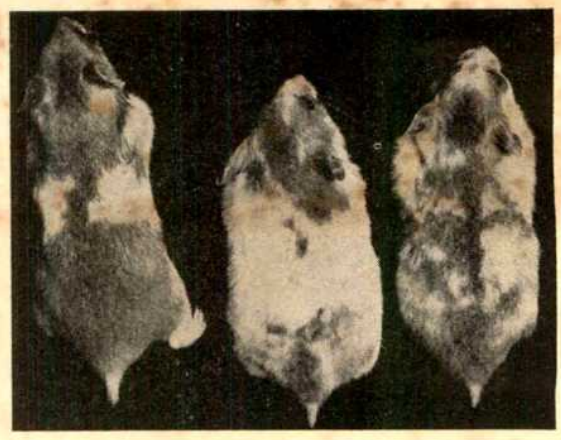

Fig. 1. Three types of white spotted hamsters; the white band (left) and the piebald (right); the central animal is genetically both white band and piebald. The only interaction observed for the two forms of white is for a broadening of the medial band

With the piebald type of spotting, the white and coloured areas of the coat are greatly intermingled. There is invariably a streak of white extending from the muzzle to between the eyes. However, with the new spotting, the white areas are confined to the trunk region of the body, are not broken up to a great extent and have not been seen to occur on the head at all (see Fig. 1). The middle specimen of the photograph is a genetic combination of the two mutant genes and phenotypically displays features of both: a median band of white, which is typically wider than that of an ordinary white band, white on the forehead together with a white brindled posterior.

An imported white band male was paired with normal females, producing an F_1 of 46 white band and 43 normal offspring. An F_2 generation from the F_1 white band consisted of 90 white band and 21 normal. A backcross of the F_1 to the normal gave 79 white band and 91 normal young. A χ^2 analysis, on the assumption that the gene is assorting in exactly 50 per cent of cases from its normal allele and that the various genotypes are of normal viability, yields $\chi^2_3 = 3 \cdot 14$ ($P > 0 \cdot 30$). This value may be partitioned into a gene segregation χ^2_1 of $0 \cdot 20$ ($P > 0 \cdot 50$) and heterogeneity between the three generations of $\chi^2_2 = 2 \cdot 94$ ($P > 0 \cdot 20$). There is the possibility that the white band gene may be lethal when homozygous, but the frequencies of the two phenotypic classes in the F_2 are a poor fit to the 2 : 1 ratio which would be expected for this eventuality ($\chi^2_1 = 10 \cdot 82$; $P < 0 \cdot 01$).

The mutant gene derives its name from a band of white which in many individuals either completely, or almost completely, encircles the body. However, the expression of the band is variable, and in a great many animals may be partially or completely interrupted by a spinal stripe of pigment, as appears on the white band shown in Fig. 1. In high-grade animals, the band is extremely wide, the belly is almost completely white, and the areas of pigmenta-

tion are restricted to the head, shoulders and lower hindquarters.

At birth the ear auricula of most white band animals are pink, but in adult animals only the basal portions of the auricula remain depigmented. The melanism in the skin around the genitalia of both sexes is suppressed.

It is possible that the gene may not be completely dominant, since the mean percentage of white in the coat of heterozygotes, *Baba*, is less than that of homozygotes *BaBa*. The mean for the white band animals of the F_1 is $15 \cdot 87 \pm 0 \cdot 75$ per cent, for the backcross (*BC*) is $16 \cdot 34 \pm 1 \cdot 10$ per cent and for the F_2 is $23 \cdot 68 \pm 1 \cdot 3$ per cent. The F_1 and *BC* means are in good agreement, as could be anticipated, since the white bands in both generations are necessarily *Baba*. In the F_2, however, one-third of the white band animals are expected to be homozygotes and, if these possess more white than the heterozygotes, the value of the mean may be expected to be raised.

This may be the case, for the mean of the F_2 is significantly higher than the means for the other two generations. The frequency distribution of percentage of white, moreover, is unimodal and positively skewed. This would appear to indicate that, if the *Ba* gene is incompletely dominant, it is so in the stochastic sense that the higher-grade animals are more likely to be *BaBa* than *Baba*. A comparison of the frequency distribution of the F_1, *BC* and F_2 would indicate that the critical point is in the region of 35 per cent white. In the F_2, 13 per cent of the white band animals have more than this amount, whereas in neither F_1 nor *BC* did a white band approach this amount of white.

The F_1 offspring were the young of a single male, and the *BC* and F_2 generations were analysed for an association with sex. The frequencies for the *BC* are 23 ♂♂ *Ba*, 23 ♀♀ *Ba*, 17 ♂♂ *ba* and 26 ♀♀ *ba*, which yields a χ_1^2 for independent assortment of 0·84 ($P > 0 \cdot 30$). The F_2 classified for sex are 39 ♂♂ *Ba*, 51 ♀♀ *Ba*, 11 ♂♂ *ba* and 10 ♀♀ *ba*, producing an associative χ_1^2 of 0·68 ($P > 0 \cdot 03$). These results indicate that the *Ba* gene does not show partial sex linkage.

In summary, the white band trait in the hamster behaves in heredity as a dominant, monogenic, autosomal entity.

I wish to thank Mrs. Margaret Beher for her assistance in obtaining specimens of white band hamsters.

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Genetic Recombination in a Common-*B* Cross of *Schizophyllum commune*

THIS communication reports the synthesis of stable common-*B* heterokaryons in *Schizophyllum commune*, and the occurrence of normal genetic recombination in fruit-bodies derived therefrom. Although common *B* heterokaryosis and the normal segregation of the *A*-factor in common-*B* fruit-bodies have been reported in other tetrapolar species[1-3], these phenomena in *S. commune* have not been demonstrated with certainty[4,5]. The nature of production of spores in such fruit-bodies, however, has not been fully determined, and "It appears uncertain whether such fruit-bodies are apomictic or functionally bipolar"[6].

Stable common-*B* heterokaryons of *S. commune* have been established by three methods:

(1) 'Illegitimate' Buller phenomenon, for example:

$$(A^{41}B^{41}p^r u_1^+ n_2^+ + A^2B^2p^s u_1 n_2) \times A^2B^{41}p^s u_1 n_2 \rightarrow (A^{41}B^{41}p^r u_1^+ n_2^+ : A^2B^{41}p^s u_1 n_2)$$

(p^s, p^r, polymyxin sensitivity and resistance, respectively; *u*, *n*, *ad*, *arg*, uracil, niacin, adenine and arginine, respectively).

(2) Isolation from the region of confluence of mated homokaryons, for example, $A^{112}B^{111} \times A^9B^{111}$.

(3) Nutritional selection on minimal medium from the region of confluence of mated homokaryons, for example, $A^{41}B^{42}arg_6^+ad_2n_3 \times A^{42}B^{42}arg_6ad_2^+n_3^+$. In all cases, two successive transfers of single apical cells were made to ensure the establishment of single mycelia.

The common-*B* heterokaryotic genotypes have been confirmed in all cases by mating type-tests with homokaryons, and in (1) also by the pattern of growth of the heterokaryons and of the resulting backcrossed dikaryons on various types of supplemented media, and the recovery of the individual homokaryotic component strains.

In culture, the common-*B* heterokaryon resembles a somewhat thin and irregular dikaryon and has relatively little aerial growth. The hyphæ are irregularly branched, and the septa are commonly provided with pseudoclamps, that is, incompleted clamp-connexions, the tips of which fail to fuse with the sub-terminal cells and often continue to grow to give side branches; these typically have pseudoclamps. As observed with phase microscopy, the number of nuclei per cell is 1–5. Secondary septation and the production of side branches seem to reduce the number of nuclei per cell, and these processes may account for the homokaryotic hyphæ that often grow to form distinct sectors. Preliminary results of the isolation of hyphal-tips and of the examination of mycelia grown from fragments following maceration give significant indication that the hyphæ lacking psuedoclamps are homokaryotic, whereas pseudoclamps appear to be reliable indicators of heterokaryotic hyphæ.

Common-*B* heterokaryons constituted of non-allelic, biochemically deficient strains grew normally on minimal medium: genetic complementation operates as in the dikaryon.

Small plugs of mycelium[5] taken from common-*B* matings of the type described in (3) gave growth on minimal medium only when taken from the area of confluence of the two strains: nuclear migration either does not occur at all, or it is severely restricted to a distance of no more than 2 mm.

In further analysis, two patterns of behaviour of the *B*-factor has been found.

(1) Nine independent heterokaryons of the composition ($A^2B^{41}p^s u_1 n_2 : A^{41}B^{41}p^r u_1^+ n_2^+$) were inoculated on fruiting medium in replicate sets of ten; fruiting bodies appeared in only a single culture about two months after inoculation. Small pieces of tissue isolated from the sterile portions of one of these fruits gave rise to a normal dikaryon, which by mating tests with homokaryons was found to be ($A^2B^*p^s u_1 n_2 + A^{41}B^{41}p^r u_1^+ n_2^+$). Among a sample of 177 monosporous progeny, there were 102 B^{41} and 75 B^*; a sample of 120 progeny was tested for

five additional pairs of markers (A_α, A_β, p, u n) and showed the segregation expected from regular meiosis in the diploid basidium. A test cross, $A^2B^* \times A^{41}B^2$, gave among 150 progeny 80 B^* and 70 B^2—but *no recovery* of B^{41}. All the B^* isolates of this cross had the 'flat' morphology typical of the common-A heterokaryon, and from these it proved to be impossible to recover morphologically homokaryotic mycelia, either by the isolation of single terminal cells or by deheterokaryotization by treatment with polymyxin. Together with the data on segregation, these results rule out the possibilities of disomic or heterokaryotic spores, and contamination as explanations of the 'flat' morphology. B^* is compatible with all 57 distinct B factors in the collection of these Laboratories; this includes B^{41}, only with which, however, B^* gives an anomalous reaction: irregular, patchy and delayed dikaryosis.

It therefore seems evident that these 'illegitimate' fruit bodies appeared as the result of a spontaneous mutation within the B^{41}, which led to a new B specificity and to spontaneous common-A heterokaryosis. The latter might be interpreted in two ways: (*a*) the new B factor is non-functional, therefore $A^2B^* \equiv (A^2B^1 : A^2B^2)$; (*b*) the new B is itself unstable and occasionally yields a derived factor, $A^2B^* \rightarrow (A^2B^* : A^2B^{**})$. Swiezynski and Day recently reported the "segregation of a new B reaction" in comparable fruits of *Coprinus lagopus*[3].

(2) A single, tiny fruit-body appeared on a common-B heterokaryon of the constitution $(A^{42}B^{42}arg_6ad_2{}^+n_3{}^+ : A^{41}B^{42}arg_6{}^+ad_2n_3)$. This fruit-body was very similar to the aberrant fruit-bodies that sporadically appear on homokaryons. All segregants of a sample of 150 progeny that were tested, however, showed only B^{42}, but five other pairs of markers showed independent assortment and crossing-over as expected from normal meiosis.

When these results are compared with previous reports in the literature, it becomes apparent that the tetrapolar fungi, as a general phenomenon, have two kinds of hemicompatible heterokaryons: (*a*) the common-A heterokaryon is initiated by extensive nuclear migration and is characterized by depressed growth of a mycelium composed of hyphæ having simple septation[3-5]; (*b*) the common-B heterokaryon is synthesized without nuclear migration and only in the region of confluence of mated homokaryons and is characterized by the normal growth of a mycelium composed of hyphæ provided with pseudo-clamps. The 'illegitimate' common-B fruit-bodies must have a normal diploid stage; therefore, they are not 'apomictic', but 'functionally bipolar'.

The results of this work will be reported in detail elsewhere.

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SOIL SCIENCE

A Plate Method for studying the Breakdown of Synthetic and Natural Silicates by Soil Bacteria

IN a previous communication[1], a plate method for detecting phosphate-dissolving micro-organisms in soil was described. We have now found that a similar technique can be used for work on the breakdown of silicates by soil micro-organisms. For this purpose the insoluble silicates are ground in a ball mill and directly incorporated into molten agar as described for the insoluble phosphates[1].

Fig. 1 shows a number of plates prepared in this way using synthetic and naturally occurring silicates. The synthetic calcium, zinc and magnesium silicates were found to be amorphous to X-rays, but the minerals wollastonite, apophyllite and olivine gave X-ray powder diffraction patterns which showed them to be substantially free of impurities. The test organism used here was an unidentified species of *Pseudomonas* isolated from soil, and the clearing around the growth can be clearly seen.

It has already been shown by Duff and Webley[2] that 2-ketogluconic acid is produced by similar soil organisms when grown in liquid culture containing insoluble phosphates and silicates. The presence of this acid in the clearer zone around the growth in the present work was demonstrated by cutting out an agar disk (3 mm. diameter) close to the growth and applying it to a paper chromatogram and allowing it to dry at room temperature. The dried disk of extracted agar could then be brushed off and when the chromatogram was developed and sprayed, as described previously[2], 2-ketogluconic acid could be easily detected. Calcium, zinc and magnesium could usually be detected as their soluble chelates by spraying with 8-hydroxyquinoline[3].

The clearer areas containing the residues of the naturally occurring minerals (wollastonite, apophyllite, and olivine) were carefully cut out and the agar was melted in hot water. The solutions were then centrifuged to sediment the insoluble residues, which on examination were found to be amorphous by X-rays. The insoluble material from the surrounding

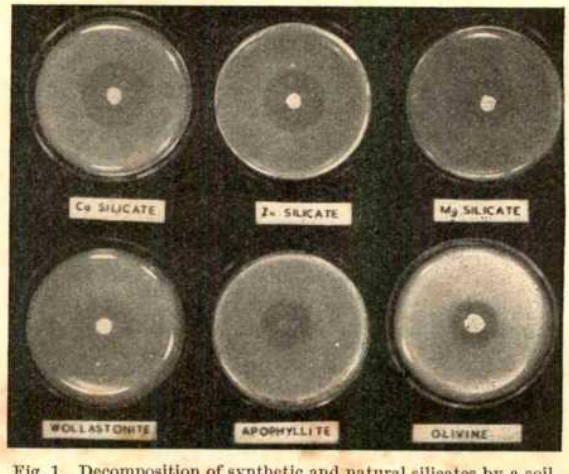

Fig. 1. Decomposition of synthetic and natural silicates by a soil bacterium. The basal medium was that used previously (ref. 1) but containing 2 per cent w/v glucose. The final concentration of the silicates was 0·25 per cent w/v. After inoculation, the plates were incubated for 4 days at 25°

cloudy zones was also extracted in the same way and gave X-ray diffraction patterns identical with those of the original powders. These results clearly showed that the crystal structure of the minerals had been destroyed.

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Some Effects of Aldrin and DDT on the Soil Fauna of Arable Land

INSECTICIDES are now extensively applied to agricultural soils, and if this practice continues there is the obvious possibility that such treatments may have harmful effects on the soil fauna. The chlorinated hydrocarbons are not readily broken down in soil[1,2], and the general use of fertilizers containing aldrin could be one source of accumulations of this material in agricultural land. The applications of insecticide may control specific pests as desired, but could also suppress certain elements of the fauna, and even cause secondary increases of some soil animals by modifications in the predator pressure.

We have studied the effects of rates of insecticides commonly used, on the soil fauna of arable land, at Cannington Farm Institute, in Somerset. The rates of insecticides used were 3 cwt. of 1·25 per cent aldrin dust, and 2 cwt. of 5 per cent DDT dust per acre, and plots were laid out in a random block consisting of four replicates of each treatment and control. The size of each plot was 6 ft. square with 6 ft. guard rows between plots. The insecticides were applied to the surface of the plots as dusts and thoroughly mixed into the soil to a depth of 6 in. by double rotovation. All plots were kept fallow throughout the period of the trial by regular application of the weed-killers CMPP and 'Dalapon'.

The soil was sampled at intervals of 2–3 months after the beginning of the experiment. Samples taken from each plot consisted of (*a*) four 2-in. diameter cores to a depth of 6 in., and (*b*) twenty-five 1-in. diameter cores also 6 in. deep. The fauna was extracted from the first sets of samples by washing through a somewhat modified Salt and Hollick[3] apparatus and then stored in vials of alcohol until the animals could be sorted into taxonomic categories by examination under a binocular microscope. The second set of samples from each plot was bulked and thoroughly mixed, and the nematodes extracted from small subsamples placed in Baerman funnels[4].

Considerable changes in population occurred in most groups of the soil fauna. Initially numbers of most groups of animals decreased because of the cultivation, but this lasted for only three months. Both insecticides significantly decreased the numbers of Acarina in the treated plots. Aldrin also brought the population of Collembola to a low level, but DDT increased numbers of these animals to a peak nine months after treatment, after which numbers fell to a level slightly above that of the untreated plots. This confirms the results obtained by Sheals[5] for soil treated with DDT and then planted with rye grass,

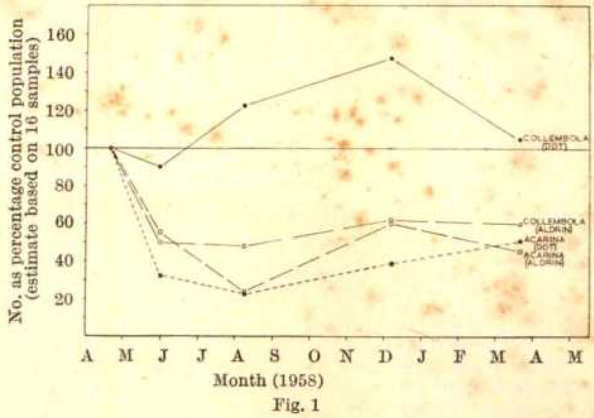

Fig. 1

and by Dobson[6], who found the Collembola population increased in arable land treated with BHC. The numbers of dipterous and coleopterous larvæ and pupæ, thrips, pauropods and symphylids were all markedly suppressed by both insecticides. Numbers of root aphids were greatly decreased by aldrin but not by DDT; neither insecticide affected the populations of small plant parasitic nematodes, earthworms and enchytraeid worms to a significant extent.

More detailed sorting of the fauna, possibly to species-level, will be necessary to show whether the increased numbers of Collembola in the DDT-treated plots result from changes in the predator–prey balance, but quite small dosages of insecticide can obviously have considerable effects on the fauna and so might eventually influence the fertility of the land.

A full account of the results will be published shortly.

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Microbiology of Some Soils from Antarctica

ANALYSES of soil from Antarctica reveal little weathering and only minute quantities of organic matter[1]. Vegetation in this area is commonly restricted to mosses, lichens, or algae. A number of samples of moss, algae and soil from the McMurdo Sound region have been examined to determine the nature of the microflora and microfauna associated with this very simple organic cycle.

Among the genera of terrestrial algae already identified are *Chlamydomonas*, *Chlorella*, *Chlorococcum*, *Stichococcus*, *Nostoc*, *Hantzschia*, *Bumilleriopsis*, *Radiosphaera*, *Heterothrix*, *Heterococcus*, all of which are typical of soils in temperate climates[2,3]. The last-named four genera have not been previously recorded from the Antarctic continent.

The bacterial flora of the moss is similar to the epiphytic flora found in temperate climates[4,5],

consisting largely of Gram-negative chromogens. The soil flora, however, appears to be more distinctive. There are more chromogenic bacteria than are normally found in soils, spore-forming bacteria are rare, and there is a large proportion of Gram-positive cocci. Attempts at isolating aerobic nitrogen-fixing bacteria were unsuccessful. Fungi are uncommon and *Streptomyces* have only been recovered from one site.

Ciliate protozoa identified include *Colpoda cucullus*, *Homalogastra setosa* and *Trichopelma sphagnetorum*, all typical soil forms[6,7], and a suctorian. Amœbæ are quite common, but testaceans have only been recovered from moss. Rotifers, tardigrades and nematodes were also present in some of the samples.

All these micro-organisms grew at room temperature, which in the case of the algae varied between 0° and 38° C. The bacteria grew both at 4° C. and at 25° C., but growth was slower at the lower temperature.

The presence of these micro-organisms, many of them typical of the soils of temperate regions, suggests the presence of an organic cycle comparable to that found in more developed soils and supports the view that the rock waste of this region may be properly referred to as soil.

Further details will be published elsewhere.

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VIROLOGY

Inactivation of Virus Hæmagglutinins by *para*-Chloromercuribenzoic Acid

IT has been found that a number of chemical agents reacting with thiol groups can impair the infectivity of certain viruses while leaving others unaffected[1,2].

In the course of a systematic study, one of these compounds, *para*-chloromercuribenzoic acid, has been tested for its effect on a number of virus hæmagglutinins.

It was found that substances in the media used to suspend the viruses did not abolish the effect of the compound in the concentrations used. The reagent dissolved in distilled water was mixed with equal volumes of virus suspensions and held at room temperature for 1 hr. The mixture was then dialysed at 4° against 0·1 *M* phosphate buffer, *p*H 7·2, except in the case of the arbor viruses, when borate saline, *p*H 9·0, was used[3].

The dialysing fluid was changed at 4 hr. and the dialysis continued overnight. Doubling dilutions of the dialysates were made in plastic plates, 1 per cent cells added and allowed to settle at room temperature (occasionally 4° C.). Human cells were used for most tests, sheep cells for the *E.M.C.* group, goose cells for the arbor viruses and rhesus cells for adenovirus type 7.

Table 1

Group	Virus strain and type		Log₂ mean reduction of titre on treatment with parachloromercuribenzoic acid 10^{-3} *M*		10^{-4} *M*	
Myxo	Influenza *A*	*W.S.*	0	(4)*	0	(1)
		Mel.	0	(1)	0	(1)
	Influenza A_2	Iksha	0	(1)	0	(1)
		A/Eng/59	0	(1)	0	(1)
	Influenza *B*	Lee	0	(3)	0	(1)
	Parainfluenza I	Sendai	0	(4)	0	(1)
	Mumps		0	(2)	0	(1)
Adeno	Adeno type 7		>2·5	(4)	>7·5	(2)
	Adeno type 9		0	(5)	—	
	Simian virus 17		0	(3)	—	
Reo	*REO* type I		>4·4	(8)	>4	(1)
	REO type II		>1·1	(3)	>7	(1)
Entero	*ECHO* 7		>3·75	(2)	—	
	ECHO 11 prototype		>2	(1)	—	
	ECHO 11 "*U*"		2·8	(5)	>5	(1)
	ECHO 12		>1·75	(2)	—	
	Theiler's virus *GD* VII		>8	(1)	>4·5	(1)
E.M.C.	*E.M.C.*		>6	(1)	>9	(1)
	Columbia *SK*		>5	(1)	—	
Arbor	Group *A*	Semliki Forest	0	(2)	0	(1)
	Group *B*	West Nile	0	(3)	—	

* Number of tests performed. —, Not tested.

The compound tested had no effect on red cell receptors[4]. The other results are shown in Table 1.

There seems to be a clear-cut division between viruses in which there is a marked destruction of hæmagglutinating activity and others which are unaffected even by high concentrations. The myxoviruses and arbor viruses seem to be unaffected while the enteroviruses and reoviruses (previously called *ECHO* 10) are inactivated. This may be a reflexion of a fundamental difference of structure between these groups. However, it can be seen that within the adenovirus group the results are not consistent and so caution would be required in using this reaction as an aid in classification. Another point of interest is that the effect of the compound on the infectivity of a virus may be quite different from that on the hæmagglutinin, for the infectivity of many myxoviruses is destroyed by this treatment whereas the infectivity of *GD* VII is unchanged.

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Intranuclear Formation of Cytomegalic Inclusion Disease Virus

HUMAN cytomegalic inclusion disease virus has been isolated in human fibroblast cultures and its cytopathogenic properties characterized by Smith[1], Rowe *et al.*[2], Weller[3], and Weller *et al.*[4]. The present communication deals with some appearances in the electron microscope. The strain used is the Kerr strain obtained from Dr. T. H. Weller which has been passaged in tissue culture about 20 times. The virus was grown in human embryonic skin-muscle fibro-

blasts[5], the medium for both growth and maintenance being Earle's saline, 0·5 per cent lactalbumin hydrolysate, 10 per cent inactivated horse serum, soya bean trypsin inhibitor and antibiotics; the *p*H was adjusted with sodium bicarbonate to 7·2. For electronmicroscopy the medium was poured off and the cells fixed *in situ* with buffered osmic acid for 1 hr. After dehydration through alcohol, the tissue was scraped off the glass and embedded in methacrylate. Thin sections were cut for examination.

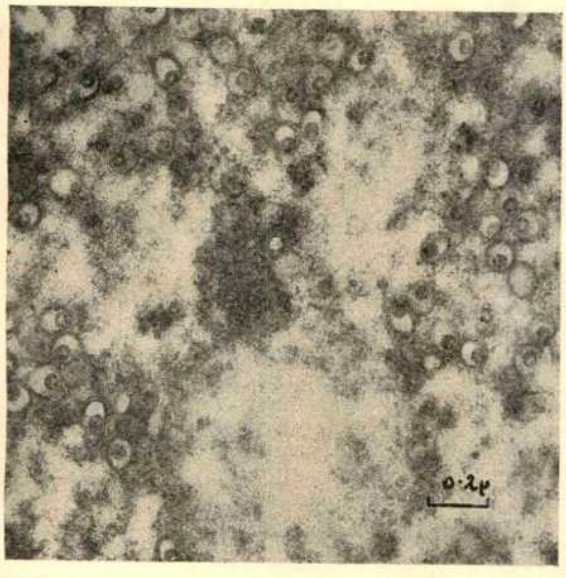

Fig. 1. Electronmicrograph showing the formation of virus particles, each possessing a single surrounding membrane, within the nucleus of the cell. (× 40,000)

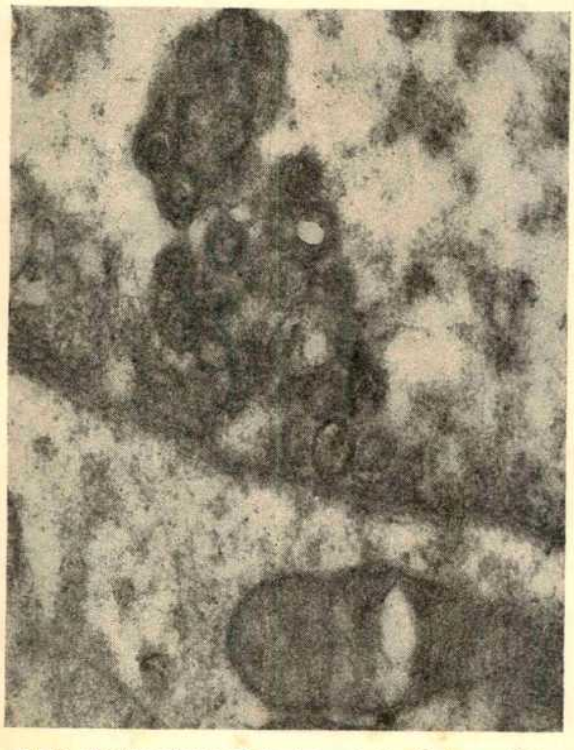

Fig. 2. Electronmicrograph showing a cluster of virus particles lying close to the nuclear membrane. The latter, which is normally double, appears to be multiple over this area and shows inward extensions which are responsible for the formation around the virus particles of second and occasionally also third surrounding membranes. The large bodies in the cytoplasm are mitochondria. (× 44,800)

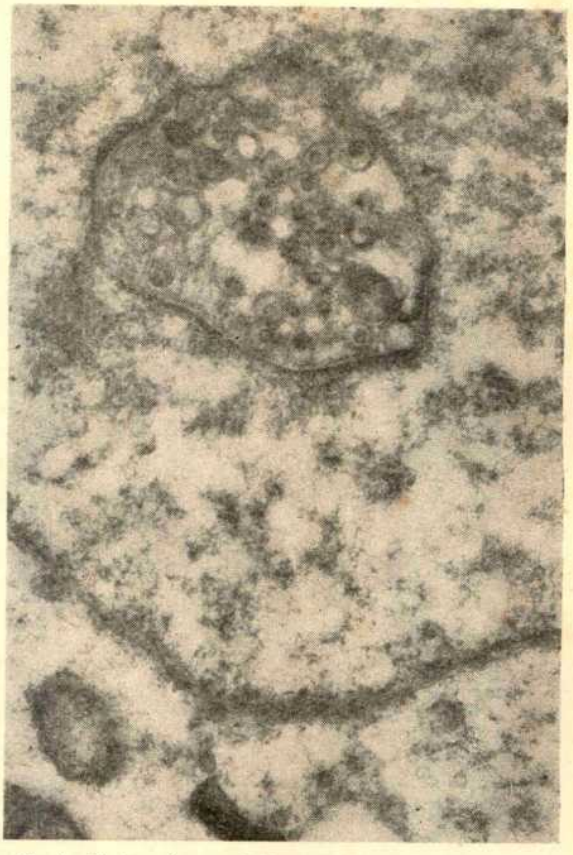

Fig. 3. Electronmicrograph illustrating a walled-vacuole within the nucleus, containing virus particles. Inward extensions from the inner layer of the vacuole are continuous with membranes forming the outer coats of some of the virus particles. (× 37,500)

The virus is formed in the nucleus of the cell. The earliest stage of virus formation as yet observed was that of masses of granular particles each possessing a single surrounding membrane (Fig. 1). The size of these particles is 80–120 mμ. Virus particles lying free in the cytoplasm, on the other hand, possess double membranes, the outer of which is acquired during passage through the nuclear membrane. There appeared to be two methods of passage into the cytoplasm. Many particles pass through the nuclear membrane singly (Fig. 2), and at such sites of passage there occurs an increase in the number of nuclear membrane layers, as described by Morgan *et al.*[6] for herpes simplex virus, and from which the virus acquires its outer coat. The nuclear membrane is normally double. The most striking finding, however, was the presence of many walled-vacuoles, containing clusters of virus particles, within the nucleus (Fig. 3). In many cases there was distinct evidence of continuity between the double membranes surrounding the vacuoles and nuclear membrane. They were in fact invaginations of the nuclear membrane. Both single- and double-coated virus particles were visible within them. In the case of the double-coated particles the outer coat often showed continuity with inward extensions of the inner membrane of the invagination. The presence of clusters of virus particles seems to stimulate inward movement of the

nuclear membrane resulting in the invaginations. The virus completes its formation by acquiring its outermost coat from the reduplicated nuclear membrane and the virus particles enter the cytoplasm either by rupture of the vacuole at the surface of the nucleus, or more probably by actual extrusion of the whole vacuole. Many of these virus-containing vacuoles are visible in the cytoplasm as also described by Luse and Smith[7]. The method of formation appears to resemble closely that found for herpes simplex virus in HeLa cells by Morgan *et al.*[6]

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Cytochemical Changes in Human Amnion Cells infected with Psittacosis Virus

BEDSON *et al.*[1] described the developmental forms of psittacosis virus using conventional staining methods and light microscopy. Subsequent studies by others, who used phase, ultra-violet[2], and electron[3] microscopy, and fluorescein-tagged antibody[4], helped to describe the complex nature of the replication-cycle. In this work, we used Feulgen staining[5] and fluorescence microscopy with acridine orange dye to demonstrate cytochemical changes in tissue cultures infected with psittacosis virus. Immunocytochemical changes were followed by fluorescent-antibody techniques[6]. Pretreatment of infected cells with ribonuclease was also used in these staining procedures.

When cells stained with acridine orange are viewed with ultra-violet light, the cytoplasm and nucleoli appear rust-red and the nucleoplasm, yellow-green. In this communication, we shall refer to the rust-red colour as ribonucleic acid staining and to the yellow-green as deoxyribonucleic acid staining.

A toxigenic psittacosis virus[7] in allantoic fluid was inoculated into a line of human amnion[8] which was propagated on coverslips in Leighton tubes. At time-intervals, cultures were fixed in acid-alcohol, washed in McIlvaine's buffer (*p*H 3·8), and stained for 4 min. in 0·01 per cent acridine orange prepared in buffer. Cultures were washed and mounted in buffer. They were examined with a Reichert Zetopan microscope and illumination system. At 2–4 hr. after inoculation, deoxyribonucleic acid-staining particles (0·3–0·6μ) were noted in the cytoplasm. Within the following 24 hr., the initial deoxyribonucleic acid-staining particle was replaced by ribonucleic acid-staining inclusion which was distinct from the surrounding cytoplasm. These inclusions increased in size (1·0–4·0μ) and in numbers (2–20) until grape-like clusters were formed. During the next 48 hr., colour differentiation of the individual inclusions within these clusters occurred in sequence from shades of red to orange to yellow to green. Afterwards, and within the next 48 hr., pin-point (0·2–0·4μ) deoxyribonucleic acid-staining particles (mature virus) were evident. Re-infection occurred, and the cycle was repeated until the entire cytoplasm was filled with mature inclusions. Infected cells eventually ruptured, thus liberating virus particles into the fluid medium. Infection did not interfere with cell division; mitotic figures were noted throughout the developmental cycle.

Treatment of infected cells with ribonuclease prior to staining with acridine orange effectively removed all ribonucleic acid-staining material from the cytoplasm and nucleoli and from the matrix surrounding the deoxyribonucleic acid-staining virus particles. During all stages of development, the deoxyribonucleic acid-staining material was Feulgen positive. Preparations of the early multicoloured (red-orange) inclusions did not react with a group-related fluorescein-tagged antibody either with or without ribonuclease pretreatment. In contrast, preparations which had reached the yellow-matrix stage were antigenic, but only after prior treatment with ribonuclease. Virus which had reached the mature green-matrix and pin-point deoxyribonucleic acid-staining stages were antigenic with or without ribonuclease pretreatment. That propagation of psittacosis virus in the tissue cultures had occurred was demonstrated by intracerebral inoculations into mice.

By means of acridine orange dye and fluorescence microscopy, the replication-cycle of psittacosis virus in human amnion cells was shown to involve deposition of a ribonucleic acid-containing matrix by the host cell around an initial deoxyribonucleic acid-containing virus particle. Since this matrix could be digested with ribonuclease, it is not considered part of the intact virus and may function as a metabolic pool provided by the host cell.

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FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, November 28

UNIVERSITY OF LONDON (at the Postgraduate Medical School of London, Ducane Road, London, W.12), at 4 p.m.—Dr. J. S. Robson: "The Renal Excretion of Water in Health and Disease".*

BRITISH SOCIETY FOR THE HISTORY OF SCIENCE (in the London Planetarium, Marylebone Road, London, N.W.1), at 5.30 p.m.—Mr. Leonard Clarke: "Greek Astronomy and Its Debt to the Babylonians".

UNIVERSITY OF LONDON (at King's College, Strand, London, W.C.2), at 5.30 p.m.—Prof. A. Bentz (Board of Soil Research, Hanover): "The North-west German Basin".* (First of three Special University Lectures on "The German Oil Fields and their Palæogeographic Conditions". Further lectures on November 29 and December 1.)

UNIVERSITY OF LONDON (in the Anatomy Lecture Theatre, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. John O. Corliss (University of Illinois): "Phylogeny and Evolution of the Ciliated Protozoa—Basic Concepts".* (Second of three lectures on "The Evolution of the Protozoa". Further lecture on December 5.)

INSTITUTION OF ELECTRICAL ENGINEERS, EDUCATION DISCUSSION CIRCLE (at Savoy Place, London, W.C.2), at 6 p.m.—Discussion on "Training for Research" opened by Prof. G. H. Rawcliffe and Dr. G. A. V. Sowter.

ROYAL AERONAUTICAL SOCIETY, AGRICULTURAL AVIATION GROUP (at 4 Hamilton Place, London, W.1), at 7 p.m.—Mr. J. B. Farrant: "The Farmer's Viewpoint".

ROYAL INSTITUTE OF CHEMISTRY, LONDON SECTION (joint meeting with the DARTFORD AND DISTRICT PHARMACEUTICAL SOCIETY, at the North-West Kent College of Technology, Miskin Road, Dartford, Kent), at 7.30 p.m.—Mr. G. L. Baldit: "Chemical Aids to Crop Protection".

Tuesday, November 29

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. L. E. Glynn: "Auto Antibodies and Diseases of Connective Tissue".* (Twelfth of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. A. F. Huxley: "Theories of Muscular Contraction—a Historical Survey" (Inaugural Lecture).*

ROYAL AERONAUTICAL SOCIETY, ROTORCRAFT SECTION (at 4 Hamilton Place, London, W.1), at 6 p.m.—Mr. R. Stanton Jones: "The Design of Ground Effect Machines".

IRON AND STEEL INSTITUTE (at the Hoare Memorial Hall, Church House, Great Smith Street, London, S.W.1), at 6.30 p.m.—Mr. L. Rotherham: "The Contribution of Metallurgy to Electric Power Generation" (Thirteenth Hatfield Memorial Lecture).

Tuesday, November 29—Wednesday, November 30

IRON AND STEEL INSTITUTE (at Church House, Great Smith Street, London, S.W.1)—Autumn General Meeting. Two symposia on: "Fluid Flow in Furnaces and Converters" and "Martensite".

Tuesday, November 29—Friday, December 2

CORROSION AND METAL FINISHING EXHIBITION (in the Empire Hall, Olympia, London).*

Wednesday, November 30

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 2.30 p.m.—Anniversary Meeting.

UNIVERSITY OF LONDON (at Bedford College, Inner Circle, Regent's Park, London, N.W.1), at 5.15 p.m.—Prof. W. F. Widdas: "Membrane Permeability and Science"* (Inaugural Lecture).

INSTITUTION OF ELECTRICAL ENGINEERS, ELECTRONICS AND COMMUNICATION SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. W. J. Bray: "The Potentialities of Artificial Earth Satellites for Radiocommunication".

ROYAL AERONAUTICAL SOCIETY, MAN-POWERED AIRCRAFT GROUP (at 4 Hamilton Place, London, W.1), at 7 p.m.—Mr. John Barlee: "Some Aspects of Bird Flight".

Wednesday, November 30—Friday, December 2

BRITISH PLASTICS FEDERATION (at Café Royal, Regent Street, London, W.1)—Second International Reinforced Plastics Conference.

IRON AND STEEL INSTITUTE (at the Hoare Memorial Hall, Church House, Great Smith Street, London, S.W.1), at 9.30 a.m. daily—Symposium on "Steels for Reactor Pressure Circuits".

Thursday, December 1

SOCIETY OF CHEMICAL INDUSTRY, CORROSION GROUP (in the Empire Restaurant, Olympia, Kensington, London, W.14), at 2 p.m.—Meeting on "The Influence of Water Movement on Corrosion". Dr. G. Butler: "Ferrous Materials"; Dr. N. V. Newman: "Non-ferrous Metals".

ROYAL INSTITUTION OF NAVAL ARCHITECTS (at 10 Upper Belgrave Street, London, S.W.1), at 4.45 p.m.—Mr. J. E. Conolly: "Strength of Propellers".

INSTITUTE OF REFRIGERATION (at the Institute of Marine Engineers, The Memorial Building, 76 Mark Lane, London, E.C.3), at 5.30 p.m.—Mr. E. J. Perry and Mr. P. D. Laing: "Positive Displacement Rotary Compressors as Applied to Refrigeration".

INSTITUTION OF ELECTRICAL ENGINEERS (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. W. R. Stevens and Mr. H. M. Ferguson: "Our Civic Lighting: Gloom or Gaiety" and "A Survey of Street Lighting and its Future".

ROYAL INSTITUTION, LIBRARY CIRCLE (at 21 Albemarle Street, London, W.1), at 5.30 p.m.—Mr. Edward Ironmonger: "William Thomas Brande (1788–1866)". (Forgotten Worthies of the Royal Institution, 1.)

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. B. Lennox: "Nuclear Sexing and Human Chromosomal Anomalies".* (Thirteenth of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

SOCIETY OF CHEMICAL INDUSTRY, MICROBIOLOGY GROUP and TEXTILE CHEMICALS GROUP (at 14 Belgrave Square, London, S.W.1), at 6.15 p.m.—Meeting on "The Microbiological Breakdown of Cellulose". Dr. J. A. Gascoigne: "The Industrial Significance of Cellulose Breakdown"; Mr. P. Russell: "Microbiological Studies in Relation to Moist Groundwood Pulp".

INSTITUTE OF METALS, LONDON LOCAL SECTION (joint meeting with the LONDON BRANCH of the INSTITUTE OF BRITISH FOUNDRYMEN (at 17 Belgrave Square, London, S.W.1), at 6.30 p.m.—Dr. D. V. Atterton: "The Origin, Detection and Elimination of Gases in Cast Metals".

ROYAL INSTITUTE OF CHEMISTRY, LONDON SECTION (joint meeting with the BATTERSEA COLLEGE OF TECHNOLOGY CHEMICAL SOCIETY, at the Battersea College of Technology, Battersea Park Road, London, S.W.11), at 7 p.m.—Sir Christopher Ingold, F.R.S.: "Nitration and Nitrosation; a Contrast".

UNIVERSITY OF LONDON (at Wye College, Wye, Ashford, Kent), at 8.15 p.m.—Prof. A. C. Schuffelen (Wageningen): "Some Aspects of Research on Soil Fertility".*

Friday, December 2

WORSHIPFUL SOCIETY OF APOTHECARIES OF LONDON, FACULTY OF THE HISTORY OF MEDICINE AND PHARMACY (at Apothecaries' Hall, Black Friars Lane, London, E.C.4), at 5.30 p.m.—Dr. A. H. T. Robb-Smith: "The Growth of Knowledge of Functions of Blood".

INSTITUTION OF ELECTRICAL ENGINEERS, MEDICAL ELECTRONICS DISCUSSION GROUP (at Savoy Place, London, W.C.2), at 6 p.m.—Discussion on "Telemetering Biological Data" opened by Dr. G. H. Byford and Dr. K. G. Williams.

BRITISH INSTITUTION OF RADIO ENGINEERS, COMPUTER GROUP (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6.30 p.m.—Mr. D. Roberts, Dr. D. S. Campbell and Mr. P. M. Thompson: "Progress in Microminiature Circuit Techniques for Digital Computers".

SOCIETY OF CHEMICAL INDUSTRY, FINE CHEMICALS GROUP (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Prof. W. H. Linnell: "Pharmacy—Art or Science".

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 9 p.m.—Prof. J. Z. Young, F.R.S.: "Control, Constancy and Change in Animal Life".

Saturday, December 3

BRITISH INTERPLANETARY SOCIETY (in the Tudor Room, Caxton Hall, London, S.W.1), at 6 p.m.—Dr. H. C. King: "The History and Future of Telescopes for Astronomical Observations".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

LECTURER (with special qualifications in poultry husbandry) IN THE DEPARTMENT OF AGRICULTURE—The Secretary, The University, Edinburgh (December 5).

SENIOR SCIENTIFIC OFFICER (with an honours degree in physics, and several years relevant experience) AT THE DEFENCE STANDARDS LABORATORIES, Department of Supply, Maribyrnong, Victoria, Australia, to take charge of a section engaged in applying X-ray crystallography and electron microscopy to structural problems arising from the chemical, physical and metallurgical work of the D.S.L., including interpretation of results; also applying X-ray diffraction to metallurgical examinations and chemical analysis—The Senior Representative (AV.82/5), Department of Supply, Australia House, Strand, London, W.C.2 (December 7).

ASSISTANT LECTURER IN PLANT PATHOLOGY IN THE DEPARTMENT OF AGRICULTURAL SCIENCES, School of Agriculture, Sutton Bonington—The Registrar, The University, Nottingham (December 9).

ASSISTANT LECTURER OR LECTURER IN APPLIED MATHEMATICS—The Registrar, The University, Sheffield (December 10).

SENIOR PHARMACOLOGIST (well versed in standard classical pharmacology); and a SENIOR PHYSIOLOGIST (well versed in mammalian experimental techniques), to take charge of sections of medical research at the Chemical Defence Experimental Establishment (War Office), Porton, Wilts—The Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting G.397/0A (December 10).

CHAIR OF FLUID MECHANICS WITHIN THE DEPARTMENT OF MECHANICAL ENGINEERING—The Registrar, The University, Leeds 2 (December 14).

UNIVERSITY DEMONSTRATOR IN ORGANIC CHEMISTRY—Dr. F. B. Kipping, University Chemical Laboratory, Lensfield Road, Cambridge (December 14).

LECTURER/SENIOR LECTURER IN PSYCHOLOGY at the University of New England, Armidale, New South Wales, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, December 15).

TEMPORARY RESEARCH ASSOCIATE or RESEARCH FELLOW (suitably qualified medical or science graduate with good experience in enzymology) IN THE BIOCHEMICAL SECTION OF THE DEPARTMENT OF PATHOLOGY, for work in connexion with possible enzyme disturbances in cancer—The Registrar, King's College (University of Durham), Newcastle upon Tyne (December 18).

LECTURER IN ELECTRICAL ENGINEERING—The Registrar, Manchester College of Science and Technology, Manchester 1 (December 19).

CHAIR OF PHYSICS; and CHAIR OF ZOOLOGY in the University College, Ibadan, Nigeria—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (December 30).

LECTURER IN BACTERIOLOGY at the University of Malaya, Singapore—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (December 31).

LECTURER or ASSISTANT LECTURER IN PHARMACEUTICS at the University of Malaya, Singapore—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London W.C.1 (December 31).

SENIOR LECTURER IN CHARGE OF THE DEPARTMENT OF PHILOSOPHY, The University College of Sierra Leone (Fourah Bay College)—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C 1 (December 31).

ANALYTICAL CHEMIST (with a first- or upper second-class honours degree in inorganic chemistry, or equivalent qualification, and a thorough grounding in this subject, with special reference to inorganic quantitative analysis) in Bechuanaland, to take charge of the Geological Survey Laboratory, and undertake the analysis of rocks, ores, minerals and ground-water, etc.—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.105/76/05.

ASSISTANT EXPERIMENTAL OFFICERS or EXPERIMENTAL OFFICERS (2) (with a degree in mathematics or statistics, or a degree in agriculture or biology with an interest in experimental work and statistics) IN THE STATISTICS DEPARTMENT, for work on agricultural and biological statistics—The Secretary, Rothamsted Experimental Station, Harpenden, Herts.

CHEMIST (with a good honours degree in chemistry, and at least two years postgraduate research experience, preferably in insecticide analysis), with the PESTICIDES RESEARCH UNIT, Tanganyika, for research into the chemical aspects of the control of tropical pests and to take charge of the chemical laboratory—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.87/8/01.

COMPUTER (with a competent knowledge of, and preferably a degree in, mathematics) IN THE DEPARTMENT OF PHYSICS, to assist research groups by computations using desk calculating machines and an electronic computer—The Professor of Physics, King's College (University of Durham), Newcastle upon Tyne 1.

LECTURERS, ASSISTANT PROFESSORS and ASSOCIATE PROFESSORS IN THE DEPARTMENT OF MATHEMATICS (either at the Edmonton branch or the Calgary branch of the University)—Professor B. S. Keeping, Mathematics Department, University of Alberta, Edmonton, Alberta, Canada.

TECHNICAL EDITOR (preferably with a pass degree or H.N.C., and experience in a related field of work), to be employed on editing, proof-reading, indexing and distribution of scientific reports, technical specifications etc., and to handle related information inquiries—The Senior Recruitment Officer, Atomic Weapons Research Establishment, Aldermaston, Berks, quoting Ref. No. B.2493/34.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Ministry of Agriculture, Fisheries and Food. Bulletin No. 146. Poultry Breeding: Genetics and Systems of Breeding. By G. E. Mann. Third edition. Pp. vi+146. (London: H.M. Stationery Office, 1960.) 7*s*. net. [188

Ministry of Agriculture, Fisheries and Food. Domestic Food Consumption and Expenditure, 1958. Annual Report of the National Food Survey Committee. Pp. vii+185. (London: H.M. Stationery Office, 1960.) 10*s*. net. [188

Department of Scientific and Industrial Research: Road Research Laboratory. Road Research Technical Paper No. 48: The Assessment of Priority for Road Improvements. By D. J. Reynolds. Pp. iv+31 (London: H.M. Stationery Office, 1960.) 2*s*. 6*d*. net. [188

Federation of British Industries. Coal: The Price Structure. Fourth edition. Pp. vi+10. (London: Federation of British Industries 1960.) 2*s*. 6*d*. [188

The Edinburgh School of Agriculture, and the Edinburgh and East of Scotland College of Agriculture. Calendar for 1960–61. Pp. 108 (Edinburgh: The Edinburgh School of Agriculture, and the Edinburgh and East of Scotland College of Agriculture, 1960.) 1*s*. [188

Department of Scientific and Industrial Research: Forest Products Research. Special Report No. 14: Theory of Cutting Part 1: Experiments in Rectilinear Cutting. By K. J. S. Walker and R. Goodchild. Pp. ii+26+4 plates. (London: H.M. Stationery Office, 1960.) 2*s*. 6*d*. net. [188

Proceedings of the Royal Society of Edinburgh. Section B (Biology). Vol. 67, Part 3: A Taxonomic Review of the British Species of *Culicoides* Latreille (Diptera, Ceratopogonidae) By Dr. J. Allan Campbell and E. C. Pelham-Clinton. Pp. 181–302. (Edinburgh: The Royal Society of Edinburgh, 1960.) 21*s*.; 3.75 dollars. [188

Other Countries

New Zealand Forest Service: Forest Research Institute. Forestry Research Notes No. 20 (September, 1959): Progress Report on the Establishment in New Zealand of *Ibalia Leucospoides* Hochenw., a Parasite of *Sirex noctilio* (F). By R. Zondag. Pp. 11. (Wellington: Government Printer, 1959.) [188

New Zealand Department of Scientific and Industrial Research: Geophysics Division. Seismological Observatory Bulletin E-187: New Zealand Seismological Report, 1956. Pp. ii+94. (Wellington: Government Printer, 1960.) [188

World Health Organization. Technical Report Series, No. 190: Expert Committee on Venereal Infections and Treponematoses—Fifth Report. Pp. 73. 3 Swiss francs; 5*s*.; 1 dollar. No. 198: European Technical Conference on the Control of Infectious Diseases through Vaccination Programmes, Rabat, Morocco, 28–31 October 1959—Report. Pp. 21. 1 Swiss franc; 1*s*. 9*d*.; 0.30 dollars. (Geneva: World Health Organization; London: H.M. Stationery Office, 1960.) [188

Berichte des Deutschen Wetterdienstes. Nr. 67 (Band 9): Die Mittlere vertikale Verteilung von Wolken in Abhängigkeit von der Wetterlage. Von Elisabeth de Bary und Fritz Moller. Pp. 28 mit 8 Tabellen im Text und 68 Abbildungen Anhang. (Offenbach a.M.: Selbstverlag des Deutschen Wetterdienstes, 1960.) [188

Oak Ridge National Laboratory, Oak Ridge, Tennessee, operated by Union Carbide Corporation for the U.S. Atomic Energy Commission. Articles published in Technical Journals, Reports Issued, Papers presented at Scientific Meetings, Theses Completed, and Inventions Disclosed during 1959 by ORNL Staff Members. Pp. v+84. (ORNL Central Files No. 60–6–49). (Oak Ridge, Tennessee: Oak Ridge National Laboratory, U.S. Atomic Energy Commission, 1960.) [188

Commonwealth Scientific and Industrial Research Organization, Australia. Division of Fisheries and Oceanography. Technical Paper No. 9: The Concentration of Plankton Pigments in Australian Waters. By G. F. Humphrey. Pp. 27. (Melbourne: Commonwealth Scientific and Industrial Research Organization, 1960.) [188

Institute of Medical and Veterinary Science, Adelaide. Twenty-first Annual Report of the Council, July, 1958—June, 1959. Pp. 100+5 plates. (Adelaide: Institute of Medical and Veterinary Science, 1960.) [188

United States Department of Agriculture: Agricultural Research Service. Technical Bulletin No. 1214: A Revision of the Genus *Trupanea* in America North of Mexico (Diptera, Tephritidae). By Richard H. Foote. Pp. ii+29. (Washington, D.C.: Government Printing Office, 1960.) 20 cents. [188

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THE GREY SEAL AND BRITISH FISHERIES

THE grey seal (*Halychoerus grypus*) appears to have increased considerably in numbers on the coasts of Great Britain during the past forty years. Except from one place, however, there are no comparative figures to show how great the increase may be, or even whether the apparent increase is real. The exception is the Farne Islands where, although the colony of grey seals had been exploited commercially on a small scale for many years during the past century, the population was estimated to number 600–800 in 1928. The National Trust came into possession of the Islands in 1925, and since then the seals have been completely protected. Counts by members of the Natural History Society of Northumberland, Durham and Newcastle upon Tyne have shown that the seal population had increased to 3,000 in 1957, and that it is now about 3,500. It is unfortunate that we have no similar comparative counts of the population in any of the other colonies of grey seals on the coasts of Britain.

For long the grey seal was believed to be a rare British animal, largely because of the vernacular name of *Phoca vitulina*, the common seal. It is difficult for people who are not familiar with the differences between the two native species to identify the animals in the water, for little except part of the head is generally visible. Consequently it has long been customary to assume that any seal seen by chance is a common seal, an assumption that is now known to be unwarranted, for on many parts of the coast the common seal is uncommon, and the grey seal is the species usually seen. It was probably largely this misapprehension that led to the passing of the unnecessary grey seals Protection Act in 1914, a private member's Bill that was slipped through Parliament late at night by a bare quorum at the instigation of a person whose interest in seals seems to have been confined to slaughtering them. This Act, and the second Act of 1932 which protects the grey seal in its breeding season during September 1–December 31, have until recently not been taken very seriously, even by Government departments.

Since 1945 the British seals have attracted the attention of a number of zoologists, who have published numerous papers on their anatomy, physiology, ethology, and general natural history. As a result of these researches, it has become plain that the grey seal is a much commoner animal than was formerly believed; but it is impossible owing to the lack of exact observations in the past to know whether this is due to an increase in the number of seals or in the number of zoologists interested in them. It is equally difficult to form an objective judgment about the complaints of the Scottish salmon netters, who capture salmon in inshore waters and estuaries, that the numbers of grey seal have increased inordinately. Past records show that salmon netters have always complained of the depredations of seals, and have used various methods to kill them or drive them away, sometimes with conspicuous success.

There is no doubt that seals do inflict considerable damage on salmon nets, and that they destroy or maul some of the salmon captured in them. It is not surprising, therefore, that the net proprietors feel aggrieved that a large population of grey seals, which is known to have increased four- or five-fold in the past thirty years, should enjoy complete protection on the Farne Islands, especially since a number of seals tagged on the Islands have been entangled and drowned in their nets. The netters wish the seal population of the Islands to be drastically reduced, but they are opposed on humanitarian grounds by many people whose material interests are not involved; unfortunately, strong emotions have been aroused on both sides. An attempt at culling some of the young pups in 1959 was unsuccessful for various reasons, and, moreover, it is not certain that control of numbers by killing unweaned pups is the best method. So far as our present knowledge goes, more than 50 per cent of the pups die from natural causes before they reach the age of one year; it therefore seems superfluous to kill pups when so many of them will be dead within twelve months even if no action is taken. Information is not yet available to show whether the killing of adult seals on their breeding grounds is an effective method of control. The breeding colonies are comparatively few, and the concentration of adults on them is high; the breeding grounds therefore appear to be the places where a large reduction of numbers could be attained easily and quickly. But isolated attempts at reducing the seal population by slaughtering some of the animals at one or two colonies do not seem likely to have any permanent effect of significance.

It is by no means certain that all the damage complained of is inflicted by seals from the Farne Islands; nothing is known about the movements of the seals from the much larger colony in Orkney which may be contributing to the damage. It seems improbable, too, that all the seals from these colonies are regularly preying on salmon and damaging the nets. The seal populations are known to total many thousands, yet the seals seen at the fishing stations are counted in dozens or less; if all the population were preying on salmon, the netters' latest returns would be expected to be the worst ever made instead of being among the best. There is some evidence that the damage is inflicted by a minority of the population, and that damage stops when this minority

is removed; but what part of the population is responsible for the damage has not yet been ascertained. There is also evidence that there is some segregation of the population into sex- and age-groups, but much more information is required on this point. The recovery of seals marked as pups has proved that some of them at least travel very long distances in the first few months of their lives, for example from the Farne Islands to Norway, Faroe, and the coasts of Germany, Holland, and Belgium. The movements of older animals have yet to be traced; regular tagging has been carried on for less than ten years, and it is probable that the methods used at first were not efficient, so that the seals lost their tags after a comparatively short time.

It is thus evident that no satisfactory policy about grey seals in relation to fisheries can be settled until the requisite knowledge about their natural history has been obtained. It is for this reason that the Nature Conservancy is at present sponsoring a three-year programme of research on the grey seal, financed partly by the Development Commissioners. In a recent paper* which should form a useful background to this investigation, Dr. B. B. Rae has attempted to gather together all that has been written about the grey and common seals in relation to fisheries since the passing of the Grey Seal Protection Act in 1914. Unfortunately, Dr. Rae mixes the vague statements of untrained observers with the relatively few proved facts, and tends to reach conclusions some of which start from false premises; he sometimes appears to abandon objectivity by straining to build up a case against the grey seal with statements that are not adequately supported by evidence. There is a *prima facie* case against the grey seal, but the solution of the problems it presents can only be found by patient research and the laying aside of all emotion and bias on both sides. The work is in hand, and if faithfully and diligently prosecuted, there is no doubt that the desired result will be attained.

* Department of Agriculture and Fisheries for Scotland. Marine Research 1960, No. 2. Seals and Scottish Fisheries. By Dr. Bennet B. Rae. Pp 39 + 9 plates. (Edinburgh and London: H.M. Stationery Office, 1960.) 15*s*. net.

MIRŒSTROL: AN ŒSTROGEN FROM THE PLANT *PUERARIA MIRIFICA*

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In 1936, Dr. S. J. Folley, working at the National Institute for Research in Dairying at Shinfield, in England, found that the injection of œstrone or œstradiol benzoate into lactating cows caused prolonged increases in both the fat and the non-fatty solids content of the milk[1]. This 'enrichment effect', as it was then called, was later confirmed and further investigated by Folley and his colleagues[2].

During the early spring of 1948, Dr. H. W. Bennetts, of Perth, Western Australia, discussed with Drs. Bartlett and Folley his findings that reproductive disorders in sheep were due to the ingestion of œstrogenic compounds apparently present in subterranean clover, which at that time was the principal diet of sheep in Western Australia. In view of this finding and the work reported above by Folley and his colleagues, it was decided to initiate work at the National Institute for Research in Dairying on œstrogens in pasture herbage. Dr. Bennetts kindly provided helpful information on the techniques which he had found useful, and advice and help was also sought and obtained from Sir Charles Dodds and his colleagues at the Courtauld Institute of Biochemistry, Middlesex Hospital, London, where also at that time D. H. Curnow, a research worker from Western Australia, was studying herbage œstrogens.

In May 1948 œstrogenic activity was demonstrated in the pasture herbage from a field adjoining the National Institute for Research in Dairying by Bartlett and his colleagues[3]. This finding posed a host of questions of practical significance for the solution of which it was clear that the resources available at that time at the Institute and the Courtauld Institute needed to be strengthened on the chemical side. Accordingly, in 1949 Dr. G. S. Pope joined the staff at Shinfield for work on œstrogens in pasture plants; the progress of this work has already been reported[4].

In the early stages of the work, when attempts were being made to isolate the œstrogens of red clover (aerial portions of the plant), attention was directed to the chemically new and highly potent œstrogen isolated in 1940 by Schoeller, Dohrn and Hohlweg[5] from the tuberous roots of a leguminous plant in Thailand, investigated from a chemical point of view by Butenandt[6] (1940). It was evident that this plant source was at least a hundred times as rich in œstrogenic activity as red clover and it became of considerable interest for two reasons. The first was that since both it and red clover are of the family Leguminosae, it seemed likely that the slight activity of red clover was due to a low content of the same new œstrogen as found in the plant in Thailand, and, therefore, that study of the latter might greatly help the work with red clover. (In the event this forecast proved to be wrong, as the activity of red clover was found to be due to the very slightly potent *iso*flavonoid œstrogens.) The second reason was a natural interest in the new, highly potent œstrogen for its intrinsic value.

At this stage, Mr. D. C. Rivett-Carnac, of the British Embassy, Bangkok, with whom the workers at Shinfield were in touch, directed attention to certain relevant information in some of the Thai scientific journals.

Kerr[7] in 1932 was the first to direct public attention to the fact that the tuberous roots of the Thai plant concerned, a woody climber found in the forests of northern Thailand and known locally as *kwao keur*, were considered to be of value as the active constituent of a rejuvenating drug. The information came to him privately from Mr. H. B. Garrett and Dr. E. C. Cort, and the conclusion reached was that the plant was *Butea superba*. Following Kerr's paper, various workers began to collect the roots, and in 1939 Vatna[8] showed the presence of œstrogen in *kwao keur*, this being confirmed by Schoeller *et al.*[5]. It became clear, however, after detailed botanical investigation in Thailand, that the name *kwao keur* was, in fact, applied to several species of plant having tuberous roots, and that those yielding the new œstrogen belonged to an unnamed species of *Pueraria*, superficially very similar to *Butea superba*. The name *Pueraria mirifica* was given to it by Lakshnakara Kashemsanta, Kasin Suvatabandhu and Airy Shaw[9].

In 1952 a gift of 6·1 kgm. of dried *Pueraria mirifica* root was received at Shinfield from Mr. Kasin Suvatabandhu, and in 1953 and 1954 batches of 9 kgm. and 4 kgm. were again obtained through the generosity of Mr. Kasin Suvatabandhu and with the assistance of British Council staff in London and Bangkok. Bioassay, using the mouse uterine growth test, of a crude methanol extract of the powdered root confirmed the high œstrogenic activity of the material. The crude methanol extract (6 per cent by weight of dried root) was then submitted to conventional solvent partition procedures giving a product (0 6 per cent by weight of dried root) which contained more than 50 per cent of the œstrogen. Further purification was effected by partition chromatography on kieselguhr columns, and certain fractions from these crystallized in part and yielded a crystalline product (58 mgm. from 6·1 kgm. dried root) when washed with ethyl acetate. Recrystallization from methanol yielded as thin rectangular plates a colourless crystalline product, melting with decomposition at 268° C. (Kofler apparatus). This product appeared to be homogeneous when chromatographed on paper in three different solvent mixtures, in each case showing as a pink spot on reacting with 5 per cent aqueous potassium carbonate and diazotized *p*-aminophenyl 2-diethylaminoethyl sulphone. It appeared, therefore, that the product, of melting point 268° C., was a pure compound, and on testing for œstrogenic activity it was found to be equal to œstradiol-17β in potency in the mouse uterine growth test, and to have one-quarter of the potency of œstradiol-17β in the rat vaginal cornification test, in each case œstrogens being administered by subcutaneous injection. The name 'mirœstrol' was given to the œstrogen; it is doubtless identical to the compound isolated by Schoeller *et al.*[5].

For further biological and chemical work, and especially for an attack on the structure of mirœstrol, much larger quantities of the tuberous roots were required. Dr. S. Bartlett was responsible for the arrangements eventually made to collect additional supplies of the root, and he personally supervised the collections on site. The only place where the plant was known to grow was in the forest near Chiengmai in northern Thailand, and it was clear that supplies could only be obtained by means of a collaborative effort with the appropriate local authorities. Those who gave generous help and advice included Prince Lakshnakara Kashemsanta, Mr. Kasin Suvatabandhu, the director and staff of the Maejo Agricultural Experimental Station at Chiengmai, and Mr. R. J. Hilton, head of the British Council Department in Bangkok.

At this time the interest of the National Research Development Corporation was sought and obtained in this work. The chemical novelty was certain at this stage; the point was whether the structure, when known, might be readily accessible by synthesis from known and abundant substances. The Corporation accordingly undertook to obtain whatever patent protection was possible in the light of prior knowledge and publication and agreed to finance an additional chemist, Dr. D. G. Bounds, at Shinfield, and certain other costs likely to be incurred in the collection of the root, the extraction of mirœstrol and the determination of its structure.

Two plant-collecting expeditions to Thailand were then undertaken by Dr. Bartlett. The first in 1954, yielding 120 kgm. of dried root, was financed mainly by a grant from Quaker Oats, Ltd., but in part by the National Research Development Corporation, and the second in 1957, which was wholly financed by the latter, yielded 200 kgm.

Mr. Suvatabandhu, a well-informed Thai botanist, knows of only two places in Thailand where quantities of the plant *Pueraria mirifica* grow; one place is at the foot of the mountain Doi Suthep near Chiengmai, and the other is nearly 100 miles farther north at Chieng Dao.

The plant clearly has a local reputation as a rejuvenator. At Chieng Dao, Dr. Bartlett and his Thai colleagues were travelling by car in search of the plant and asked one of the men who were repairing the road if he knew the plant, and he replied, "Yes, we eat it!" The tubers of the plant are almost flavourless and somewhat turnip-like in consistency, and as the Thais are not short of food it may be assumed that *Pueraria mirifica* is eaten for some purpose other than as ordinary food. Further evidence of local interest in the plant may be gleaned from the fact that Mr. Puk Pakkasem, a member of the office staff at the British Consulate at Chiengmai, was able, when requested, to obtain in a few hours thirty local inhabitants who were able to locate the plant in the forest and dig it.

An interesting episode occurred in November 1954, when Dr. Bartlett visited the Siam City Bank in Chiengmai accompanied by Mr. Suvatabandhu. During casual conversation the bank manager, Mr. Kraisri Nimmanahaeminoa, showed great interest in the fact that they were collecting *kwao* and said his grandfather used to make medicine from the plant and had written a pamphlet about it. Mr. Nimmanahaeminoa provided a copy of the pamphlet and a pot of 'medicine', which appeared to be a 50 : 50 mixture of dried kwao and honey; it was made in 1953. The pamphlet, in the Thai language, was kindly translated by Mr. Stuart Simmonds, of the School of Oriental and African Studies, University of London, and gave the following information: On the cover was a diagrammatic but accurate sketch of the plant and the description: "Treatise on the Drug made from the Tubers of the Kwao Vine by Luang Anusar Sunthon, Special Commissioner, Chiengmai. Printed at the Upati Pongs Printing House, 3000 copies, May 1931". The main source of information for the pamphlet was a treatise written on palm leaves by 'ancients' and stored in a temple at Pagan, the old capital of Burma. The temple was wrecked by lightning, and the treatise then came to light.

The drug is said to be well known in Burma, where it is called 'paukse', and is stated to rejuvenate old men and women, but should not be taken by young people. One man who took the drug was reputed to have lived to 280 years of age. This local folklore, which appears to ascribe remarkable properties to the *kwao* (or *Pueraria mirifica*) in Burma and Thailand, may well be responsible for the comparative scarcity of the plant. It is not known whether it grows in Burma, but the area of Pagan mentioned in the pamphlet is now said to be an arid desert due to the forest having been cut down in order to build temples.

The pharmaceutical properties of *Pueraria* are considered, in Thailand, to include toxicity, and a careful study of the constituents of the plant has been made in the Chemistry Department of the University of Bangkok. At the Ninth Pacific Science Congress at Bangkok in November 1957, an interesting paper was presented on the "Constituents of the Tuberous Roots of *Pueraria mirifica*" by the Thai workers, T. Nilanidhi, B. Kamthong, K. Isarasona and D. Shiengthong (unpublished work), in addition to a joint one by the Thai and United Kingdom workers, Lakshnakara Kashemsanta, Kasin Suvatabandhu, Bartlett and Pope, on "The Œstrogenic Substance (Mircœstrol) from the Tuberous Roots of *Pueraria mirifica*"[10].

The collaboration of the Director of the Royal Botanic Gardens at Kew was sought in an attempt to grow plants of *Pueraria mirifica* there. The first two attempts were unsuccessful, but the third plant, kindly sent from Thailand by Col. E. H. Jacobs-Larkcom, grew and is still growing vigorously. In December 1958 Miss Joy Jacobs-Larkcom collected a number of additional plants in Chiengmai, and these are now also planted in Kew Gardens.

The roots obtained by the expeditions to Thailand were utilized for the following purposes in the studies on mircœstrol.

(*a*) *Improvement of the method of isolation.* The method of isolation has been simplified, and recovery of around 15 mgm. mircœstrol per kgm. dried root is now a routine procedure. Paper chromatography, using periodate as reagent, which provides a very sensitive and almost specific colour test for mircœstrol, gives efficient analytical control.

(*b*) *Determination of physical properties.* Mircœstrol has been found to crystallize in two forms, a stable hydrated form (stout needles), which after desiccation quickly regains its water of crystallization when exposed to moist air, and a non-hygroscopic, anhydrous form (thin rectangular plates). The latter form has a sharp melting point of 268° C., with some decomposition on melting (Kofler apparatus, rheostat setting 350° C.). Like many steroid hormones, mircœstrol has a high dextrorotatory power, $[\alpha]_D^{17}$ + 301° (1·08 gm./100 ml. in ethanol). Its ultra-violet and infra-red absorption curves have also been useful criteria of the purity of the various specimens isolated.

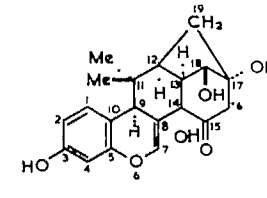
(*c*) *Determination of œstrogenic potency.* In addition to the properties already noted, mircœstrol has been found to have high œstrogenic potency when given orally: approximately three times that of stilbœstrol in the immature mouse uterine growth test[11] and two-thirds that of stilbœstrol in the rat vaginal cornification test. It has also 70 per cent of the activity of œstradiol-17β when administered by subcutaneous injection, in promoting mammary duct growth in the rat, and is 2·2 times as active as œstrone by a similar test in the mouse[12].

(*d*) *Preliminary chemical studies.* Elementary analysis and molecular weight determination in Dr. Dorothy Hodgkin's laboratory, University of Oxford, using the X-ray method, gave $C_{20}H_{22}O_6$ as the molecular formula for mircœstrol, or less probably $C_{20}H_{24}O_5$. Analysis of the monomethyl ether and monoacetate, in each case the phenolic hydroxyl (see below) having reacted, supported this finding. Other derivatives of mircœstrol were then prepared, details of which have been reported elsewhere[13], and from the ultra-violet and infra-red absorption curves of these and their chemical properties it was concluded that mircœstrol is a monohydric phenol possessing one carbonyl and at least two alcoholic hydroxyl groups.

(*e*) *Preparation of a derivative of mircœstrol for X-ray analysis.* The complete elucidation of the structure of mircœstrol solely by chemical methods appeared likely to be very difficult with the small amount of material available. It was therefore decided to employ X-ray crystallographic analysis to solve the problem, using three-dimensional methods on a heavy-atom derivative. This work was carried out by Dr. Dorothy Hodgkin and her colleagues at Oxford.

Dr. D. G. Bounds succeeded in making a monobromo-substitution product of mircœstrol. At first, bromination of mircœstrol with one molecular proportion of bromine gave complex mixtures, but reaction conditions were eventually found which gave a mixture containing only two main products. These were isolated by partition chromatography, and from the elementary analysis and ultra-violet and infra-red absorption curves of one of these compounds, it was concluded that in this compound a single bromine atom had entered the mircœstrol molecule replacing a hydrogen atom and that no other chemical changes had taken place. The fact that the monobromo-mircœstrol isolated coupled much less readily than did mircœstrol with diazotized *p*-aminophenyl 2-diethylaminoethyl sulphone was taken as good evidence that the bromine atom was present as a substituent in the benzene ring of mircœstrol.

(*f*) *X-ray studies.* X-ray crystallographic measurements on monobromomircœstrol were made by Dr. Noel E. Taylor, and the crystal structure was solved in collaboration with Dr. Hodgkin and Dr. J. S. Rollett through a series of three-dimensional electron density calculations carried out on *Deuce* at the National Physical Laboratory. The positions of the atoms found by these calculations are illustrated in Figs. 1 (*a*) and (*b*). They lead to the structural formula I, for mircœstrol itself:



(I)

Full details of this work have been reported elsewhere[14].

Biogenetically, it seems possible to dissect the nucleus into an isoprene unit and a partly reduced *iso*flavene nucleus. This dissection relates it, on one hand, to the many plant products in which isoprene units are found linked to condensed ring systems (cf.

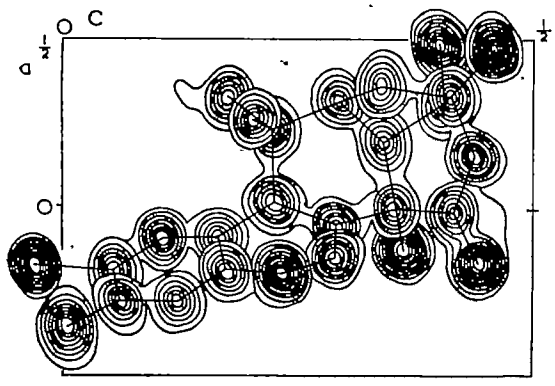


Fig. 1 (a). Electron density-levels over the peaks in ρ3 in bromomircœstrol. The structure is seen projected along [010]. Contours at intervals of approximately 1 el./A.³ except over the bromine atom, where the intervals are 4 el./A.³

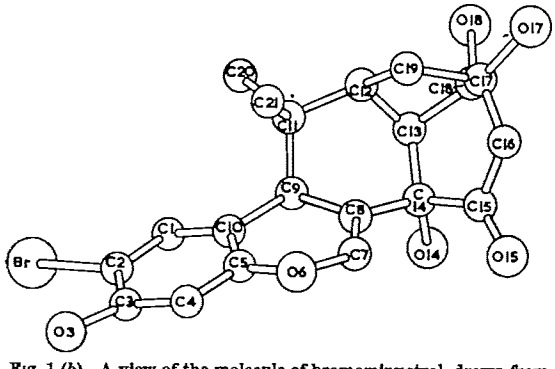


Fig. 1 (b). A view of the molecule of bromomircœstrol, drawn from the atomic positions in ρ3

Robinson[15]), and, on the other, to those *iso*flavones and *iso*flavenes which have been shown to have œstrogenic properties. Mircœstrol is not a steroid, and the biological activity is probably a consequence of accidental features of molecular geometry. The actual distance from the 3-OH in mircœstrol to the 18-OH is 10·3 Å., which is very near the distance to be expected from models of the 3-OH to the 17-OH of œstradiol. When, however, one compares the disposition of the 17-OH of mircœstrol and the 16-OH of œstriol relative in each case to the 3-OH, the similarity is not so close; but perhaps it is worth noticing in this connexion that mircœstrol is the more potent œstrogen.

(*g*) *Limited clinical trial*. The trial was carried out by Dr. P. M. F. Bishop and his colleagues at the Chelsea Hospital for Women, London.

Mircœstrol has been administered to ten women suffering from amenorrhœa (primary, two cases; secondary, seven cases) or artificial menopause (one case). 5 mgm. daily was given on six occasions and 1 mgm. daily on another six occasions. Marked œstrogen response was noted with both these doses on the vaginal smear, the maximum rise in the cornification index usually occurring during the second or third week after treatment commenced. This peak usually occurred, therefore, after the treatment had been discontinued. Œstrogen withdrawal bleeding failed to take place on six occasions (three with doses of 1 mgm. daily from 5 to 10 days; three with doses of 5 mgm. daily from 2 to 14 days), though withdrawal bleedings had usually occurred in these patients when they had been previously treated with œstrogens. Withdrawal bleeding did take place on five occasions, however, 7–18 days after the cessation of treatment. The withdrawal interval is much longer, therefore, than with most other oral œstrogens. No toxic effects were complained of on three occasions, the doses being 1 mgm. daily for 7 days, 5 mgm. daily for 8 days and 5 mgm. daily for 14 days, respectively. Toxic effects were rather marked on the remaining nine occasions and consisted of malaise, headache, nausea and in some instances vomiting. They did not seem to be appreciably less severe on the 1-mgm. doses than on the 5-mgm. doses. Work with 0·1-mgm. doses is being undertaken. On four occasions there was enlargement and tenderness of the breasts. These changes were more severe and more frequent on the 5-mgm. doses. On two occasions they were accompanied by marked pigmentation of the nipples, which persisted for some time. In the patient who had received an artificial menopause the hot flushes diminished in frequency and severity for the first week of the 14-day course, but began to return by the fifth day after treatment had been discontinued.

In the light of the limited experience described, it would seem that mircœstrol produced marked œstrogenic response in the vaginal smear; is rather slow to act and its effect takes some time to wear off. It does not always induce a withdrawal bleeding, and in the doses so far employed is apt to give rise to rather disagreeable toxic effects.

In view of the undesirable side-effects of mircœstrol, it appears unlikely that this substance itself will be suitable for use in medicine in spite of its high level of œstrogenic activity by the oral route. It is possible that modifications of its structure might lead to useful œstrogens, but it is evident that a total synthesis of the whole molecule would be difficult, and not likely to be commercially feasible; also although the mircœstrol structure is new, it is, as noted above, related in part to already known œstrogens, and therefore does not display as great a novelty in regard to its structure/action relationship as was at first thought possible; nevertheless, mircœstrol presents some features of interest, and further investigations of its biological properties are proceeding.

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HIGH-ENERGY PHYSICS

TENTH ROCHESTER CONFERENCE

THE annual international conference on high-energy physics, known more commonly as the 'Rochester Conference', has, over the past decade, produced a sequence of elaborate progress reports on the status of current experimental and theoretical research in one of the most rapidly growing fields of physics. Under the leadership of Prof. Robert E. Marshak, it began in 1950 as an informal seminar at which a handful of specialists considered the implications of the newly discovered π-mesons. When even newer classes of particles were observed in cosmic radiation, and when the great accelerators began to operate, the scope of the conference naturally widened, so as gradually to encompass all the problems that make up the modern science of particle physics. The size of the delegation increased as well, reflecting the growth in the number of physicists engaged in these problems. At the tenth Conference, which was recently held in Rochester, 350 delegates from more than twenty nations gathered in order to assess the results of their most recent research, and to plan the work that lies ahead. The meeting lasted from August 25 until September 1. During the first two days, detailed reports were presented in four simultaneous sessions. These were followed by four plenary sessions during which the earlier discussions were summarized by *rapporteurs*, and three sessions of invited papers on topics of general interest. It is impossible to give a useful account of all these proceedings in abbreviated form, particularly when it is addressed to an audience of non-specialists. I have therefore chosen to review the set of fundamental principles toward the study of which the work at high energies is being directed. I shall then describe some of the more prominent features of the tenth Conference, emphasizing those reports that appear to provide new links in the chain of argument.

Outside gravitation, which seems to play no significant part in nuclear physics, there are three kinds of forces in Nature. The most familiar of them is the electromagnetic interaction, for which the classical theory was developed by Maxwell and Lorentz. Its extension to microscopic phenomena has been achieved in a quantum theory of electrodynamics. The theory describes the interaction in terms of the typical virtual process $e \rightarrow e + \gamma$, where e is any charged particle and γ is a photon. The symbol e also represents the unit of charge, of which all natural charges appear to be exact multiples. The strength of the interaction is measured by the dimensionless universal constant $e^2/\hbar c = 1/137$, $\hbar$ being Planck's constant and c the speed of light in vacuum. The theory has scored many successes, and its essential validity, except possibly at very high energies, is not questioned.

The second kind of force encompasses the 'strong' interactions between particles of certain classes. A quantum field theory of the strong interactions has developed from the original work of Yukawa, and is typified by the virtual process $p \rightarrow n + \pi^+$, where p is a proton, n a neutron, and π^+ a positively charged pion. The dimensionless coupling constant for the pion-nucleon interaction is $g^2/4\pi\hbar c \simeq 14$, where g has the physical dimension of charge. The fundamental significance of the charge g is no more clearly understood than that of the electric charge e. Furthermore, the coupling constants associated with other strong interactions are presumably different, but all are believed to be of the same order of magnitude. Because of several technical difficulties the theory of strong interactions has proceeded cautiously, guided closely by new experimental discoveries. But certain simplified forms of the theory, developed principally by Chew and his collaborators, have provided semi-quantitative descriptions of many phenomena.

We encounter finally the 'weak' interactions, which are the most mysterious of all the forces. They are typified by the β-decay of a nucleon; for example, $n \rightarrow p + e^- + \bar{\nu}$, where $\bar{\nu}$ is an antineutrino. Weak interactions couple other classes of particles as well. There is no experimentally identified field quantum, analogous to the photon and the pion, associated with the weak interactions. The present description of the phenomena is a development of the original work of Fermi. In his theory, the coupling constant characteristic of a weak interaction is not immediately dimensionless, but it is conventionally written in units that involve the Compton wave-length of the charged pion. Weak couplings so defined have strengths of the order of 10^{-14}, a number to be contrasted with 10^{-2} for the electromagnetic coupling, and with 10 for strong coupling. It appears that weak interactions have at least roughly the same strengths in all their manifestations. This observation has led to the hypothesis of the universality of weak interactions, but a precise formulation of the principle has not yet been made, nor has it been applied quantitatively to experimental data in an unambiguous way. A great advance in our knowledge of weak forces was recently initiated by Lee and Yang. Their suggestion that the interactions need not be invariant to spatial reflexion has been experimentally verified in many different ways, and has led to important clarifications of symmetry principles underlying all physics.

The particles of physics, among which the three types of forces are supposed to act, are separated first into two general groups: the bosons and the fermions. By definition, bosons have spins (intrinsic angular momenta) that are integral multiples of $\hbar$. Fermions have half-integral spins. Bosons are regarded as the quanta of the several kinds of field. Thus photons, with spin unity, are quanta of the electromagnetic field; pions, with zero spin, are quanta of the strong nuclear field. If quanta of the weak field exist, they are also presumably bosons. There is no conservation principle governing the number of bosons that may be created or destroyed in a collision. It is only necessary that energy, momentum, angular momentum, and charge be conserved. The number of fermions, on the other hand, is believed to be subject to strict conservation laws which I shall discuss shortly.

The bosons specifically associated with strong interactions are called 'mesons', and two classes of these particles have so far been observed. In addition to the pions (π) with masses near 0·14 BeV., there are the heavier 'kaons' (K) with masses near 0·50 BeV. (By the 'mass' of a particle I mean, of course, its rest mass. It is most convenient to write rest masses as rest energies in units of MeV. (10^6 electron-volts) or BeV. (10^9 electron-volts).)

There are two sets of fermions. One consists of particles lighter than the mesons, and are called 'leptons'. It includes the neutrino (ν), the electron (e^-), and the muon (μ^-). (Although once called the 'μ-meson' because of its intermediate mass, the muon does not conform to the modern definition of a meson.) The neutrino has zero mass, the electron mass is about 0·5 MeV., and the muon mass is about 106 MeV. The other set of fermions consists of particles heavier than mesons, and is called the set of 'baryons'. It includes the nucleons (N) with masses of about 0·94 BeV.; the Λ-hyperon, with mass 1·12 BeV.; the Σ-hyperons, with masses near 1·19 BeV.; and the Ξ-hyperons, with masses of about 1·31 BeV. The spins of all fermions are almost certainly 1/2. The baryons interact strongly with each other and with the mesons, and weakly with the leptons.

One may well wonder about the meaning of the term 'elementary particles'. The early periods of modern physics were characterized by searches for ultimate constituents of matter, and there were times when it appeared that the search had ended. The current point of view on this matter is somewhat different. The concept of an elementary particle is now thought to be useful only within a specific context of the contemporary experimental and theoretical situation, taking into account the types of interaction that one is investigating, and the particle properties that one regards as fundamental. In this sense the present list of elementary particles need not be final, even if no new species are discovered.

So far I have mentioned ten classes of particles (γ, ν, e^-, μ^-, π, K, N, Λ, Σ, Ξ). A further subdivision occurs when we take account of the different states of electric charge which most of the mesons and baryons can assume. Thus the π has three charge states (π^+, π^0, π^-); the K has two (K^+, K^0); the N has two (p, n); the Σ has three (Σ^+, Σ^0, Σ^-); and the Ξ has two (Ξ^-, Ξ^0). We then have a total of 17 particles. Furthermore, there is believed to be an antiparticle associated with each particle, having properties that are very simply related to those of the particle. This would give a total of 34. However, four of the antiparticles ($\bar{\gamma}$, $\bar{\pi}^+$, $\bar{\pi}^0$, $\bar{\pi}^-$) are experimentally indistinguishable from four of the particles. In this way, we arrive at the 30 unique objects which are under study in high-energy physics.

The multiplicity of charge states bears much formal resemblance to the multiplicity associated with ordinary spin. This observation has led to the idea of an 'isotopic spin vector', I, connected with a given particle or system of particles, and an isotopic spin space in which the vector resides. The z-component of isotopic spin, I_z, selects one of the possible multiplets of the system. For example, the vector I has magnitude unity for the π, with three possible projections on the z-axis representing a triplet (π^+, π^0, π^-). The importance of isotopic spin to the subject rests in the observation that I appears to be strictly conserved in strong interactions. The idea has not yet been given significance in the description of leptons.

The mathematical transformation of a particle into its antiparticle is called 'charge conjugation', and is denoted by the operator C. It is equivalent to a reflexion in isotopic spin space. Under the assumption that particle physics conforms to the principles of special relativity, it has been shown that perfect symmetry exists between a particle and its antiparticle. The two have the same mass, spin, lifetime, and modes of decay; they have opposite charge and magnetic moment. This symmetry is beautifully apparent in the electron-positron pair, on which precise experiments have been done. One believes not only that each of the other antiparticles exists (some of the antihyperons have yet to be discovered) but also that it must exhibit the same symmetry. Another powerful theorem based on relativity has been proved by Pauli and Lüders. It asserts that all interactions are invariant under the combined operation CPT, where C is charge conjugation, P is spatial reflexion (the parity operation), and T is time inversion.

All the conservation and invariance principles that are currently accepted in particle physics can now be stated in summary form. Some are taken over from classical physics, but most have only recently come to light as generalizations from new experiments. The list is as follows:

(A) Principles valid in all interactions:
1. Conservation of energy and momentum.
2. Conservation of angular momentum.
3. Conservation of charge.
4. Conservation of baryons (number of baryons minus number of antibaryons).
5. Conservation of leptons (number of leptons minus number of antileptons).
6. Lorentz invariance (CPT theorem; symmetry of particle and antiparticle).
7. Invariance under T (time inversion).

(B) Principles valid in strong and electromagnetic interactions, and violated in weak interactions:
8. Invariance under charge conjugation.
9. Invariance under spatial reflexion.
10. Conservation of I_z.

(C) Principle valid in strong interactions, and violated in electromagnetic and weak interactions:
11. Conservation of I.

In addition to these strict principles, there are several recently formulated selection rules for which much evidence has accumulated. The most completely confirmed of them states that, when mesons or baryons decay into one another, the magnitude of I for the system changes by $\frac{1}{2}$. This rule and some of the conservation principles can be illustrated by considering the modes of decay of the Λ-hyperon. The particle is electrically neutral, has half-integral spin, and has zero isotopic spin. There are several decay modes which are consistent with principles 1–5. Those that involve no more than three decay particles are:

$$\Lambda \rightarrow n + \pi^0 \quad (1) \qquad \Lambda \rightarrow p + \mu^- + \bar{\nu} \quad (5)$$
$$p + \pi^- \quad (2) \qquad n + \nu + \bar{\nu} \quad (6)$$
$$n + \gamma \quad (3) \qquad n + e^+ + e^- \quad (7)$$
$$p + e^- + \bar{\nu} \quad (4)$$

Since the first two modes involve only baryons and mesons, which are strongly coupled to each other, we might expect that the decay would proceed very

rapidly through these channels. But notice that the isotopic spin of the system $N + \pi$ must be a combination of two vectors the magnitudes of which are $\frac{1}{2}$ and 1 respectively. The only isotopic spin states allowed for this system are $I = 1/2$ and $3/2$. Therefore neither I nor I_z can be conserved, and a decay through strong interactions is impossible. The non-conservation of I_z also inhibits the radiative decay (3). We see in addition that, although decay modes of the type $\Lambda \rightarrow N + \overline{K}$ would satisfy conservation of isotopic spin, the mass of the final state exceeds that of the Λ and the mode is impossible if energy is to be conserved. We have thus shown that the particle cannot decay through strong interactions. Furthermore, since the decay does in fact proceed slowly through channels (1) and (2), we know that a weak interaction couples the particles, and we can use the decay rate to obtain an estimate of its strength. (If the Λ could decay through a strong interaction, its life-time would be of the order of 10^{-23} sec. The observed life-time is about 10^{-10} sec.)

Of the remaining modes of decay, (4) and (5) are not forbidden by any known rules, and can be expected to occur as poor competitors of (1) and (2). The remaining modes are forbidden by selection rules that have not been mentioned. Finally, it is to be noted that the $\Delta I = \frac{1}{2}$ rule requires the $N + \pi$ system in the Λ decay to occur only in the $I = \frac{1}{2}$ state. One can deduce from this that the mode $p + \pi^-$ should occur twice as frequently as $n + \pi^0$, a prediction that is well confirmed by experiment.

The fact that Λ cannot decay promptly permits us to regard it as an elementary particle, even though its life-time is short by ordinary standards. The situation is similar for all the unstable elementary particles, which constitute a majority of the list already given. Outside the stable particles (γ, ν, e^-, p), the longest lived is the neutron with a mean life of 10^3 sec., and the shortest lived is probably the Σ^0-hyperon, the life-time of which, although not yet measured, is expected to be in the neighbourhood of 10^{-19} sec. This example also illustrates the kinds of experiments that must be done in particle physics, and it gives a hint about their difficulty. In order to produce a Λ under controlled conditions, and to observe such a decay mode as $n + \pi^0$, one needs a large accelerator and detectors of considerable refinement. Notice that all the particles are neutral, and so do not produce ionized tracks.

Although the foregoing review constitutes a mere sketch of the high-energy field, it may serve as an adequate background for a short summary of the tenth Rochester Conference. I shall begin with developments concerning the weak interactions. Feynman has looked carefully at the question of universality, with particular attention to the life-time of the muon. Using recent experimental data on the beta decay of oxygen-14, he calculates a muon life-time of $2{\cdot}251 \pm 0{\cdot}012$ μsec. This is slightly longer than the best measured life-time, the discrepancy of about 2 per cent being considerably larger than the combined error. He concludes that the principle as commonly formulated is not quantitative, and he finds further that high-order corrections to the theory only aggravate the discrepancy. Gell-Mann reported on many recent speculations about this general question. He outlined a more abstract formulation of the universality idea, which might be able to cope with the weak interactions of all particles.

Several new experimental results have lent support to other ideas about weak interactions. Ljubimov (Moscow) described an investigation of the 'helicities' of muons in cosmic radiation. According to current theory, the muons in the decay $\pi^+ \rightarrow \mu^+ + \nu$ should spin in the left-handed sense around their direction of motion. The muons from π^- decay should be right-handed. Experiment confirms both predictions. Chuvilo (Dubna) reported on new observations of the decay modes of K^0, and showed that they are in agreement with predictions based on the $\Delta I = \frac{1}{2}$ rule. Additional support for the rule, based on asymmetry measurements in pionic decay of Σ and Λ, was reported by Cronin. It might be said here that none of the many experiments recently carried out has cast any doubt on the invariance principles and selection rules outlined above. With regard to strong interactions, I might first mention the current status of one of the oldest problems in nuclear physics. It concerns the force between nucleons. Early research brought out little more than qualitative facts about the strength and range of the force, without clarifying its details. With the advent of the synchrocyclotron, nucleon scattering could be done at energies up to several hundred MeV. It was discovered that such collisions lead to a strong polarization of the scattered beam, and this phenomenon has become an important tool in the most recent measurements of the interaction. At the conference, representatives of the groups at Harwell, Rochester, Harvard, and Dubna reported that almost all their results now fit into a unique and concise empirical scheme, which it is the aim of theorists to explain. With regard to the theory, one can say that the force at relatively large distances (down to about 3×10^{-13} cm.) is now well understood in terms of a single pion exchange potential. The behaviour at shorter distances, where multiple meson exchange is important, has not yet been dealt with quantitatively.

The strong interactions of K, Λ and Σ particles have also been studied intensively in recent work at the higher energies. The reports from Cornell, Saclay, Brookhaven, Berkeley, Dubna and CERN constitute an enormous library of new data on processes of many different kinds. A particularly interesting result was reported by Good (Wisconsin), who has studied the reaction $K^- + p \rightarrow \Lambda + \pi^- + \pi^+$, and has measured the momentum spectra of the pions. He finds structure in the spectra, suggesting the existence of quasi-stationary states of the $\pi - \Lambda$ system.

Bernardini (CERN) reported progress on the design of experiments for the utilization of energetic neutrino beams derived from the great accelerator in Geneva. It is expected on certain theoretical grounds that the cross-sections for neutrino reactions will be much larger at high energies than they are at low energies. For example, Lee and Yang have speculated about the reaction $\nu + N \rightarrow W + \mu + N$, where W is the hypothetical boson associated with weak interactions. The calculated cross-section for this reaction is 10^{-35} cm.^{2} at high energies; the cross-section for the only neutrino reaction carried out to date ($\bar{\nu} + p \rightarrow e^+ + n$) is 10^{-41} cm.^{2} at low energy.

Another important experiment still in the preparatory stage was described by Panofsky. It will investigate colliding beams of electrons, produced in the Stanford linear accelerator and stored in two magnet rings. The equivalent laboratory energy of the collision will be several thousand BeV.. and will in

this sense represent by far the highest controlled energy available to physics. It is hoped that the beams can be used to examine the validity of quantum electrodynamics in an energy region which has so far only been accessible in rare cosmic ray events.

Finally, I shall discuss a report by Heisenberg on progress being made in his theoretical group (Munich) toward the development of a general theory of elementary particles. They assume that the most general symmetry principles of the type summarized above are sufficient to specify a differential equation, the eigenvalues of which are connected with properties of the particles. Thus the symmetry principles rather than the particles themselves are regarded as the elementary notions of physics. A prototype of such theories is the relativistic wave equation proposed thirty years ago by Dirac, who was able to give a deductive account of electron spin and to anticipate the discovery of the positron. Several years ago, Heisenberg and Pauli proposed a non-linear spinor equation to which they were led by symmetry considerations. It appears that, since then, some significant steps have been taken toward illuminating the mathematical properties of the equation and deducing some of its physical consequences. There is as yet, however, no strong experimental evidence for or against the theory. Aside entirely from computational difficulties, the theory is open to certain conceptual objections. One of them stems from the fact that, for the equation to have non-trivial solutions, it must deal with an indefinite metric in Hilbert space. This leads to probability amplitudes of negative norm, for which no interpretation can be given in the usual formulation of quantum mechanics. Heisenberg hopes, however, that all such cases will correspond to virtual states of physical systems, and that negative probabilities may for this reason not be incompatible with the present structure of physics.

It may be clear from this sampling of the conference that the physics of high energies is active on many fronts. It should also be clear that there are fundamental questions still unanswered. Are there still more classes of particles? Are the strict principles of present theory applicable at very small distances and at very high energies? Is there a 'universal' weak interaction, and is there a field quantum associated with it? Are the particles themselves to be regarded as the ultimate entities of physics, or are their properties derivable from a set of simple principles? At any stage in the development of our knowledge there is always a class of questions which seems inaccessible to the methods of physics, but which is nevertheless eventually answered within the context of later developments. It is with a faith strongly supported by this observation that physicists are attacking the provocative questions now before them.

E. M. HAFNER

NEWS and VIEWS

Cloud Physics at the Imperial College of Science and Technology, London: Prof. B. J. Mason

DR. B. J. MASON has been appointed to a newly created chair in cloud physics at the Imperial College of Science and Technology as from October 1960, thus gaining academic recognition for sustained original work in this field over the past decade or so. He joined the Department of Meteorology at the Imperial College of Science and Technology in 1948, following graduation in physics with first-class honours at University College, Nottingham, in 1947 and some research with Dr. G. D. Yarnold on surface tension in the following year. Mason was led to take up research in cloud physics on reaching the Imperial College of Science and Technology, and he soon formed around him an active group of research students concerned mainly with microphysical processes, while his colleague, Dr. F. H. Ludlam, led parallel work on the macrophysics of clouds, to the benefit of the subject as a whole. Cloud microphysics, in Mason's hands, has advanced mainly by his skill in exploiting laboratory techniques and he has designed a number of quite beautiful experiments. Notable among these is the use of the diffusion cloud chamber, in collaboration with Dr. J. Hallett, to determine the forms—needles, plates, prisms, dendrites—in which ice is deposited as a function of temperature and supersaturation. This work has contributed not only to meteorology but, quite notably also, to modern solid-state physics. Mason was awarded the D.Sc. of the University of London in 1956, and was appointed Warren Research Fellow of the Royal Society in 1957. His authoritative text, "The Physics of Clouds", was published in 1957, and he has served on the Councils of the Royal Meteorological Society and the British Association and on Government research committees. Prof. Mason may now, with extra facilities and his noted enthusiasm, be expected to make an increasing impact on the study of cloud physics in Great Britain.

Physics in Hong-Kong: Prof. W. D. Chesterman

DR. W. D. CHESTERMAN has been appointed to the vacant chair of physics in the University of Hong-Kong. Dr. Chesterman graduated at the University of Bristol in 1934. He then became a student apprentice at the British Thomson-Houston Co. and on completion of his apprenticeship was appointed to the staff of the Company, where he remained until 1939, when he joined the Admiralty. His work in the Admiralty has been mainly in the fields of photographic and optical techniques and in underwater acoustics. He became a Fellow of the Institute of Physics in 1943 and of the Physical Society in 1945. During the past ten years he has gained an international reputation for his work on photographic techniques. He has published a book and a number of papers on high-speed photography, which have been very well received. During 1956–58 he was chairman of the International Committee on High Speed Photography, and in 1958 he was elected a Fellow of the Royal Photographic Society. In 1959 he was awarded the degree of doctor of science by the University of Bristol. The papers put forward for his doctorate included published accounts of his work in the fields of underwater acoustics, illumination optics, high-speed photography and oceanographic research.

Parliamentary Secretary to the Minister for Science

IN moving the second reading of the Ministers of the Crown (Parliamentary Secretaries) Bill in the House of Commons on November 18, the Financial Secretary to the Treasury, Sir Edward Boyle, said that the Bill was designed first and foremost to give the Government greater flexibility in the deployment of Parliamentary Secretaries between Departments, and also, more specifically, it authorized the payment of a salary, not exceeding £2,500 a year, to a Parliamentary Secretary to the Minister for Science. He would be Parliamentary Secretary to the Minister and not to the Ministry, and if the appointment was made questions falling within the responsibility of the Minister would be answered in the House of Commons by the Parliamentary Secretary. Dr. R. Bennett, speaking as chairman of the Parliamentary and Scientific Committee, welcomed the provision as something for which that Committee had been pressing and also paid a generous tribute to the ability of the present Minister for Science. In replying on the debate, Sir Edward Boyle suggested that provision of a Parliamentary Secretary would assist the Minister to pursue his studies in greater detail and that the Parliamentary Secretary would also be able to reply to debates on all the main subjects for which the Minister was responsible. These responsibilities embraced first the Atomic Energy Authority; secondly, the four main executive research councils; and thirdly, those very important advisory bodies, the Advisory Council on Scientific Policy, with its Scientific Man-power Committee, the Overseas Research Council, and the Steering Group for Space Research. If, on the adjournment, members wished to raise the whole question of the work of the Department of Scientific and Industrial Research, or of the advisory bodies, there would be a junior Minister responsible for replying specifically on these subjects.

British Patents and Designs

ON moving the second reading of the Patents and Designs (Renewals, Extensions and Fees) Bill in the House of Lords on November 15, the Earl of Dundee explained that while the Industrial Property Convention of October 1958 made some improvements in existing practice, the only one which needed legislation in Great Britain was the proposed extension from three months to six months in the period of grace allowed for the application for a renewal of a patent or copyright protection for a design. This is done under Clause 1 of the Bill, which also corrects a mistake inadvertently in our own Registered Designs Act but not in the Patents Act of 1949. Clause 2 proposes to repeal the first schedule to the Patents Act, 1949, which specifies certain maximum fees for the registration and renewal of patents but not designs and not trade marks. This schedule to the Act of 1949 is identical with that in the Patents and Designs Act, 1884, and the Earl of Dundee said that it was not proposed to control fees under a statutory instrument as was already done for trade marks or designs, in place of introducing a new schedule. He indicated that if the Bill was passed in its present form the Patent Office proposed to increase the application fee for a patent from £1 to £2, and that for filing the complete specification from £4 to £8. Nearly all the expenses of the Patent Office were in connexion with filing the initial application and the complete specification, and it was proposed to make no increase in the renewal fees, which varied from a maximum of £5 in the first year to £20 in the sixteenth year, and were mostly still less than the set maxima. While welcoming the first part of the Bill, Lord Silkin urged strongly that the clause relating to revised fees should be withdrawn and introduced as a specific single-clause measure, and this was also supported by Lord Cowley and Lord Ferrier, the former of whom thought the present Clause 2 was contrary to the advice of the Swan Committee in 1947. In his reply, the Earl of Dundee maintained that the procedure proposed by the Government was the most advantageous, and said that the Government had already discussed the matter with interested commercial organizations, none of which had raised any objections to the fixing of fees by statutory instruments rather than by a schedule in an act of Parliament.

International Patent Conventions

THE Catalogue of the Derwent Information Service describes briefly the various publications and services provided (Derwent Patents Abstracts—Catalogue. Pp. ii+38. London: Derwent Information Service, Theobalds Road, W.C.1, 1960. 2*s*. 6*d*.). These include reports on British, German, Commonwealth, Belgian and Russian patents in certain specified fields, journals containing abstracts of fine chemicals, plastics, petrochemicals and metallurgical patents, and a series of other patents bulletins dealing with more limited fields. Besides information on patenting procedure in various countries, the catalogue includes an article by M. Hyams on Russian patent law and procedure based on discussions with the Committee for Inventions in Moscow.

Museum of Science and Industry, Birmingham

BIRMINGHAM City Council recently approved a scheme for extending the Museum of Science and Industry in Newhall Street. The new building will replace old property which is structurally unsound and increase the floor area of the Museum to 150,000 sq. ft. The whole scheme is estimated to cost £590,000 and will take not less than six years to complete. The work of rebuilding will be undertaken in three phases; these comprise the erection of a galleried single-storey unit to house, among other large exhibits, the Pacific locomotive *City of Birmingham*; a six-storey administrative, workshop and stores block and another single-storey unit with galleries, in that order. Provision has been made for a lecture room, two cafés and numerous rest rooms. When the scheme is completed public access will be from Fleet Street (which runs at right angles to Newhall Street) by a bridge over the Birmingham–Fazeley Canal.

The site and buildings now occupied by the Museum were once the premises of Elkington and Co., Ltd. (who are well known for the manufacture of silver-plate), until they were taken over by the Committee of the City Museum and Art Gallery in 1950 to house the newly formed Department of Science and Industry. During the past ten years the old factory has been systematically adapted for Museum purposes and opened to the public as each section was completed. The Museum exhibits small arms, veteran, vintage and modern motor-cars and motor-cycles, machine tools, steam engines which are run periodically on live steam, internal combustion engines and scientific instruments covering a wide field. The annual attendances now exceed 400,000.

Science in France

THE second issue of *French Science News*, published by the French Foreign Office and distributed by its Embassy in London, contains considerable information about major French scientific investigations and developments in science and technology. The main articles are concerned with developments in petrology and astronomy while, among pure research items, summaries of work are given on the fundamental theory of corpuscular systems and the concept of the centre of gravity; ultrasonic absorption and dispersion in polyatomic gases; paramagnetic ion relaxation; the production of tritium in thorium by protons of 135 MeV.; the spectra of conversion electrons and K and L Auger electrons resulting from the disintegration of thulium-170 to yttrium-170; the basic functions of definite symmetry for the wave-functions of a system of three identical particles; the absorption spectra of selenium and tellurium in ultra-violet light; the equilibrium diagrams of the zircon–oxygen systems of the rare earths; the reactions of the system calcium sulphide–vanadium pentoxide and the preparation and identification of sodium orthonitrates and orthonitrites. Accounts are also given of new developments in apparatus and equipment in various laboratories as well as in engineering. In medicine, details are given of the phosphodiuresis test provoked by parathormone, and the diagnosis of pseudo-hypoparathyroidism in the infant and the risk involved in radiological examinations. Other information includes particulars of new courses at higher education centres, recent books and awards to outstanding men of science. The journal would be considerably improved if the final editing were entrusted to a French-speaking English-born man of science. M. Jean Rostand might then have enjoyed even more his International Kalinga Prize "for scientific Vulgarization . . . for the entirety of his work".

Introducing Pedology

MARIAN RAY, of 36 Villiers Avenue, Surbiton, Surrey, has provided an admirable series of filmstrips showing the origin, composition and use of soil. There are five strips in the series, each of which could form the basis of a lesson to scholars taking the Ordinary Level General Certificate of Education examination in biology, or agricultural students at farm institutes. The first, "Rocks and Erosion", describes the main types of rocks and the action of weathering; the second, "Plants and Decay", is concerned with the elements of plant nutrition and their re-circulation. "Soil Profiles" shows how soil formation is influenced by climate, animals and topography; "Soil Composition" describes the physical and chemical bases of soil; while "Soil and Farming" includes such varied topics as soil erosion, pests and diseases, the effects of teaching crop rotation, the effects of fertilizers, farm machinery and different types of British farming. Each strip is in colour and supported by a booklet with concise text and a short bibliography.

U.K. Population Statistics

THE Registrar General's Quarterly Return for the second quarter of 1960 was published in October. The usual periodical returns show a continuation of the relatively high birth-rate, and it is likely that births in 1960 will exceed the figure of 750,000 registered in 1959 and will be higher than in any year since 1948. Stillbirth and infant mortality-rates continue to decline, and are lower than in any previous corresponding quarter. It is noteworthy that the already low rates have been reduced by 25 per cent during the 1950's. The Return contains an abridged life table for 1957–59, showing an expectation of life at birth of 68·0 years for men and 73·7 for women. The high excess of deaths among males continues, and at ages 55–65 male death-rates were approximately double those of females of the same age. Another table shows the number of years of working life lost per 10,000 population. Among males, cancer, accidents and coronary disease accounted for 40 per cent of the loss; among females, the three most important causes were cancer, bronchitis, and pneumonia and other cardiac diseases (No. 446. Pp. 28. London: H.M. Stationery Office, 1960. 2*s*. net).

Quarterly Journal of the Royal Astronomical Society

THE *Monthly Notices of the Royal Astronomical Society* has hitherto contained both original papers and material primarily concerned with the affairs of the Society. The increasingly specialized character and growing quantity of papers being published in the *Monthly Notices* has led to the appearance of the new *Quarterly Journal* (1, No. 1 (September 1960). Double issue. Pp. 128. 24*s*.; Annual subscription 40*s*.; 6 dollars. Single issues 12*s*.; 1.80 dollars. (London: Royal Astronomical Society.) 1960). It will contain all that was in *Monthly Notices* other than the original papers. Presidential addresses, George Darwin lectures, reports of observatories, and Council notes will be included, together with articles of the type previously appearing in *Occasional Notes*. The latter publication has been terminated. *Monthly Notices* will in future contain only original research papers. The new journal will appear in future in March, June, September and December each year; but, for technical reasons, two double issues are being published in 1960. It will be sent to all subscribers to *Monthly Notices* and to all Fellows of the Society, and will be on sale to others at £2 per annum. The contents of the first issue, dated September 1960, include an address by Prof. R. O. Redman on the work of the Cambridge Observatories, and articles by Prof. F. Hoyle on the origin of the solar nebula and by Dr. B. E. J. Pagel on the surfaces of stars.

The Transvaal Museum, Pretoria

THE report of the Trustees of the Transvaal Museum, Pretoria, for the year ended March 31, 1960, again refers to the shortage of work, storage and exhibition space which prevents the Museum from exercising its proper function to the community (Pp. 46. Pretoria: Transvaal Museum, 1960). The imposition of an entrance fee of 1*s*. led to a decrease of about one-third in the total attendance. On the other hand, it has eliminated the disinterested and undesirable visitor who formerly used the Museum as a rest-house and caused much trouble. Two major expeditions to the Gobabeb area of the Namib Desert and Somalia have been organized during the year. The former was made possible by a generous private donation and produced much material and information concerning life under extreme desert conditions.

Fulbright Travel Grants

Under the provisions of the Fulbright programme, travel grants are available to citizens of the United Kingdom and dependent territories, to go to the United States for an academic or educational purpose, provided that they have adequate financial support in dollars for the visit, and have been accepted by an American institution of higher learning. Grants cover the cost of direct travel between a candidate's home and the American university or institution. They are available during June 1–August 15, 1961, for which application must be received by March 15, 1961; and August 16, 1961–April 1, 1962, for which applications must be received by June 1, 1961. Application forms and further information can be obtained from the United States Educational Commission in the United Kingdom, 71 South Audley Street, London, W.1.

"McGraw-Hill Encyclopedia of Science and Technology"

The McGraw-Hill Publishing Co., Ltd., has just published a 15-volume "Encyclopedia of Science and Technology". It is of handy format, each volume consisting of 600–700 double-column pages, and the last volume includes an index to the whole. It is claimed that the work involves 7,200 articles, varying in length from 100 to 1,500 words, contributed by more than 2,000 scientists and technologists from the United States, among whom are many with an international reputation. Continuous revision, the bugbear of any form of encyclopædia, is to be provided by means of "Year Books", beginning in 1962, each consisting of articles on outstanding developments of the preceding year, and shorter notes on important discoveries, new products and applications. The pre-publication price is £61 11*s*. 6*d*. (159 dollars); after December 15 the price will be £67 16*s*. 6*d*. (175 dollars).

University News:

Birmingham

The following appointments have been made: *lectureships*, Dr. C. F. Wells (chemistry), Dr. F. Bakhtar (mechanical engineering), Dr. J. L. Jinks (honorary lecturer in the Department of Genetics); *research associateships and fellowships*, G. Lines (medical biochemistry and pharmacology), P. Johnson (medical biochemistry and pharmacology), R. H. Hollier (Tube Investments Senior Research Fellow in the Department of Engineering Production), G. R. Izaak (nuclear physics).

The University has accepted the offer by Joseph Lucas, Ltd., to second to the University each year an American professor, nominated by the University, to hold a Joseph Lucas visiting professorship in the Department of Engineering Production.

Leeds

Dr. H. M. N. H. Irving, of the University of Oxford, has been appointed to the chair of inorganic and structural chemistry, from a date to be arranged.

London

Prof. B. G. Neal, professor of civil engineering at the University College of Swansea, has been appointed to the University chair of applied science with special reference to engineering tenable at the Imperial College of Science and Technology.

Sheffield

Among the appointments to be announced recently are the following: N. Moray, to be lecturer in psychology; J. E. Enderby, to be lecturer in physics; Dr. J. V. S. Mani, to be I.C.I. Research Fellow in the Department of Fuel Technology and Chemical Engineering.

Sydney

Dr. W. N. Christiansen has been appointed to the Peter Nicol Russell chair of electrical engineering in succession to Prof. D. Myers. For twelve years prior to his appointment he was engaged in research on radio astronomy in the Commonwealth Scientific and Industrial Research Organization. Dr. L. C. Birch has been appointed to the Challis chair of zoology, which became vacant on the retirement early this year of Prof. P. D. F. Murray. Dr. Birch was appointed to a senior lectureship at the University in 1948 and later became reader in zoology.

Announcements

Viscount Amory has been appointed chairman of the Medical Research Council, in succession to the Earl of Limerick.

Dr. George W. Corner, For. Mem. R.S., historian of the Rockefeller Institute, New York, and director emeritus, Department of Embryology of the Carnegie Institution of Washington, has been appointed executive officer of the American Philosophical Society, Philadelphia. He will retain a connexion with the Rockefeller Institute as visiting professor.

The third international symposium on "Comparative Endocrinology" is being sponsored by the Zoological Society of Japan, and is to be held during June 5–10, 1961, at Oiso. Further information can be obtained from the chairman of the symposium, Dr. Kiyoshi Takewaki, Department of Zoology, University of Tokyo.

An international pharmacological meeting is being organized under the auspices of the Section of Pharmacology of the International Union of Physiological Sciences, and is to be held in Stockholm during August 22–25, 1961. The general theme of the meeting will be "Mode of Action of Drugs". Further information can be obtained from the First International Pharmacological Meeting, Karolinska Institutet, Stockholm 60, Sweden.

"New Polish Publications" lists new and forthcoming books published in Poland, with annotations in English. The books of scientific interest are classified under the headings: philosophy, psychology, education; economics, social sciences; biology; agriculture, forestry; medicine; mathematics, astronomy, chemistry; geology, geography, geophysics; and techniques. Issues Nos. 1–5, 1960, include some 126 entries under these headings (Agpol Foreign Trade, Advertising and Publishing Agency, Warsaw).

Under the title "United Kingdom Postgraduate Awards 1960–62" the Association of Universities of the British Commonwealth has issued a list of such awards tenable at universities in the United Kingdom, and a short list of awards for United Kingdom graduates tenable at universities outside the United Kingdom (Tenth Edition. Pp. ii+136. London: Association of Universities of the British Commonwealth, 1960). There are a subject index to each list and also an index to the named awards. This tenth edition is in a new and larger format, and it is proposed to publish subsequent editions every two years.

HIGH-VOLTAGE ACCELERATORS

As attendance at international conferences tends to become larger and the programmes more congested, there is an unfortunate tendency for papers to become shorter and more specialized, so that the proceedings of such conferences are largely unintelligible to workers outside a narrow field. In fact, many of the short papers contributed to such meetings present detailed experimental data which arouse little discussion and would be more adequately dealt with by straight publication in journals of the learned societies. An entirely different situation occurs in meetings where the number of papers is limited, and adequate time is available for experts in neighbouring fields to present a more general review of present status, tendencies and difficulties in their respective subjects. With adequate time for discussion, attendance at such meetings can be very profitable not only by allowing informal interchanges between specialists but also by providing others with a feeling for the prevailing current of thinking in each subject, which cannot be obtained by reading the specialist literature.

The advantages of this second type of conference were brought out very clearly at the second Accelerator Conference which was held during October 4–6 at the Krasnapolsky Hotel, Amsterdam. Sponsored by the High Voltage Engineering Co., this meeting brought together more than three hundred scientists from twenty-four countries, either designing or using high-voltage accelerators for a variety of scientific purposes. A total of twenty-two lectures was given, and these brought out strongly the wide range of studies in which such accelerators have become essential. The session on the first day was devoted to applications in nuclear physics; the second to the new tandem accelerators and the types of experiments on which these are now used. Separate sessions on the morning of the third day were devoted to varied topics in neutron physics, isotopes separation, activation analysis, solid state research. The concluding session in the afternoon of the third day outlined contributions in radiobiology, industrial and medical applications and future accelerators for high-power applications.

A major feature of many of the lectures and ensuing informal discussions was the interchange of views on future applications and requirements for high-voltage accelerators. In many nuclear physics problems, highly monochromatic beams of very short duration are needed, whereas for industrial applications lower voltages and less-uniform beams are quite acceptable if the cost per kW.hr. could be reduced. In this connexion the forecasts of accelerator designers are most encouraging. Already the cost has sunk to between 2 and 10 dollars per kilowatt for a 10-kW. machine. With re-design, longer life of components and higher output ratings, we may expect to obtain high-voltage radiation at a total cost of less than 1 dollar per kW.hr., and 5,000 dollars per kW. installed. Although these figures are high compared with electrical energy from 240-V. mains supply, they are very favourable when related to the costs from electrical accelerators at present installed, or the present cost of radioactive isotopes such as cobalt-60. A single accelerator producing 20 kW. of high-energy radiation has the same energy output as several million curies of cæsium-137, which is far greater than the total world production from fission products. Since one kW.hr. of high-energy radiation, if fully absorbed, can give a sterilizing dose of 2·5 megarads to 300 lb. of material, the cost of radiation is no longer an economic handicap in a number of industrial processes. Attempts to discover industrial applications for high-energy radiation have been carried out in a number of industrial laboratories. It is unfortunate that for commercial reasons the more successful applications have not so far received much publicity. The paper contributed by S. H. Pinner and W. H. T. Davison gives an interesting compilation of patents involving radiation which have already been published. These indicate clearly the considerable interest in the polymer field, where a large change can be obtained with a relatively modest radiation dose.

On the nuclear physics side, Prof. P. M. Endt (Utrecht) discussed the use of proton- and gamma-rays in the study of nuclear resonance-levels, and Dr. T. Huus (Copenhagen) summarized work on Coulomb excitation. Prof. L. Katz (Saskatchewan) diverged from his original script to outline his requirement for a research linear accelerator. On the premise that he was only allowed one such equipment for research he laid down the very stringent specification required. The scientists and designers concerned with accelerator design were prepared to meet this technical challenge if the physicists undertake responsibility for finding the necessary money. It was not clear how the many earnest seekers after scientific truth could all congregate at the feet of this valuable, but extremely expensive, oracle.

By using ultra-fast microwave pulse techniques, lifetime measurements of the order of 7×10^{-11} sec. were determined in some odd argon rare earth nuclei by Dr. G. Goldring (Rehovoth). Dr. E. Cotton (Saclay) also gave a short review on nuclear widths and life-times and Dr. A. Schoch (CERN, Geneva) discussed colliding beam techniques.

Electrostatic machines have considerable advantage in the production of continuous beams, and the voltage can be readily adjusted, but there is a limit of roughly 5 MeV. beyond which they cannot operate satisfactorily. This limit had been overcome by the use of tandem generators in which negative ions are accelerated from earth potential to about this voltage, then stripped to give positive ions which continue their path in the same direction. By this means the energy of the beam is doubled. The first of these new tandem generators was installed at Chalk River in February 1959, and Dr. H. Gove (Atomic Energy of Canada, Ltd.) gave details of experiments with this new equipment. In spite of its novel character 80 per cent operational time has been attained with a two-shift programme. The problems studied include proton cross-sections, giant resonance in carbon-14 and silicon-28, and thresholds and yields, departures from Rutherford scattering and narrow resonance structure. Dr. K. W. Allen (Atomic Weapons Research Establishment) also dealt with the advantage of a tandem generator as compared with the

linear accelerator or the betatron for their nuclear work, which involves bombardment with p, d, t and ^{3}He ions in the energy-range of up to 10–12 MeV. and direct measurement of nuclear life-times of 10^{-11}–10^{-14} sec.

There is an obvious need for accelerators going to even higher voltages, and Dr. P. Rose (High Voltage Engineering Co.) described plans for three-stage accelerators giving 15 MeV. He also foresaw accelerators furnishing 30-MeV. beams of 10 m.amp. within ten years. Other potential improvements in high-voltage accelerators include millimicrosecond pulsing as compared with the 2-μsec. pulse at present available (R. Connor, High Voltage Engineering Co.) and more powerful generators using the 'Amplitron' instead of the klystron or magnetron (J. C. Nygard, High-Voltage Engineering Co., and R. F. Post, California).

Ion sources of high efficiency, capable of separating μgm. quantities of rare materials, were described by Prof. J. Kistemaker (Amsterdam), while Prof. R. Fleischmann (Erlangen) discussed polarized ion beams, and Dr. K. Beckurts (Karlsruhe) dealt with pulsed neutron sources and neutron life-time in moderators.

In radiation research, high-voltage beams are valuable in solid-state investigations, as outlined by Dr. P. Baruch (Paris) and have also been used in chemical analysis, either by gamma or neutron activation (J. W. Otvos, Emeryville). Radiation effects in biological systems, as presented by Dr. W. Huber (Stanford), particularly emphasized aspects of interest to radiation physicists and chemists dealing with radiation damage in much simpler systems.

The time-scale permitted adequate time for private discussions on many specific aspects which could not be raised at the formal sessions. Social activities included a banquet given by the High Voltage Engineering Co., at which Prof. H. B. G. Casimir of the Philips Research Laboratories delivered a witty speech and a reception was held by the Mayor and Aldermen of Amsterdam. This included a Van Gogh exhibition which was very much appreciated. Scientific education is sometimes described as narrow and non-cultural. Perhaps we may hope that students of the humanities who hold this view also relax from their learned meetings by attending exhibitions of classical scientific experiments and reading or discussing recent developments in atomic structure, relativity and quantum theory, the basic concepts of which have an increasingly important influence on the outlook of the modern thinking man.

The full proceedings of the conference will be published at the end of the year in *Nuclear Instruments and Methods*.

A. CHARLESBY

FLOW MEASUREMENT IN CLOSED CONDUITS

FLOW measurement is one of the less-spectacular aspects of fluid dynamics, and perhaps for this reason it has not received the attention it deserves. Nevertheless, flow-metering is as old as the engineering applications of fluid dynamics, since in almost every application it is desirable or important to know the volume or mass flow per unit time passing through the system. For example, the distribution of water in a water grid, the flow of air in an air-conditioning plant, the supply of steam to a turbine, the regulation of the flows in the continuous production of chemical engineering products. The fluids may be gases or liquids and the latter may be corrosive or contain solid suspensions as in sewage or wood pulp. The rate of flow may be small as in a blood vessel or great as in large hydraulic turbine installations and in gas turbines. The nature of the fluid, the size of installation, the speed of flow and the accuracy required, all influence the choice of meter.

Of the more common types of flow-meter, the simplest and most accurate for measurements in liquids consists of a large vessel on a weighbridge into which a given mass of liquid is timed. The National Engineering Laboratory, East Kilbride, possesses a 30-ton weighing tank. Alternatively, a somewhat less accurate but more convenient method is that which uses a vessel designed on the pipette principle, into which a definite volume of liquid is timed. These two methods are generally used as standards against which more compact and convenient flow-meters may be calibrated. The pitot-static pressure head has been widely investigated, and used by aerodynamicists for measuring the velocity at a point in air flows, and is regarded by them as a fundamental instrument. By traversing the instrument across a duct the velocity distribution and hence the flux can be found. Small rotating vanes coupled to counting devices and known as current meters can also be used to find the velocity at a point after calibration, and hence the volume flow can be found by integration. A great many meters in practical use utilize a pressure difference brought about by a change of cross-sectional area of the duct. In nozzles and venturi meters this change of area is smooth and gradual, and such meters introduce little loss into the duct system, but they are fairly sensitive to upstream disturbances. In the orifice-plate type of meter the change of section is sudden, and a large resistance is offered to the flow, which gives rise to a large pressure difference. Another method, used in hydraulic power installations, involves the steady injection of a solution of salt at a known rate. Samples are then taken downstream where the mixing is complete, and from the dilution the mass flow can be found. A variant of this makes use of radioactive isotopes. Some methods attempt to measure the mass or volume flow directly without introducing any obstruction into the duct. An interesting example is the magnetic flow-meter, in which a magnetic flux is set up at right angles to the flow of a conducting liquid, and a current flows between two electrodes in the pipe wall which can be related to the volume rate-of-flow. The meter is of particular value in water-borne sludges. Another example of considerable practical importance is the Gibson method. In this the fairly rapid closure of a valve, or of the inlet guide vanes of a hydraulic turbine, causes a pressure variation with time between two stations in the pipe line. The integral of this over the time of closure is related closely to the

destruction of momentum and so to the mass-rate of flow.

During September 27–30 a symposium on "Flow Measurement in Closed Conduits" was held in the new James Watt building of the National Engineering Laboratory. It was the first of a series which are to be held there, and so far as can be discovered, it was the first symposium devoted solely to flow measurement which has been held anywhere. Some 150 delegates were present; about 50 coming from countries of Western Europe, the United States and the Dominions and the remainder from British manufacturers, industrial users, official establishments and universities. The symposium occupied four days, and on the last evening the delegates attended a dinner at the Central Hotel, Glasgow, given by the director, Dr. D. G. Sopwith, to the authors of the papers. On the last afternoon, the delegates were invited to look around the various laboratories of the National Engineering Laboratory.

Dr. Sopwith was chairman at the opening session when the first item was the presentation of a film made by the National Engineering Laboratory at the Kinlochleven power-station, showing the comparative testing of a number of flow-meters. This was followed by the 'opening address' given by Vice-Admiral Sir Frank Mason, chairman of the Steering Committee of the National Engineering Laboratory. The remaining six sessions were devoted to the discussion of twenty-nine papers.

Session *A* was concerned with current meters and pitot tubes, and included contributions from the United States (1), Italy (1), France (2), and the United Kingdom (2). Session *B* discussed orifice plates, with papers from the United States (1), United Kingdom (2), France (1). Venturi-meters formed the subject of Session *C*, with papers from the United States (1), Belgium (2), and the United Kingdom (1). Session *D* dealt with the various other pressure difference devices, with contributions from the United Kingdom (2), West Germany (1), Austria (1), and the United States (1). Session *E* was devoted to salt dilution and salt velocity methods, with papers from the United States (1), France (1) and the United Kingdom (2). Session *F* discussed the Gibson method, with papers from Norway (1), and the United Kingdom (1). Session *G* was concerned with special methods, and papers were presented from the United Kingdom (3), West Germany and Holland (1). All papers were in English and the discussions were in English, and though translator services were available these were required but once. The papers and the discussions are to be published as a bound volume. The excellent organization of the symposium by the deputy director, Dr. Hutton, and by Dr. Winternitz and his staff of the Fluid Mechanics Division of the National Engineering Laboratory, ensured that the maximum time was available for the discussion of the papers. The discussions were frank and helpful and were enlivened by certain overseas visitors with a nice sense of humour.

The theme of most of the papers and the discussions was the question of accuracy or constancy of the calibration coefficient. This is a very important feature of any flow-meter, and it was clear from the papers that considerable effort is being made to improve existing flow-meters in this respect. Present-day standards of accuracy for most flow-meters fall far short of those for physical measurements; for example, a reliable accuracy of 1 per cent must be regarded as rare. There are good reasons for this, since most flow-meters are affected by scale effects (Reynolds number), effects arising from upstream installations, such as bends and changes of section, turbulence and compressibility (in the case of gases), by erosion, corrosion and solid deposits which can cause deterioration with time. This question of accuracy is, in many cases, of great practical importance. In chemical engineering, accurate metering and regulation of the flow of the various products in continuous-flow processes is desirable on both technical and economic grounds. The manufacturers of pumps and turbines are frequently called on (in the case of large units) to meet very stringent performance specifications, which involve quantity flow, and it is essential that the manufacturer and the user should agree on the flow-metering accuracy. Since many countries export turbo-machinery, flow-metering has an international importance. One of the important results achieved by the symposium was not only the bringing together of the manufacturers, users and research workers, but also the achieving of this on an international level, so that a wide variety of experience was pooled and important personal contacts were made.

In conclusion, therefore, it can be stated that the symposium was timely and a great success, due mainly to the excellent arrangements made by the Fluid Mechanics Division of the National Engineering Laboratory.

J. H. PRESTON

PROGRESS IN CALORIMETRY

THE fifteenth annual Calorimetry Conference was held at Gatlinburg, Tennessee, during September 7–10, with Oak Ridge National Laboratory acting as host and Dr. J. P. McCullough (Petroleum Thermodynamics Laboratory, Bureau of Mines) serving as chairman. In the pleasant surroundings of the Great Smoky Mountains, 106 calorimetrists from the United States, Canada and Europe heard and discussed thirty-one technical papers on recent work on many phases of calorimetry and engaged in informal discussions of calorimetric problems. Among the topics discussed were calorimetry at temperatures as low as 0·1° K. and as high as 2,800° K., precision reaction and bomb calorimetry, solution calorimetry, applications of calorimetry to solid-state problems, application of calorimetry to radiation dosimetry, improvements in temperature measuring devices, and data processing by digital computers. At the Conference banquet, Dr. A. M. Weinberg, director of Oak Ridge National Laboratory, shared his experiences and observations on a recent trip to the U.S.S.R. with the chairman of the U.S. Atomic Energy Commission, illustrating his talk with a number of interesting slides. Dr. D. W. Osborne

(Argonne National Laboratory) was programme chairman, and Dr. R. H. Busey (Oak Ridge National Laboratory) was local arrangements chairman.

The Hugh M. Huffman Memorial Lecture, established in memory of the founder of the Calorimetry Conference, was given by Prof. J. W. Stout (University of Chicago) on the subject "Magnetic Entropy in Ionic Crystals". Prof. Stout gave a stimulating lecture on the magnetic contribution to the entropy of ionic salts of the transition metals, discussing the theoretical considerations and the results obtained from low-temperature heat-capacity measurements and from experiments on magnetic susceptibility, paramagnetic resonance, and optical absorption.

Several papers were devoted to a perennial concern of the Conference: the improvement of temperature-measuring devices. Further tests of the germanium resistance thermometers developed at the Bell Telephone Laboratories were described, with H. Plump reporting on "Low Temperature Thermometry at the National Bureau of Standards" in the range 2–20° K., and C. van Rijn, H. van Dijk and M. Durieux (Kamerlingh Onnes Laboratorium, Leyden) reporting on "Calibration of a Germanium Resistance Thermometer at Liquid Helium and Liquid Hydrogen Temperatures". These devices show such encouraging promise for precision temperature measurements from 1° to 20° K. that a committee has been seeking a manufacturer of additional germanium thermometers for further testing. P. Lindenfeld (Rutgers University), chairman of the committee, reported that the Minneapolis-Honeywell Regulator Co. has become interested, and G. Halverson of that Company showed several pilot models.

Results in a quite different temperature region were presented by J. P. Evans (National Bureau of Standards), who described the development of platinum resistance thermometers for the International Temperature Scale from 630·5° to 1,063° C. It is expected that the use of such thermometers will simplify and smooth the scale, as well as provide greater precision and reproducibility than is possible with present thermometric instruments. Also, the use of thermistors for measuring small changes of temperature in solution calorimetry was described in several papers. A notable example was the paper by G. R. Argue, E. E. Mercer, and J. W. Cobble (Purdue University) on "An Ultrasensitive Thermistor Microcalorimeter" for the determination of the heats of solution of the heavy elements with quantities as small as 5 or 10 μgm.

Several authors reported on applications of calorimetric techniques to solid-state physics. J. E. Kunzler (Bell Telephone Laboratories), for example, discussed methods for the observation of very small amounts of energy—between 10^{-2} and 10^{2} ergs—and the application of these techniques to investigations of magneto-thermal oscillations of single crystals of bismuth and the adiabatic demagnetization and heat capacity of ferrimagnets.

A subject of great interest to calorimetrists measuring or analysing heat capacities was presented by B. N. Brockhouse (Atomic Energy of Canada, Ltd.) in an invited paper on "Dispersion Curves and Frequency Distributions of Lattice Vibrations from Neutron Scattering". A novel cryostat for low-temperature calorimetry from 4° to 80° K. was described by V. Mathot (Free University of Brussels), along with experimental results on the heat of mixing of hydrogen and deuterium liquids. Another interesting new type of cryostat, a helium-3 cryostat with a lead wire thermal switch for cooling the calorimeter to 0·3° K., was depicted by D. L. Martin (National Research Council of Canada).

The Conference is deeply interested in the adequate presentation of calorimetric and thermodynamic data. For this reason the fifteenth Calorimetry Conference considered carefully and adopted a "Resolution on Publication of Calorimetric and Thermodynamic Data" which is intended to be a guide for authors, editors and referees of calorimetric papers. This resolution is a revision of one adopted in 1953 that has been valuable to authors and editors alike.

Plans were announced for the next conference, which will be an International Calorimetry Conference and will be held at Ottawa during August 14–17, 1961. The meeting will be jointly sponsored by the Calorimetry Conference and by the Subcommission on Experimental Thermochemistry of the Commission on Chemical Thermodynamics of the International Union of Pure and Applied Chemistry. The host organization will be the National Research Council of Canada.

At the annual election the following officers were elected: *chairman*, Dr. D. W. Osborne (Argonne National Laboratory); *chairman-elect*, Dr. J. E. Kunzler (Bell Telephone Laboratories); *secretary-treasurer*, 1960–63, Dr. G. T. Furukawa (National Bureau of Standards); *directors*, 1960–62, Dr. G. T. Armstrong (National Bureau of Standards) and Dr. J. K. Logan (Naval Research Laboratory). Other directors of the Conference are: Dr. J. P. McCullough, Prof. David White (Ohio State University), Prof. N. E. Phillips (University of California, Berkeley), and Prof. J. M. Sturtevant (Yale University).

THE INTERNATIONAL ASSOCIATION OF VOLCANOLOGY

THE International Association of Volcanology, under the ægis of the International Union of Geodesy and Geophysics, met in Helsinki during July 25–August 6, with Prof. A. Rittmann, who is a Swiss citizen, as president.

Mr. G. R. Laclavére, in his capacity as interim secretary in place of Prof. F. Signore, who died on December 2, 1959, reported that since the last general assembly in Toronto in 1957, five parts of the *Bulletin Volcanologique* and six parts of the Catalogue of Active Volcanoes (Africa, Melanesia, Central America, Kurile Islands, Kamchatka and the U.S.A.) had been published, and in September 1958 fifty-four volcanologists, from twelve countries, had met in Paris for a symposium.

In Helsinki, under the presidency of Prof. A. Rittmann, and with the assistance of the local secretary, Prof. Th. G. Sahama, the work of the Association was arranged in four sections: (1) active volcanoes (six papers and six reports); (2) physics of volcanoes

(four papers, also five papers combined with section 1); (3) physical chemistry and chemistry of magmas, volcanic waters and volcanic gases (eighteen papers); (4) palæovolcanology and plutonism (fourteen papers).

Altogether fifty-five contributions were submitted to the Association from fourteen countries, distributed as follows: U.S.S.R. 15, United States 8, France 6, Japan 6, Australia 4, Great Britain 4, Belgium, Italy, Portugal and Switzerland 2 each, India, Mexico, Netherlands and Norway 1 each. Of these contributions forty-three were read and discussed. In addition, two papers on lunar volcanoes were submitted. Prof. A. Rittmann's presidential address dealt with the geochemistry of basalts and the mechanism of their eruption. The national reports on recent volcanic activity were contributed by Australia, India, Japan, Mexico, United States, U.S.S.R.

Several joint symposia also were held on the subjects of: (1) isotope geology and experimental petrology; (2) the age of minerals, Pre-Cambrian rocks and meteorites; (3) island arcs and the ocean floor.

Two discussions were held under the combined auspices of the International Association of Volcanology, the International Association of Seismology and the Geochemical Commission of the International Union of Pure and Applied Chemistry, on the question of the position of geochemistry within the International Union of Geodesy and Geophysics and other international scientific unions. As a result, a request was made to the Council of the International Union of Geodesy and Geophysics for the establishment of an *ad hoc* committee on 'Geochemical Problems'. The function of the committee would be: (1) to arrange meetings in the field of geochemistry under the auspices of the committee, or under the joint sponsorship of the committee and other sections of the Union; (2) to promote the furtherance of geochemistry by investigating the possibility of a relationship between the International Union of Geodesy and Geophysics, the International Union of Pure and Applied Chemistry, and any other international body in the field of geology which may be formed.

During the Assembly two volcanological colour films of outstanding interest were shown, illustrating a spectacular basaltic eruption in Hawaii, and also the remarkable achievements of the Belgian expedition which recently studied the lake of molten lava far down in the crater of the Congolese volcano Nyiragongo.

The president, Prof. A. Rittmann (Catania University), announced a decision, taken jointly by the Department of Volcanology of Catania University in Sicily and the Belgian National Centre of Volcanology, to explore the possibility of creating an International Institution for Volcanological Research in Catania, close to Etna.

The Association expressed approval of the Executive Committee's plan to hold two symposia before the next General Assembly, the first to be on the formation of ignimbrites, hyaloclastites and related deposits, and to be held in Catania during October 1961, and the second on the prediction of time and place of volcanic eruptions and the relationship between magmas and the nature of volcanic eruptions, to be held in Tokyo (Japan) during May–June 1962.

The Association also approved the proposal that a *Bulletin of Volcanic Eruptions* should be instituted. Such a publication, recording briefly current volcanic phenomena, should appear up to four times a year, and it should be distributed to National Sub-Committees for Volcanology and to certain individuals. It is anticipated that the Volcanological Society of Japan will agree to undertake and finance publication and distribution.

Office bearers for the triennium 1960–63 were elected as follows: *president*, Prof. A. Rittmann (Switzerland); *vice-presidents*, Prof. V. I. Vlodavetz (U.S.S.R.) and Mr. Gordon A. Macdonald (United States); *secretary*, Prof. F. Penta (Italy); *chairman of Section I*, Dr. M. Neumann van Padang (Netherlands); *chairman of Section II*, Dr. G. S. Gorshkov (U.S.S.R.); *chairman of Section III*, Prof. H. Kuno (Japan); *chairman of Section IV*, Prof. B. Gèze (France).

UNIVERSITY DEVELOPMENT IN BRITAIN

THE statement issued by the Association of University Teachers on the problems of university development is one which should be carefully studied by all who are concerned with policy-making in this vitally important field*.

The Association is concerned about the arbitrary way the University Grants Committee has recommended that university expansion should cater for two scientists against one entrant for all other faculties, including medicine and agriculture, and asks that this matter be reconsidered.

Agreeing with the University Grants Committee's estimate that the number of university students in Britain by 1970 should be about 170,000, the Association believes that present standards of entrance to the university should be maintained, and is of the opinion that there should be sufficient applicants of quality to maintain that standard for at least 170,000 places, and that this figure may have to be exceeded.

To cater for the additional 70,000 students for whom places will have to be found in the next ten years, a major operation will be required. This can be done by increasing the size of existing universities or by founding new ones. Recognizing all the attendant dangers to institutions which grow too large, the Association recommends that at least six new universities should be started during the next two years.

The arguments for new universities are strong. Their building cost can be shown to be no greater than that of expanding existing universities, while the difficulty and cost of acquiring land must be less. The contribution that they can make in terms of variations in teaching methods and added range of research is considerable. There should be a deliberate

* "Some Problems of University Development". Pp. 7. (London: Association of University Teachers, 21 Dawson Place, W.2, 1960.) 1*s*. 6*d*.

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policy of preserving the pattern of university life to be found in the smaller and medium-sized universities; this cannot be achieved without creating new universities.

It has been argued that because new universities have to be created and built, no appreciable contribution can result during the next decade. The Association believes that this depends on the urgency of the approach to the problem.

The Association makes a clear recommendation that new universities should be planned from the beginning for what is regarded as their likely size. Thus, a university planned for 3,000–3,500 should start with the appropriate building plans, which may be phased but should not require subsequent revision. A maximum of 4,500 should leave ample scope for later expansion to accommodate whatever specialism an individual university may adopt. The new campus should be built with all the buildings going up simultaneously. The intake in each of the first three years might be 750–800 undergraduates, building up in the three following years to 900, leaving the balance for postgraduate places. To do this requires an approach to planning and construction comparable with large industrial organizations.

The planning of the university itself as a centre of research and learning should be approached in an equally dynamic fashion. There is no time for a consultative committee to work out the charter for each university and its range of subjects. The experience gained in the creation of universities in North Staffordshire and at Brighton should be drawn on immediately, and a draft charter should be devised for each university which would be expressed in terms allowing a flexible approach by the universities concerned, and each such charter should be revised at the end of ten years.

To meet the urgency of the situation, it is suggested that the vice-chancellor, the deans of faculties, the librarian and the senior administrative officers be appointed immediately the university is created, the heads of departments should be appointed eighteen months before the first students are admitted, and other staff should be recruited during the ensuing period. An approach of this nature would enable a university to open its doors four years after the decision to create it, and seven years from the decision being taken one could expect to find 2,500 students in residence, and 3,000 ten years later. If this procedure were followed for six or more new universities, there would be a solution to the likely balance of demand before the end of the 1960's.

The Association believes that the new universities should be located in towns with not less than 50,000–100,000 population. They should be broadly based, and not of the character of either a liberal arts college or a two-faculty university. There should be opportunities for the individual development of rarer faculties. In each there should be found arts, social science, science and applied science. The applied sciences should be linked with the region in which the university is established.

GENERAL RELATIVITY AND LORENTZ-INVARIANT THEORIES OF GRAVITATIONS

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DESPITE the initial successes of Einstein's general theory of relativity, attempts to produce a satisfactory Lorentz-invariant theory of gravitation have persisted until the present day. The three well-known Einstein tests are all obtained from the Schwarzschild metric, that is the general relativity solution of the one-body problem. There has been no direct confirmation of the field equations of the theory; but in time it should prove possible to test the results of the two-body problem in the theory as far as terms of order $1/c^2$.

Although more cogent in its æsthetic and general intellectual appeal than rival theories, general relativity is not unique in the results it predicts for the motion of perihelion, deflexion of light-rays and gravitational red-shift in the one-body problem. The same results are obtained in some Lorentz-invariant theories of gravitation. No general analysis has previously been made of these theories, nor have the results predicted by them been systematically compared with the corresponding formulæ derived from general relativity. We have therefore recently made a thorough review of Lorentz-invariant theories, and the details of our analysis will be published later. It is the object of the present communication to present our principal conclusions.

We have considered seven possible tests in all: the three well-known tests obtained for the one-body problem; the secular acceleration of the centre of mass and the advance of periastron in the two-body problem; and the two additional effects introduced into the one-body problem when the axial rotation of the central body is taken into account. The formulæ for these effects have all been obtained previously in general relativity, at least to order $1/c^2$. Corresponding formulæ for some of these effects have previously been obtained in some Lorentz-invariant theories. We have derived the required formulæ for all the theories that we have considered.

Before setting out the comparative tables of results, we must explain our method of classifying Lorentz-invariant theories, which includes some not previously discussed. Attention is, of course, restricted to theories which satisfy the condition that they reduce to the Newtonian form when c is replaced by infinity. (The basic reason for seeking to replace the Newtonian theory of gravitation is that the theory is applicable only when c can be taken as effectively infinite.) First we consider in turn theories in which the gravitational potential is (i) a scalar, (ii) a vector and (iii) a second-order tensor.

Scalar Theories

Under this heading, we consider Nordstrom's theory[1] and a generalization which includes as special cases theories due to D. E. Littlewood[2] and O. Bergmann[3]. In this generalization Laplace's operator in Poisson's equation for the potential φ is replaced by D'Alembert's operator, and the equations of motion are obtained from the variational principle:

$$\delta \int \exp\{-f(\varphi/c^2)\} ds = 0$$

where ds^2 is the Minkowski metric, and:

$$f(x) = x + qx^2 + \ldots$$

Nordström's own theory is given by $f(x) = x$, whereas Littlewood's and Bergmann's theories, although derived from different initial assumptions, are both given by $f(x) = -\log(1-x)$

A different type of scalar theory, associated with a uniformly expanding world-model, was devised by E. A. Milne[4] and considered further by G. L. Camm[5], G. J. Whitrow[6], A. G. Walker[7] and W. S. Krogdahl[8]. In this theory the mutual potential energy of a particle of mass m_1 at x_1^a ($a = 1, 2, 3$) at time t_1 and a particle of mass m_2 at x_2^a at time t_2 is given by:

$$-\frac{m_1 m_2 c^2}{M_o} \frac{X_{12}}{(X_{12}^2 - X_{11}X_{22})^{1/2}}$$

where $X_{rs} = t_r t_s - x_r^a x_s^a/c^2$, $M_o = c^3 t/G$, t being the present epoch and G the constant of gravitation. The condition $X_{11} = X_{22}$ is imposed.

In all these theories it is assumed that the velocity of light c is a constant. We have, in addition, considered two types of scalar theory involving a variable velocity of light (function of the field):

(i) derived from the variational principle:

$$\delta \int ds = 0$$

where $ds^2 = c^2 dt^2 - dx^a dx^a$. (This leads to the same equations of motion as were obtained in 1912 by Einstein[9].)

(ii) Derived from the variational principle:

$$\delta \int \exp(-\psi/c^2) ds = 0$$

where $ds^2 = dt^2 - dx^a dx^a/c^2$, ψ satisfies the modified Poisson equation (with D'Alembert's operator), and $c^2 + 2\psi =$ constant. (This is of Nordström's form, except that c is now a function of the field.)

Vector Theories

Under this heading, we have examined first a generalized Maxwell type of theory not previously considered in which the vector potential φ^α ($\alpha = 0, 1, 2, 3$) satisfies the equations:

$$\Box \varphi^\alpha = 4\pi \frac{G\rho}{c^2} \frac{dx^\alpha}{ds}$$

where $\Box$ denotes D'Alembert's operator, ρ is the density, and the equations of motion are of the form:

$$\frac{d^2x^\alpha}{ds^2} = g^{\alpha\beta}\left(\frac{\partial\varphi_\beta}{\partial x^\gamma} - \frac{\partial\varphi_\gamma}{\partial x^\beta}\right)\frac{dx^\gamma}{ds} + p\frac{d\varphi_\beta}{ds}\left(g^{\alpha\beta} - \frac{dx^\alpha}{ds}\frac{dx^\beta}{ds}\right)$$

where $g^{\alpha\beta}$ is the contravariant Minkowski tensor and p is a constant. If $p = 0$, these equations of motion are of Maxwell type and are derivable from the variational principle:

$$\delta \int (ds - \varphi_\alpha dx^\alpha) = 0$$

We have also examined a wide class of vector potential theories with several disposable parameters recently introduced by P. Kustaanheimo[10]. He postulates equations of motion of the form:

$$\frac{d^2x^\alpha}{ds^2} = \frac{\partial\varphi^\eta}{\partial x^\varepsilon} B^{\alpha\varepsilon}_{\beta\gamma\eta}(\varphi^\delta)\frac{dx^\beta}{ds}\frac{dx^\gamma}{ds}$$

where φ^δ satisfies the first equation in this section and $B^\alpha_{\beta\gamma\eta}$ are general tensor functions of φ^δ.

Tensor Theories

Under this heading (which, strictly speaking, includes general relativity) we consider Birkhoff's theory[11], Whitehead's theory[12] and the generalization of the latter due to A. Schild[13].

In Birkhoff's theory the distribution of matter is represented by the energy-momentum tensor:

$$T^{\alpha\beta} = \rho \frac{dx^\alpha}{ds}\frac{dx^\beta}{ds} - \frac{p}{c^2} g^{\alpha\beta}$$

where ρ is the density, p the pressure and $g^{\alpha\beta}$ the Minkowski tensor. The condition $p = \frac{1}{3}\rho c^2$ was imposed by Birkhoff in order that the effects of small disturbances be propagated with velocity c. The gravitational tensor potentials $h^{\alpha\beta}$ are defined as the solutions of:

$$\Box h^{\alpha\beta} = (8\pi G/c^2) T^{\alpha\beta}$$

subject to the boundary conditions that all $h^{\alpha\beta}$ are zero at points infinitely distant from gravitating matter. Birkhoff assumed that the equations of motion of a test-particle are given by:

$$\frac{\partial T^{\alpha\beta}}{\partial x^\beta} = f^\alpha$$

where f^α is the body-force per unit volume. He also postulated that f^α is perpendicular to dx^α/ds, is linear in the first derivatives of the tensor potentials, quadratic in dx^α/ds and proportional to the proper density of the particle. The equations of motion then reduce to the form:

$$\frac{d^2x^\alpha}{ds^2} = g^{\alpha\beta}\left(\frac{\partial h_{\beta\gamma}}{\partial x^\delta} - \frac{\partial h_{\gamma\delta}}{\partial x^\beta}\right)\frac{dx^\gamma}{ds}\frac{dx^\delta}{ds}$$

Whitehead's theory is an action-at-a-distance theory in Minkowski space-time, particles interacting through retarded gravitational potentials. In 1924, Eddington[14] showed that the equations of motion for the one-body problem in Whitehead's theory are formally identical with the corresponding equations in general relativity if the Schwarzschild metric is represented in a suitable co-ordinate system. Later this suggestion led Schild to construct an infinite set of theories of Whitehead's type, that is, action-at-a-distance theories in Minkowski space-time. The metric tensor for the Schwarzschild solution can be written:

$$\sigma_{\alpha\beta} = g_{\alpha\beta} + h_{\alpha\beta}$$

where $g_{\alpha\beta}$ is the Minkowski metric tensor, and:

$$h_{00} = -\frac{2GM}{c^2}, \quad h_{0a} = h_{a0} = 0,$$

$$h_{ab} = \frac{-2GM/c^2 r}{1-2GM/c^2 r}\frac{x^a x^b}{r^2},$$

$r = (x^a x^a)^{1/2}$, and $a,b = 1, 2, 3$. Schild introduces a general transformation $x^0 \to \bar{x}^0$, $x^a \to \bar{x}^a$, of the form:

$$x^0 = \bar{x}^0 - \frac{2GM}{c^3}\,\psi\left(\frac{2GM}{c^2 r}\right)$$

$$x^a = \bar{x}^a\left\{1 + \varphi\left(\frac{2GM}{c^2\bar{r}}\right)\right\}$$

where $\bar{r} = (\bar{x}^a\bar{x}^a)^{1/2}$. To order $1/c^2$, we write, where b is a constant:

$$\varphi\left(\frac{2GM}{c^2\bar{r}}\right) = b\left(\frac{2GM}{c^2\bar{r}}\right)$$

Whitehead's original theory corresponds to the choice $\varphi = 0$, $\psi(v) = \log\{v/(1 - v)\}$. The paths of test-particles are given by the variational principle:

$$\delta \int d\sigma = 0$$

where

$$d\sigma^2 = \sigma_{\alpha\beta} dx^\alpha dx^\beta$$

and light-paths by the condition $d\sigma = 0$. Further, it is assumed that the period of an atom at rest is given by equal intervals σ.

In addition to the above theories, we have also examined a different type of Lorentz-invariant theory due to Poincaré.

Poincaré's Theory

In this theory[15] the inverse-square law of gravitation was re-expressed in Lorentz-invariant form. The equations of motion for a particle of mass m_1 at position x_1^a at time t_1 in the field of a particle of mass m_2 at position x_2^a at time $t_2 = t_1 - r/c$, where $r^2 = (x_1^a - x^a)\,(x_1^a - x_2^a)$, are of the form:

$$\frac{d^2x_1^a}{ds_1^2} = -\frac{Gm_2}{c^2\rho_2^3}\,\gamma^n\left(x_1^a - x_2^a - \frac{\rho_1}{\gamma}\frac{dx_2^a}{ds_2}\right)$$

where

$$\rho_r = g_{\alpha\beta}\frac{dx^\alpha}{ds_r}\,(x_1^\beta - x_2^\beta)$$

for $r = 1, 2$, $g_{\alpha\beta}$ is the covariant Minkowski tensor,

$$\gamma = g_{\alpha\beta}\frac{dx_1^\alpha}{ds}\frac{dx_2^\alpha}{ds}$$

and n is a constant.

The One-Body Problem

In the following table for the three Einstein tests (obtained in general relativity from the Schwarzschild metric), the units employed are as follows: (1) the advance of perihelion per revolution is expressed in units of $6\pi GM/c^2a(1 - e^2)$ radians, where M is the mass of the central body, a is the semi-major axis and e the eccentricity of the orbital ellipse; (2) the deflexion of a light-ray is expressed in units of $4GM/c^2R$ radians, where R is the minimum distance of the light-ray from O the centre of mass of the central body; (3) the gravitational red-shift is expressed by the value assigned to:

$$\frac{\delta\lambda/\lambda}{GM/c^2r}$$

where λ is the wave-length of a standard spectral line emitted by an atom at 'infinity', that is, where the gravitational field of the central body is negligible, and $\lambda + \delta\lambda$ is the wave-length of the corresponding line emitted by an atom at distance r from O.

Table 1

Theory	Advance of perihelion	Deflexion of light	Gravitational red shift
1. General relativity	1	1	1
2. Nordstrom's (generalized):			
$q = 0$ (Nordstrom)	$(q-1)/3$	0	1
$q = 1/2$ (Littlewood, Bergmann)	$-1/3$	0	1
$q = 4$	$-1/6$	0	1
3. Milne's	1	0	1
4. Scalar potential with a variable velocity of light.	$-1/6$	—	—
Theory (i)	2/3	1/2	1
Theory (ii)	1	1/2	1
5. Vector potential: $p = 0$	1/6	0	0
$p > 0$	$(1+2p)/6$	$p\pi GM/8c^2R$	—
6. Kustaanheimo's*	1	1	1
7. Birkhoff's	1	1	1
8. Whitehead's (generalized)	1	1	1
9. Poincaré's: $n < 2$	$n/6$	0	0
$n > 2$	$n/6$	—	—
$n = 2$	1/3	1/2	1

*This theory contains a large number of arbitrary parameters. Conditions have been imposed on them *ad hoc* so that the theory predicts the same results as general relativity for all three effects.

The Two-Body Problem

Although it has not proved possible to formulate a complete solution of the two-body problem in general relativity, approximate solutions can be obtained. Levi-Cività[15] reached the conclusion that, to order $1/c^2$, the centre of mass of two unequal bodies would be automatically accelerated along the major axis of the relative orbit, in the direction of the periastron of the larger mass. Since the periastron always slowly revolves, Levi-Cività's result would imply that a binary star considered as a whole would describe a circle. However, when the problem was re-examined by Eddington and Clark[16], working to the same order of approximation, they found that an error had been made by de Sitter in calculating a general formula, used by Levi-Cività, for the line-element due to n bodies. The effect of the resulting correction was to make the secular acceleration of the centre of mass of the two-body system zero, at least to order $1/c^2$.

In 1954, Clark[17] considered the two-body problem in Whitehead's original theory and found that the centre of mass would have a secular acceleration towards the periastron of the more massive component. In his paper in 1955, Schild conjectured that "all theories of Whitehead's type violate the law of action and reaction, and that they all predict a secular acceleration of the centre of mass in the two-body problem". We have found that, although this is true in general, for certain functions φ (all those for which $b = 1/4$) there is, to order $1/c^2$, no secular acceleration of the centre of mass.

In Table 2 are listed the results which we have obtained for the respective theories, correct to order $1/c^2$ for the following:

(1) the acceleration of the centre of mass of a binary system towards the periastron of the orbit of the more massive component expressed as an increase of velocity in this direction per revolution in units of:

$$\frac{\pi G^{3/2} m_1 m_2 (m_1 - m_2) e}{\{ma(1 - e^2)\}^{3/2} c^2}$$

cm. per sec. per revolution, where m_1, m_2 are the respective masses, m is the total mass, and a, e are the semi-major axis and eccentricity, respectively, of the relative orbital ellipse; (2) the advance of periastron per revolution expressed in units of $6\pi Gm/c^2a(1 - e^2)$ radians.

Table 2

Theory	Acceleration of centre of mass	Advance of periastron
1. General relativity	0	1
2. Nordstrom's (generalized):	$2q-1$	$\frac{q-1}{3} - \frac{(2q-1)}{3}\frac{m_1m_2}{m^2}$
$q = 0$ (Nordstrom)	-1	$-\frac{1}{3} + \frac{1}{3}\frac{m_1m_2}{m^2}$
$q = 1/2$ (Littlewood, Bergmann)	0	$-1/6$
4. Scalar potential with a variable velocity of light:		
Theory (i)	3	$\frac{2}{3} - 2\frac{m_1m_2}{m^2}$
Theory (ii)	5	$1 - \frac{8}{3}\frac{m_1m_2}{m^2}$
5. Vector potential	p	$\frac{1+2p}{6} - \frac{p}{3}\frac{m_1m_2}{m^2}$
6. Kustaanheimo's*	0	1
7. Birkhoff's	1	$1 - \frac{2}{3}\frac{m_1m_2}{m^2}$
8. Whitehead's (generalized):	$1-4b$	$1 + \frac{(4b-1)}{3}\frac{m_1m_2}{m^2}$
$b = 0$ (Whitehead)	1	$1 - \frac{1}{3}\frac{m_1m_2}{m^2}$
$b = 1/4$	0	1
9. Poincaré's	0	$n/6$

* Conditions have been imposed *ad hoc* on the arbitrary parameters in this theory so that it predicts the same results as general relativity for the effects listed in both Table 1 and Table 2.

Additional Effects in the One-body Problem

Two additional effects arise in the one-body problem when due account is taken of the axial rotation of the central body: there is an additional advance of perihelion, and the normal to the plane of the orbit precesses about the axis of rotation of the central body. Effects of this type were first obtained in general relativity by Lense and Thirring[18], working to order $1/c^2$. We have calculated similar effects in Lorentz-invariant theories to the same order of approximation. Since Poincaré's theory was not originally formulated so as to apply to continuous distributions of gravitating matter, we have extended his theory by the same method as that followed by Rayner[19] in the case of Whitehead's theory in its original form ($b = 0$).

In Table 3 we list for the respective theories:

(1) The *additional* advance of perihelion, expressed in units of:

$$\frac{2\pi}{5}\frac{(GM)^{1/2}}{\{a(1-e^2)\}^{3/2}}\frac{\omega R^2}{c^2}\cos\alpha$$

radians per revolution, where R is the radius of the central body (a sphere of mass M), ω its angular velocity, α the angle between its axis of rotation and the normal to the plane of the orbit of the test-particle (to the order of approximation considered this angle remains constant in all theories), and a, e are the semi-major axis and eccentricity of the orbital ellipse. (The expression can also be written in the concise form:

$$\left(\frac{I\omega\omega'}{Mc^2}\right)\frac{\pi\cos\alpha}{(1-e^2)^{3/2}}$$

where $I = 2MR^2/5$, that is, the moment of inertia of the homogeneous sphere about a diameter, and ω' is the mean angular velocity in the orbital ellipse.)

(2) The rate of precession of the normal to the plane of the orbit about the axis of rotation of the central body, expressed in units of:

$$\frac{\pi}{5}\frac{(GM)^{1/2}}{\{a(1-e^2)\}^{3/2}}\frac{\omega R^2}{c^2}$$

radians per orbital revolution.

In the case of Whitehead's theory, a further advance of perihelion arises due to the fact that the central body is no longer being treated as if it were of zero radius[20]. Thus, even if ω were zero the perihelion advance would not be the same as that given by general relativity, but would be:

$$\frac{6\pi GM}{c^2a(1-e^2)}\left\{1 + \frac{(4+e^2)}{10(1-e^2)^2}\left(\frac{R}{a}\right)^2\right\}$$

For e^2 small, the ratio of this additional term to the term when $R = 0$ is approximately $2R^2/5a^2$. It is therefore appreciable if a is not too large compared with R.

Conclusions

(1) On inspecting Table 1, we note that the gravitational red-shift is the least sensitive of Einstein's tests for general relativity. The same effect is predicted by almost all Lorentz-invariant theories. For, apart from Poincaré's theory with $n < 2$ and the vector potential theory with $p = 0$, the only exceptions are those theories in which it has not been possible to make the calculation. We may therefore conclude that this effect is essentially a special relativity effect arising when the ideas of that theory are applied to the study of gravitational fields.

(2) On the other hand, with the exception of Kustaanheimo's theory (which contains a large number of unspecified parameters), the only theories which agree with general relativity in their predictions for both the advance of perihelion and the deflexion of light in the one-body problem are the tensor theories of Birkhoff and Whitehead-Schild.

(3) If, however, we take into account the finite radius of the central body, then Whitehead's theory yields an additional term for the advance of perihelion in the one-body problem, irrespective of whether the central body is rotating.

(4) In the case of the two-body problem (Table 2), there arise two highly sensitive tests for general relativity. For, with the possible exception of Kustaanheimo's theory, there is complete agreement with general relativity only in one particular instance of the Whitehead-Schild set of theories and in Poincaré's theory with a particular value of n ($n = 6$).

(5) Turning to Table 3, we note that no theory agrees with general relativity in all five tests of the one-body problem, for even in the case of Whitehead's theory there is a discrepancy due to the effect of the non-zero radius of the central body. The discrepancy between Kustaanheimo's theory and

Table 3

Theory	Additional advance of perihelion due to rotation of central body	Rate of orbital precession
1. General relativity	-8	8
2. Nordstrom's (generalized)	0	0
5. Vector potential	$-(p+2)$	$p+2$
6. Kustaanheimo's*	-6	arbitrary
7. Birkhoff's	-6	6
8. Whitehead's†	-8	8
9. Poincaré's	$-(n+1)$	$n+1$

* Conditions have been imposed *ad hoc* on the arbitrary parameters in this theory so that it predicts the same results as general relativity for the effects listed in both Table 1 and Table 2.

† We have considered here the only original Whitehead theory.

general relativity is particularly striking in view of the large number of arbitrary parameters occurring in the former theory. Whatever particular values are assigned to these parameters to make the predictions of that theory agree with those of general relativity in Tables 1 and 2, it is impossible to make the two theories agree in the first column of Table 3.

(6) We may therefore conclude that no Lorentz-invariant theory of gravitation predicts all the effects considered here in complete agreement with general relativity.

(7) Finally, as regards possible practical application, it is of interest to consider the orders of magnitude of the respective effects for artificial satellites moving in orbits about the Earth with suitably chosen values of a. For an artificial satellite moving around the Earth at a mean height above the surface of the order of 1,000 km., the advance of perigee (uncorrected for the effect of the Earth's rotation) is of the order 10 sec. of arc per year, whereas the rotation correction effect is of the order 0·3 sec. of arc per year in the case of general relativity. The biggest observable discriminating effect would arise, however, in connexion with the additional advance of perigee in Whitehead's theory due to the finite radius of the Earth. For this could amount to about a quarter of the uncorrected advance, whereas it would be zero in the case of general relativity.

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UTILIZATION OF NITRIC OXIDE BY MICRO-ORGANISMS AND HIGHER PLANTS

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ALTHOUGH the metabolism of inorganic nitrogen compounds has been the subject of intensive investigation in recent years, the intermediates have not been unequivocally identified. It is generally considered that nitrate assimilation and nitrification occur in a series of two-electron steps[1-3]. Nitric oxide, which is formed by a one-electron reduction of nitrite, has long been recognized as a product of denitrification[4,5]; but it has not been suggested as an intermediate in the assimilatory reduction of nitrate[3,6]. During the course of work on the dissimilatory reduction of nitrate by *Pseudomonas aeruginosa*[6-8] and the assimilation of nitrate in *Neurospora crassa*[3], we have obtained evidence that nitric oxide may well be a common intermediate, and we have therefore re-examined the position of nitric oxide in various pathways of inorganic nitrogen metabolism.

Denitrification

Several early workers[9-11] reported the production of brown fumes during the fermentation of beet and identified them as nitrogen dioxide formed by the oxidation of nitric oxide. More recently nitric oxide has been found to be a product of denitrification in soil[12,13] and also in silage fermentation[14]. Bacteria known to produce nitric oxide during the dissimilatory reduction of nitrate or nitrite include *Bacillus licheniformis*[15], *Thiobacillus denitrificans*[16], *Pseudomonas aeruginosa*[8] and *Micrococcus denitrificans*[17]. There have also been several reports of the production of nitrogen gas from nitric oxide by bacteria[16-19]. Chung and Najjar[18] partially characterized a nitric oxide reductase from *P. stutzeri* and concluded that it was a flavoprotein requiring both iron and copper for its activity. The dialysis techniques used by these workers to establish the metal requirements are open to question since iron, copper and, to a smaller extent, zinc reactivated the enzyme after it had been subjected to prolonged dialysis against salicylaldoxime. The metal effects could therefore have resulted from the removal of residual chelate bound to the enzyme since the reversal of the inhibition was in the order of the affinities of the metals for salicylaldoxime.

Nitric oxide reductase purified 25-fold from *P. aeruginosa*, as shown in Table 1, is a metallo-flavoprotein[7]. The activity of the purified enzyme, which utilized reduced pyocyanine but not reduced pyridine nucleotides as the hydrogen donor, was maximal at pH 8·0. Sulphydryl groups appear to be required for the enzyme activity since glutathione partially offset the inhibition of p-chloromercuribenzoate, as shown in Table 2. A flavin requirement for the enzyme was indicated by the reversal of mepacrine inhibition with flavin mononucleotide (FMN) or flavinadenine dinucleotide (FAD) and confirmed by precipitating the enzyme three times with ammonium sulphate (pH 7·0), when its activity, diminished by about 70 per cent, was reconstituted by FMN or FAD (Michaelis–Menten constant, $Km = 4 \times 10^{-5}$ M). At a concentration of 2×10^{-3} M the iron and copper chelating agents, α,α'-dipyridyl, o-phenanthroline, potassium ethyl xanthate and 2 : 9 dimethyl 1 : 10 phenanthroline, inhibited the enzyme by more than 40 per cent. Salicylaldoxime, α-benzoin oxime and sodium diethyldithiocarbamate, however, which chelate copper but not iron between pH 7 and 8 (ref. 20), reduced the enzyme activity by less than 10 per cent. There is some evidence for the concentration of iron, but not

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Table 1. PURIFICATION OF NITRIC OXIDE REDUCTASE FROM *Pseudomonas aeruginosa*

Fraction	Procedure	Volume (ml.)	Total protein (mgm.)	Protein (mgm./ml.)	Total units (μl. NO/hr.)	Specific activity (μl. NO/mgm. protein/hr.)	Recovery (per cent)	Purification
1	Supernatant solution after centrifuging at 18,000 *g*	17·5	301	17 2	1,350	4 5	—	—
2	Precipitate from 0–43 per cent ammonium sulphate saturation of Fraction 1, centrifuged at 5,000 *g* for 5 min. dissolved in 0·005 *M* phosphate buffer (*p*H 8·0)	17·5	155	8·86	1,260	8·1	93	1·8
3	Fraction 2 was added to a diethylaminoethyl cellulose column. The column was eluted with 20 ml. aliquots of 0 01 *M* phosphate buffer (*p*H 8·0). Activity of the fourth aliquot	22·0	8·6	0·39	960	113·5	71	25

Actively denitrifying cells of *P. aeruginosa* (NCIB 8704) were grown in a nitrate–peptone medium (ref. 27) under anaerobic conditions for 24 hr. at 37° C. The harvested cells were washed and stored at − 15° C. 5 gm. frozen cells were suspended in 5 ml. 0·1 *M* phosphate buffer (*p*H 8·0) and disrupted with an ultrasonic probe (20 kc./sec.) for 15 min. at 4° C. The homogenate was diluted to 20 ml. with the same buffer and centrifuged at 18,000 *g* for 45 min. The supernatant solution was used as the source of the crude enzyme. The enzyme activity was assayed using the following Warburg reaction mixture. Main vessel, 1·0 ml. enzyme, 1·1 ml. 0 1 *M* phosphate buffer (*p*H 8·0), 0·1 ml. 10^{-4} *M* pyocyanine; side-arm, 0 1 mgm. crystalline alcohol dehydrogenase, 0·1 ml. 2 per cent v/v ethyl alcohol, 0·1 ml. (300 mμ*M*) reduced diphosphorpyridine nucleotide; centre well, 0 2 ml. 20 per cent w/v potassium hydroxide. Gas phase, 25 per cent NO/75 per cent nitrogen. Temp. 30° C. Boiled enzyme controls were included. Protein contents were determined by the Folin method (ref. 28).

copper, in partially purified preparations of the enzyme. Extracts of cells deficient in iron contained decreased nitric oxide reductase activity (25 per cent of normal cells) whereas those of cells deficient in copper, molybdenum, zinc or manganese were unaffected. It seems unlikely, therefore, that copper is required for nitric oxide reductase activity in this organism.

Nitrate Assimilation

McNall and Atkinson[21] showed that *Escherichia coli B*, which reduced nitrate but not nitrite, did not reduce nitric oxide. After repeatedly subculturing the organism on a nitrate medium they obtained a strain (*E. coli, Bn*) which could utilize nitrate or nitric oxide as the sole nitrogen source for growth. Similarly Steinberg[22] succeeded in growing *Aspergillus niger* and *Nicotiana tabacum* on nitrohydroxylaminate ($N_2O_3^{=}$) which is a hydrate of nitric oxide. We have therefore examined a range of bacteria, fungi, algae and higher plants to determine whether nitric oxide reductase activity is a universal enzyme in organisms which assimilate nitrate. The results in Table 3 show that the uptake of nitric oxide by cells and their extracts was limited to organisms grown with nitrate. Micro-organisms grown on ammonium-nitrogen only showed little or no nitric oxide reductase activity. The effect with higher plants was less clear because of the difficulty of growing them in the complete absence of nitrate or nitrite which are almost invariably produced in the culture solution by nitrifying organisms. Indeed, the majority of plants showed undiminished nitrate and nitric oxide reductase activities when grown on ammonium-nitrogen under non-sterile conditions. Roots of wheat seedlings, however, grown under strictly aseptic conditions with nitrate, had five times the enzyme activity of those grown with ammonium chloride as the only nitrogen source. The rate of nitric oxide uptake was very similar to that of nitrate reduction in the same homogenates of micro-organisms or higher plants, for example, *Neurospora crassa* grown on a nitrate medium had a nitric oxide reductase activity of 15 μl. NO (650 mμ *M* NO)/mgm. N/hr. and a nitrate reductase activity of 580 mμ *M* NO_3^- reduced/mgm. N/hr.

Although nitrite reductases from *Neurospora* and higher plants have been studied in some detail[3] the

Table 2. EFFECT OF SOME INHIBITORS ON NITRIC OXIDE REDUCTASE ACTIVITY

Compound	Final conc of inhibitor (*M*)	Inhibition (per cent)
Potassium cyanide	5×10^{-4}	100
Sodium ethylenediamine tetraacetate	2×10^{-3}	33
α,α'-Dipyridyl	2×10^{-3}	59
o-Phenanthroline	2×10^{-3}	73
Potassium ethyl xanthate	2×10^{-3}	40
2 . 9-Dimethyl 1 : 10-phenanthroline	2×10^{-3}	54
α-Benzoin oxime	saturated	0
Salicylaldoxime	2×10^{-3}	10
Sodium diethyldithiocarbamate	2×10^{-3}	0
Mepacrine hydrochloride	5×10^{-3}	60
,, ,, + 0 2 μ*M* FAD	5×10^{-3}	20
p-Chloromercuribenzoate	2×10^{-3}	40
,, + 0·5 μ*M* glutathione	2×10^{-3}	15

The enzyme (Fraction 3, Table 1) was assayed in the presence of the appropriate compound. The reaction mixture was as described in Table 1. A boiled enzyme control was included for each compound.

Table 3. UTILIZATION OF NITRIC OXIDE BY BACTERIA, FUNGI AND GREEN PLANTS

Nitric oxide uptake: μl. NO/mgm. N/hr.

Organism		Nitrogen source during growth	
		NH_4^+	NO_3^-
Bacterium	*Escherichia coli* (B)*	2	16
Fungi	*Aspergillus niger* (M)	6	24
	Neurospora crassa (wild type *Em*, 5297*a*)	10	29
	Candida utilis	23	31
	Cryptococcus diffluens	2	14
	Hansenula anomola	1	11
	Torulopsis versatalis	0	3
Alga	*Chlorella pyrenoidosa* (211–8c)	7	17
Higher plants	*Cucurbita pepo* (marrow)†		
	leaf laminæ	24	22
	root tissue	8	6
	Fragaria ananassa (strawberry)†		
	leaf laminæ	—	12
	Brassica oleracea (cauliflower)†		
	leaf laminæ	12	14
	Triticum vulgaris (wheat)‡		
	root tissue	7	34

* Adapted to grow on nitrate as sole nitrogen source.
† Grown under non-sterile conditions.
‡ Grown under strictly aseptic conditions.

Dr. F. W. Beech supplied the yeast cultures and Dr. E. J. Hewitt and Dr. R. A. Webb some of the plant material.

The nitric oxide uptake was measured in homogenates of various organisms with the following Warburg reaction mixture: Main vessel, 1·0 ml. homogenate, 1·2 ml. 0·1 *M* phosphate buffer (*p*H 7·5); side-arm, 0·1 mgm. crystalline alcohol dehydrogenase, 0·1 ml. 2 per cent v/v ethyl alcohol, 0·1 ml (300 mμ*M*) reduced diphosphopyridine nucleotide; centre well, 0 2 ml. 20 per cent w/v potassium hydroxide. Gas phase, 25 per cent NO/75 per cent N_2. Temperature, 30° C. Boiled enzyme controls were always included. Nitrogen contents were determined as described by Nicholas and Fisher (ref. 29).

Table 4. UTILIZATION OF NITRIC OXIDE BY ORGANISMS WHICH FIX ATMOSPHERIC NITROGEN
The reaction mixture as described in Table 3
Nitric oxide uptake: μl. NO/mgm. N/hr.

Organism		Nitrogen source during growth		
		NH_4^+	NO_3^-	N_2
Bacteria	*Azotobacter vinelandii* (O)	3	29	23
	Clostridium pasteurianum (*W-S*)	10	23	44
Blue-green algae	*Anabaena cylindrica* (1403–2)	3	18	12
	Nostoc muscorum (1453–12)	0	10	8
Higher plants (symbiotic nitrogen fixers)	*Vicia faba* (broad bean)			
	root tissue	—	—	6
	nodular tissue	—	—	20
	Casuarina equisetifolia			
	root tissue	—	—	2
	nodular tissue	—	—	7

Dr. H. E. Davenport supplied the *C. equisetifolia*.

product of the reduction has not hitherto been identified. Walker, of this laboratory, however, using the nitrite reductase from *Neurospora*, has shown that there is a stoichiometric reduction of nitrite to nitric oxide (unpublished work).

Nitrogen Fixation and Nitrification

During the course of investigations on the utilization of nitric oxide it became evident that nitrogen-fixing organisms possessed an active nitric oxide reductase, as shown in Table 4. Thus the bacteria *Azotobacter vinelandii* and *Clostridium pasteurianum* and the blue-green algae *Anabaena cylindrica* and *Nostoc muscorum* all took up nitric oxide when grown with nitrogen gas or nitrate-nitrogen, but not when grown with ammonium-nitrogen. Similarly the nodular tissue of the legume *Vicia faba* (broad bean) and of the non-legume *Casuarina equisetifolia* utilized the gas more rapidly than did the neighbouring root tissue. Nitric oxide inhibited the hydrogenase activity of *A. vinelandii* and *C. pasteurianum* when methylene blue was the hydrogen acceptor[22], but sodium nitrate, nitrite or hyponitrite, nitrous oxide, hydroxylamine or ammonium sulphate were without effect.

Anderson, of this Station, has shown that cell-free extracts of *Nitrosomonas europeae*, which oxidize hydroxylamine to nitrite aerobically[24], produce nitric oxide under anaerobic conditions (unpublished work).

Conclusions

The results presented in this paper support the view that nitric oxide, or a compound with which it equilibrates, is an intermediate in both assimilatory and dissimilatory nitrate reduction. The significance of the nitric oxide uptake in nitrogen-fixing organisms is less clear, but *Rhizobium*, *Azotobacter* and *Clostridium* also contain nitrate, nitrite and hydroxylamine reductases[17,25,26] and these enzymes could all be induced by nitric oxide should it be formed by an initial oxidative step in the fixation process. Preliminary results indicate that nitric oxide may also be formed during the nitrification of hydroxylamine. Thus nitric oxide may well be a key intermediate in the metabolism of inorganic nitrogen compounds in micro-organisms and in higher plants.

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PRESENCE OF CELL WALLS LIKE THOSE OF BACTERIA IN *RICKETTSIAE*

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THERE has been uncertainty about the taxonomic position of *Rickettsiae*, organisms that produce disease in man and parasitize a wide range of animals. All pathogenic *Rickettsiae* are considered to be obligate intracellular parasites, and no unequivocal evidence has been obtained of their multiplication in cell-free media. Under the light microscope *Rickettsiae* appear as small Gram-negative rods in the cytoplasm of infected cells. When examined by the electron microscope in air-dried preparations and in ultra-thin sections the organisms appear to have double limiting membranes[1]. Preparations of membranes of *Rickettsia mooseri* were made by Schaechter *et al.*[2], who reported that they contain amino-acids, glucose, hexosamine, glucuronic acid and galactose. These compounds are present in a wide range of organisms, but all bacteria so far studied—and only bacteria—have as a component of their cell walls mucopeptides

containing muramic acid[3]. In the present work, membranes of *R. burneti* have been shown to have muramic acid, and like the cell walls of bacteria to be digested by lysozyme.

Rickettsia (*Coxiella*) *burneti* was grown in embryonated eggs, inoculated at 6 days and harvested after a further 6 days incubation at 35°. Tests for bacterial contamination were negative. Suspensions of organisms were purified as described elsewhere[4], omitting formalin treatment. The suspensions were incubated with 1 per cent sodium deoxycholate in 0·1 *M tris* (hydroxymethyl) amino-methane buffer, *p*H 7·0, for 4 hr. at 45° with constant agitation. Cell-wall preparations similar to those described by Schaechter *et al.* were obtained. These preparations were not morphologically changed by digestion at 37° for 2 hr. with crystalline trypsin (Armour) at a concentration of 100 μgm. per ml. in 0·1 *M tris* buffer, *p*H 7·6. However, digestion for 2 hr. with crystalline egg-white lysozyme, 50 μgm. per ml. in 0·1 *M tris* buffer, *p*H 8·0, containing 0·01 *M* sodium ethylenediamine tetraacetate, resulted in the disappearance of morphologically recognizable cell walls. These are the conditions under which lysozyme digests the walls of Gram-negative bacteria[5]. No precipitation was visible and digestion with heated enzyme did not change the appearance of the cell walls, from which it seems unlikely that aggregation in the presence of the highly basic protein, lysozyme, was responsible for their disappearance. Lysozyme was also shown to liberate material giving a reaction for N-acetyl amino-sugars from suspensions of *R. burneti*, just as it does from the cell walls of many species of bacteria[6]. Suspensions of *R. burneti* were treated with egg-white lysozyme under the conditions described above for 3 hr. at 37°. The material was brought to *p*H 9·0 and shown to contain material giving the Morgan–Elson reaction for N-acetyl amino-sugars[7].

Analyses of suspensions of *R. burneti* have also established that they contain muramic acid. The organisms were precipitated with 5 per cent w/v trichloracetic acid. The precipitates were hydrolysed in sealed ampoules with 4 *N* hydrochloric acid at 105° for 4 hr. After removal of excess hydrochloric acid *in vacuo*, hexosamines in the hydrolysates were first concentrated by chromatography on a column of 'Dowex 50' (H^+). The hexosamine peak was transferred to a charcoal–'Celite' column, and glucosamine was eluted with water[8]. The 10 per cent ethanolic eluate, subjected to paper chromatography in butanol–pyridine–water (6 : 4 : 3), showed a spot in the position expected of muramic acid. Material eluted from this spot when submitted to the Elson–Morgan test[9] gave an absorption curve with a maximum at 510 mμ (505 mμ overnight), identical with that of authentic muramic acid isolated from the cell walls of *Staphylococcus aureus* and unlike that of glucosamine (Fig. 1). Such a curve is typical of hexosamines substituted at position 3 (ref. 10), and muramic acid is the only naturally occurring material of this type likely to have withstood the conditions of hydrolysis used. Furthermore, both the acetylated derivative and the substituted pentose obtained on treatment with ninhydrin under appropriate conditions[11] showed identical mobilities on paper chromatography with those of authentic muramic acid derivatives.

Preliminary tests have shown that muramic acid is present in *R. typhi* grown under the same conditions as *R. burneti* and in the mouse pneumonitis

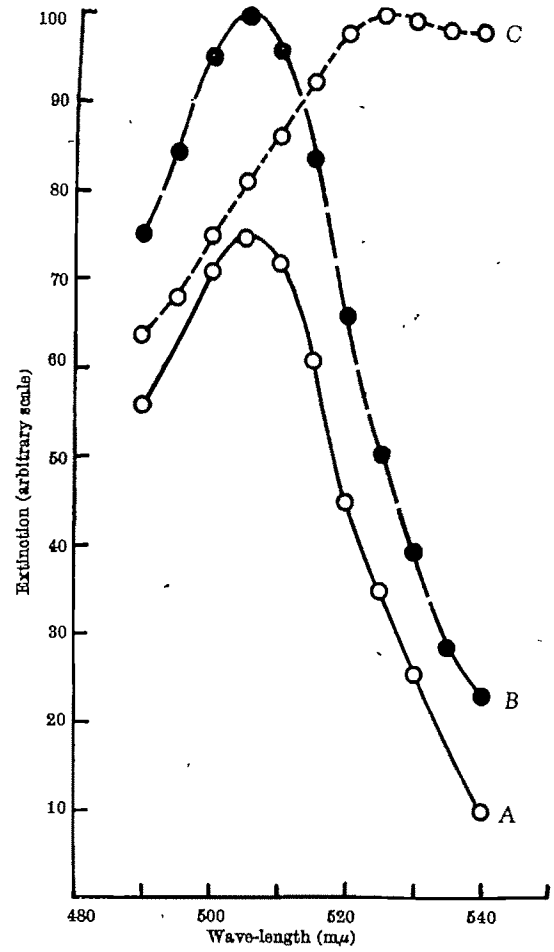

Fig. 1. Absorption curves in Rondle and Morgan tests of: *A*, authentic muramic acid from *Staphylococcus aureus*; *B*, material from *Rickettsia burneti*; *C*, glucosamine

organism (Nigg) grown in mouse embryo cell cultures; the latter belong to the psittacosis-lymphogranuloma group. No trace of muramic acid was detectable in control preparations from uninfected yolk sacs, or in highly concentrated suspensions of vaccinia virus grown in chorioallantoic membranes or influenza virus grown in the allantois of embryonated eggs.

The present work has shown that *Rickettsiae* have cell walls similar to those of bacteria. Since penicillin inhibits bacterial cell wall synthesis[12], the sensitivity of the *Rickettsia* and psittacosis-lymphogranuloma groups of organisms to penicillin may be attributable to their possession of cell walls of this type. In a number of other respects these organisms resemble bacteria rather than true viruses: (1) they have both deoxyribonucleic acid and ribonucleic acid[3,13], whereas true viruses have one or the other (Allison, A. C., and Burke, D. C., unpublished observations); (2) they multiply by binary fission[14], which is not the case in the true viruses; (3) they are sensitive to chloramphenicol and tetracyclines, and purified suspensions of organisms have some capacity for incorporation of amino-acids into protein, which is abolished by chloramphenicol[15].

All these findings suggest that *Rickettsiae* are probably bacteria that have become adapted to intracellular multiplication. Perhaps they have lost the capacity to synthesize certain enzymes necessary for growth and replication, and so have become

obligate intracellular parasites. The apparent inability of suspensions of *Rickettsiae* to utilize glucose, even though they can metabolize tricarboxylic acid cycle intermediates[16], may be a case in point. There is a substantial body of opinion that *Rickettsiae* were originally insect parasites, and among the *Rickettsiae* of insects there seems to be no sharp line of distinction between intracellular and free-living forms[17].

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IDENTIFICATION OF THE RECOMBINANT PRODUCTS OF CANINE AND HUMAN HÆMOGLOBINS

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WHEN a mixture of canine carbonmonoxyhæmoglobin and human carbonmonoxyhæmoglobin A is dissociated at either *p*H 4·7 (ref. 1) or *p*H 11·0 (ref. 2) for 20 min. or more and then recombined at neutral *p*H, two additional electrophoretic components are produced. In slightly acidic buffer, in which all the components are cationic, canine hæmoglobin migrates more slowly than hæmoglobin A; one of the new components migrates more slowly than canine hæmoglobin; and the other migrates more rapidly than hæmoglobin A (Figs. 1 and 3). The exchange reaction:

$$\alpha_2^{A}\beta_2^{A} + \alpha_2^{can}\beta_2^{can} = \alpha_2^{A}\beta_2^{can} + \alpha_2^{can}\beta_2^{A} \qquad (1)$$

though it accounts for the appearance of two new components, does not specify which of the postulated products corresponds to the new fast or the new slow electrophoretic component. Probable compositions of these components have now been determined by recombination of canine hæmoglobin with human hæmoglobins known to be abnormal in either the α-chain or the β-chain.

All dissociations of the equimolar mixtures of canine–human carbonmonoxyhæmoglobin to be described were done at *p*H 4·7, Γ/2 0·10 (acetate buffer) for 24 hr. except where otherwise noted. Dissociation was followed by dialysis in potassium phosphate buffer of *p*H 6·8, Γ/2 0·02 or *p*H 6·3, Γ/2 0·02 at 5° C. for approximately 18 hr. The control and recombined 1 per cent carbonmonoxyhæmoglobin mixtures were analysed by moving-boundary electrophoresis in the same phosphate buffer used for dialysis for 5 hr. at 0·5° with potential gradients of 9·3 (at *p*H 6·8) and 8·5 (at *p*H 6·3) V./cm.

A recombined mixture of canine and S hæmoglobins showed little change in the electrophoretic pattern other than asymmetry of the faster (S) boundary. Electrophoresis of a recombined mixture of canine and C hæmoglobins showed one new component migrating between canine and C in the approximate position of hæmoglobin A and asymmetry of the fastest (C) boundary. Recombination of a mixture of canine, S, and C hæmoglobins which had been dissociated for

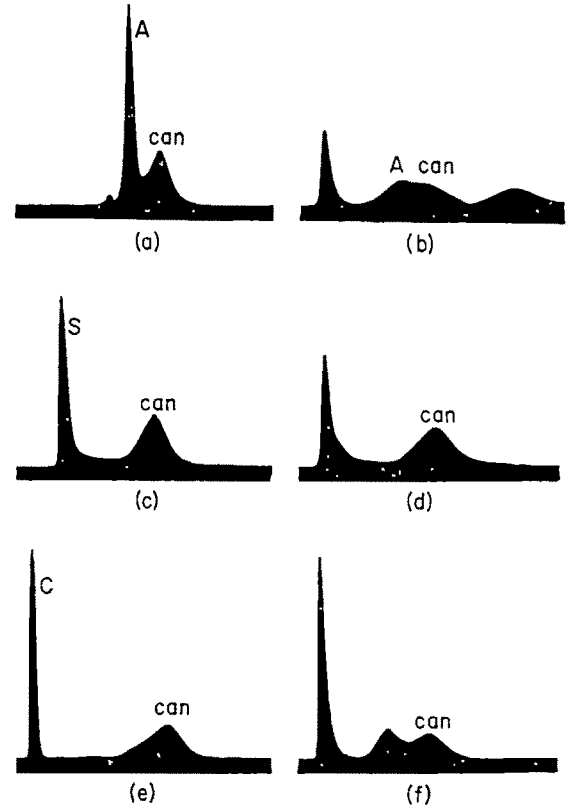

Fig. 1. Ascending limb electrophoretic patterns of 1 per cent carbonmonoxyhæmoglobin in phosphate buffer of *p*H 6·8, Γ/2 0·02. The direction of migration is from right to left. *a*, A, canine control; *b*, A, canine recombined; *c*, S, canine control; *d*, S, canine recombined, *e*, C, canine control; *f*, C, canine recombined

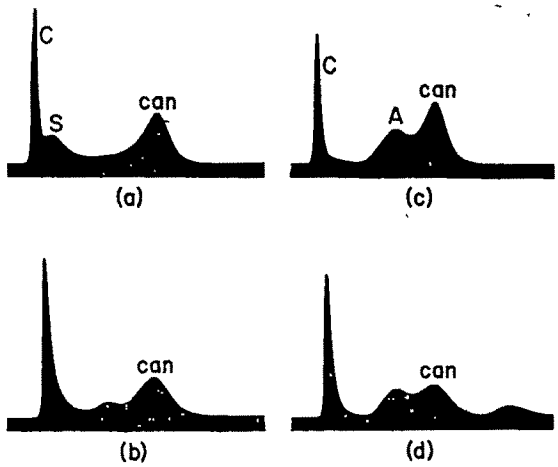

Fig. 2. Ascending limb electrophoretic patterns of 1 per cent carbonmonoxyhæmoglobin in phosphate buffer of pH 6·8, $\Gamma/2$ 0·02. The direction of migration is from right to left. *a*, C, S, canine control; *b*, C, S, canine recombined; *c*, C, A, canine control; *d*, C, A, canine recombined. *b* and *d* were recombined after dissociation for 4 hr.

4 hr. yielded one new component in the approximate position of hæmoglobin A with merging of the original S and C boundaries into one fast unsymmetrical boundary. No component migrating more slowly than canine or more rapidly than C appeared in these experiments. Dissociation (4 hr.) and recombination of a mixture of canine, A, and C hæmoglobins gave one new electrophoretic component migrating more slowly than canine.

At pH 6·3, hæmoglobin I migrates more slowly than canine hæmoglobin. Recombination of a dissociated canine–I hæmoglobin mixture (I was isolated from an A–I sample by column chromatography[3]) again yielded only two electrophoretic components, but both boundaries were decidedly skewed and were more widely separated from each other than in the control experiment. Hopkins-2 hæmoglobin (partially purified from Hopkins-2 trait by column chromatography[3]) migrates with canine hæmoglobin as one electrophoretic component at pH 6·3. On dissociation and recombination a new component migrating more slowly than canine and Hopkins-2 was observed as well as an increase in the proportion and mobility of the component in the position of hæmoglobin A. A new fast component was also present, but the amount was much less than in the canine-A experiments. The electrophoretic patterns of all experiments are shown in Figs. 1, 2, and 3.

Not one of the results is as clear-cut as the results of I–S[4] and canine–A recombinations, in which each reactant and product was resolved as a separate electrophoretic component. A self-consistent interpretation is nevertheless possible if the observed results and the postulated products of all recombinations are correlated. The exchange reactions of canine hæmoglobin with hæmoglobins S and C, which have altered β-chains[5,6], and with hæmoglobins I[7] and Hopkins-2 (ref. 1), which have altered α-chains, can be represented as follows:

$$\alpha_2^{can}\beta_2^{can} + \alpha_2^{A}\beta_2^{S} = \alpha_2^{can}\beta_2^{S} + \alpha_2^{A}\beta_2^{can} \quad (2)$$

$$\alpha_2^{can}\beta_2^{can} + \alpha_2^{A}\beta_2^{C} = \alpha_2^{can}\beta_2^{C} + \alpha_2^{A}\beta_2^{can} \quad (3)$$

$$\alpha_2^{can}\beta_2^{can} + \alpha_2^{I}\beta_2^{A} = \alpha_2^{can}\beta_2^{A} + \alpha_2^{I}\beta_2^{can} \quad (4)$$

$$\alpha_2^{can}\beta_2^{can} + \alpha_2^{Ho-2}\beta_2^{A} = \alpha_2^{can}\beta_2^{A} + \alpha_2^{Ho-2}\beta_2^{can} \quad (5)$$

The new electrophoretic component of lower mobility than canine hæmoglobin in the canine–A recombination did not appear in either the canine–S or the canine–C recombinations. $\alpha_2^{can}\beta_2^{A}$, a product of reaction (1), but not of reactions (2) or (3), must therefore be the new slow component, and $\alpha_2^{A}\beta_2^{can}$, the common product of all three recombinations, must be the new fast component. The mobility of $\alpha_2^{A}\beta_2^{can}$ probably lies between those of S and C since it is not resolved electrophoretically from either. Consideration of reactions (4) and (5) adds support to identification of the new fast component as $\alpha_2^{A}\beta_2^{can}$. This species, which is not postulated as a product in either reaction, was absent in the canine–I recombined mixture and was present in the canine–Ho-2 recombined mixture only in an amount compatible with the proportion of hæmoglobin A known to be present as a contaminant before recombination. A new electrophoretic component appeared in the canine–Ho-2 recombination in the same position and amount as the new slow component of the canine–A recombination, a result consistent with the identification of the new slow component as $\alpha_2^{can}\beta_2^{A}$ since it is a postulated product in both reactions (1) and (5). No new electrophoretic component was resolved in the canine–I recombination; however, the presence of $\alpha_2^{can}\beta_2^{A}$ as postulated by reaction (4) is not excluded because the mobility of this species is similar to that of I.

Identification of the new fast component of the canine–A recombination as $\alpha_2^{A}\beta_2^{can}$ and the new slow component as $\alpha_2^{can}\beta_2^{A}$ permits estimation of the

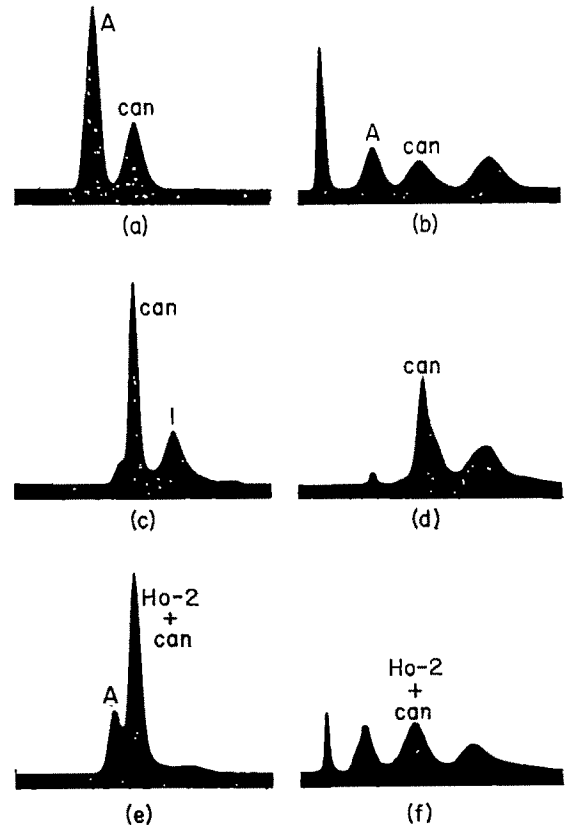

Fig. 3. Ascending limb electrophoretic patterns of 1 per cent carbonmonoxyhæmoglobin in phosphate buffer of pH 6·3, $\Gamma/2$ 0·02. The direction of migration is from right to left. *a*, A, canine control; *b*, A, canine recombined; *c*, canine, I control; *d*, canine, I recombined; *e*, (A), Ho-2, canine control; *f*, (A), Ho-2, canine recombined

Table 1. COMPOSITION OF CANINE AND HUMAN HÆMOGLOBIN MIXTURES BEFORE AND AFTER RECOMBINATION

Mixture		Electrophoretic Composition (in order of increasing mobility)
can + A	Control	41% $\alpha_2^{can}\beta_2^{can}$; 59% $\alpha_2^{A}\beta_2^{A}$
	Recombined	31% $\alpha_2^{can}\beta_2^{A}$; 24% $\alpha_2^{can}\beta_2^{can}$, 21% $\alpha_2^{A}\beta_2^{A}$, 24% $\alpha_2^{A}\beta_2^{can}$
can + S	Control	50% $\alpha_2^{can}\beta_2^{can}$, 50% $\alpha_2^{A}\beta_2^{S}$
	Recombined	54% $\alpha_2^{can}\beta_2^{S} + \alpha_2^{can}\beta_2^{can}$, 46% $\alpha_2^{A}\beta_2^{S} + \alpha_2^{A}\beta_2^{can}$
can + C	Control	49% $\alpha_2^{can}\beta_2^{can}$ 51% $\alpha_2^{A}\beta_2^{C}$
	Recombined	26% $\alpha_2^{can}\beta_2^{can}$, 22% $\alpha_2^{can}\beta_2^{C}$; 52% $\alpha_2^{A}\beta_2^{C} + \alpha_2^{A}\beta_2^{can}$
can + I	Control	40% $\alpha_2^{I}\beta_2^{A}$; 60% $\alpha_2^{can}\beta_2^{can}$
	Recombined	44% $\alpha_2^{I}\beta_2^{A} + \alpha_2^{can}\beta_2^{A}$; 56% $\alpha_2^{can}\beta_2^{can} + \alpha_2^{I}\beta_2^{can}$
can + Ho–2 (+ A)	Control	80% $\alpha_2^{Ho-2}\beta_2^{A} + \alpha_2^{can}\beta_2^{can}$, 20% $\alpha_2^{A}\beta_2^{A}$
	Recombined	31% $\alpha_2^{can}\beta_2^{A}$; 37% $\alpha_2^{Ho-2}\beta_2^{A} + \alpha_2^{can}\beta_2^{can}$; 23% $\alpha_2^{A}\beta_2 + \alpha_2^{Ho-2}\beta_2^{can}$; 9% $\alpha_2^{A}\beta_2^{can}$

mobilities of the other products postulated in reactions (2) to (5) if it assumed that the mobilities of $\alpha_2^{A}\beta_2^{can}$, $\alpha_2^{Ho-2}\beta_2^{can}$ and $\alpha_2^{I}\beta_2^{can}$ are related in the same way as those of hæmoglobins A, Ho-2 and I, and that the mobilities of $\alpha_2^{can}\beta_2^{A}$, $\alpha_2^{can}\beta_2^{S}$ and $\alpha_2^{can}\beta_2^{C}$ are related in the same way as those of hæmoglobins A, S and C. The probable composition of each electrophoretic component in a recombined mixture can then be determined as shown by the following example. No new component was resolved in the S-canine recombination, and one new component with the mobility of hæmoglobin A appeared in the canine–C recombination. The new component of the canine–C recombination must be $\alpha_2^{can}\beta_2^{C}$ since the other postulated product is $\alpha_2^{A}\beta_2^{can}$, which migrates more rapidly than A. Thus the mobility of canine hæmoglobin lies between the mobilities of $\alpha_2^{can}\beta_2^{A}$, the new slow component of the canine–A recombination, and $\alpha_2^{can}\beta_2^{C}$. According to the relative cationic mobilities of hæmoglobins A, S and C (A < S < C) the mobility of $\alpha_2^{can}\beta_2^{S}$ also lies between the mobilities of $\alpha_2^{can}\beta_2^{A}$ and $\alpha_2^{can}\beta_2^{C}$. Consequently the slow component in the recombined S–canine mixture is probably composed of two species of similar mobility, canine hæmoglobin and $\alpha_2^{can}\beta_2^{S}$. The constituent or constituents of the electrophoretic components in all recombined mixtures were determined in this manner and the results summarized in Table 1. It is seen that the observed proportions of the components are consistent with their postulated compositions and with asymmetrical recombination.

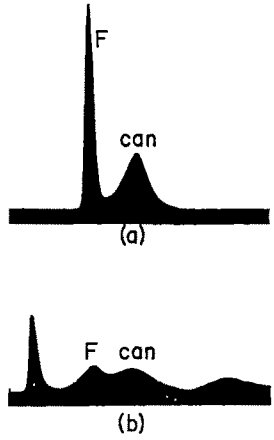

Fig. 4. Ascending limb electrophoretic patterns of 1 per cent carbonmonoxyhæmoglobin in phosphate buffer of pH 6 8, Γ/2 0 02 The direction of migration is from right to left. *a*, F, canine control, *b*, F, canine recombined

Knowledge that the new slow component of the canine–A recombination carries the β-chain of hæmoglobin A, and the new fast component the α-chain, makes possible the use of canine hæmoglobin to identify the aberrant chain of an abnormal human hæmoglobin. Its advantages for this purpose over previously characterized abnormal hæmoglobins such as S and C are that it differs from hæmoglobin A in both chains and is readily available in large quantity. If, for example, a human hæmoglobin is normal in the α-chain (α^{A}) but altered in the β-chain, recombination of this hæmoglobin with canine hæmoglobin should yield the same new fast component of the canine–A experiments ($\alpha_2^{A}\beta_2^{can}$), but the other new component should migrate in a position different from that of $\alpha_2^{can}\beta_2^{A}$. Recombination of fœtal hæmoglobin ($\alpha_2^{A}\gamma_2$)[8–10] and canine hæmoglobin yielded just such a result although the relative mobilities of hæmoglobins A and F are such that $\alpha_2^{can}\beta_2^{A}$ and $\alpha_2^{can}\gamma_2$ migrate in nearly identical positions (Fig. 4). It would be of interest to investigate such hæmoglobins as H (β_4^{A})[11] and 'Bart's' (γ_4)[12] in this manner.

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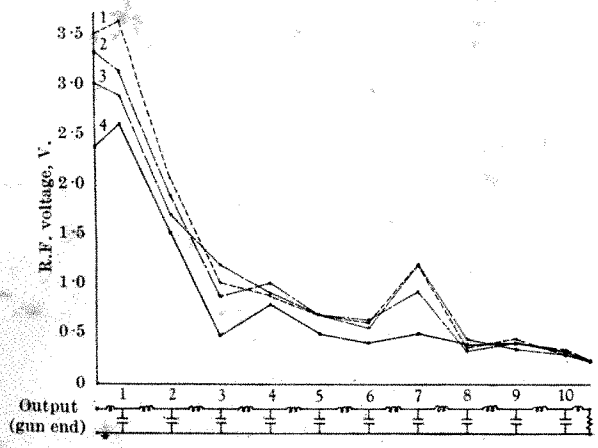

Fig. 2. R.F. voltage distribution on delay line

	D.C. beam voltage (V_0 volts)	D.C. beam current (I_0 m.mA.)
Curve 1	449	3·52
Curve 2	470	3·46
Curve 3	425	3·40
Curve 4	450	2·65

determination of the voltage distribution since the fact that the oscillator becomes stabilized at a finite amplitude at all is a consequence of the non-linearity of the system.

In order to obtain meaningful results great care has to be taken to ensure that the line is correctly matched and that the measuring probe presents an effective open-circuit to the structure. Although the latter condition was realized in these measurements some slight standing wave was present on the line. The amplitude of this was, however, small and does not affect the conclusion drawn above.

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GEOPHYSICS

Physical Parameters of the Atmospheric Escape Layer

Nicolet[1] and Urey[2] have made estimates of such physical parameters of the atmospheric escape layer as the height of this critical level, its temperature, and the corresponding scale height, by extrapolation of results of the Rocket Panel[3]. Since the data of the Rocket Panel extend to a height of only 220 km., considerable extrapolation is necessary. Recent results obtained by observation of satellite orbits extend to altitudes sufficiently high to permit direct inference of physical parameters of the atmosphere at the critical level. It is the purpose of this communication to report such results from the data of King-Hele and Walker[4]; the salient feature which emerges is a diurnal variation in the physical parameters associated with the escape layer.

From a result of Spitzer[5], the height ζ of the escape layer above the Earth's surface is fixed by the requirement that:

$$nh = (\pi \sigma^2)^{-1} \qquad (1)$$

at this level, where n is the number density of atmospheric particles, h is the scale-height, and σ is the mean collision diameter of an atmospheric particle. The analysis of King-Hele and Walker yields the scale height h directly, but not the number density n. The latter quantity is fixed in terms of the directly inferred density ρ of the atmosphere by:

$$n = (\rho/M)N \qquad (2)$$

where N is Avogadro's number and M is the mean molecular weight of the air. In default of measurements by mass spectrometer at these high altitudes, one must estimate M, which introduces a basic uncertainty into the results. In agreement with King-Hele and Walker, M will be taken as 22 at a height of 200 km., decreasing linearly with height to $M = 16$ at 500 km., and constant thereafter. Urey's choice $\sigma = 3 \cdot 15 \times 10^{-8}$ cm. will be taken for the mean collision diameter[2].

As computed on this basis, the values of nh from the data of King-Hele and Walker are shown as a function of altitude in Fig. 1. Above a height of 300 km., the data points fall on two branches, corresponding to day and night, which actually represent averages for early afternoon and past midnight, respectively. The corresponding heights ζ of the escape layer determined by equation (1) are shown in the second column of Table 1. One notes that ζ is greater for day than for night conditions. This fact is in qualitative accord with my result[6] that the height

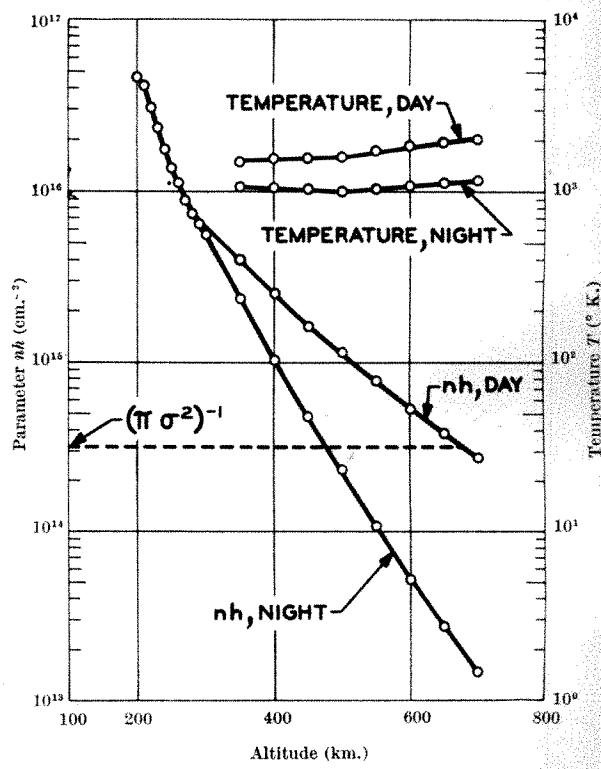

Fig. 1. The parameter nh and the absolute temperature T in the atmosphere as a function of altitude for day and night conditions, from the data of King-Hele and Walker

A Silicon γ-Ray Spectrometer

CURRENT pulses produced by the passage of an ionizing particle through a semi-insulator have been reported in the literature[1]. Since most of these materials are, as yet, not available in commercial quantities, we decided to investigate the use of high-resistivity silicon, available as 5,000 ohm cm. *p* type. We estimated that current pulses of about 10^6 ion pairs might be detectable, particularly if the specimen volume is restricted, and the working temperature is lowered to that of liquid air.

Ohmic contacts are made to the specimen by alloying into a boron-diffused surface layer with gold–gallium wire. A number of devices have been prepared most of which detect radiation. The variation of performance between detectors indicates that the processing is not yet under complete control. However, the following performances have been recorded. Gamma-rays from cobalt-60 have produced pulses up to a maximum of 2 mV., for which the signal to noise ratio is greater than 50 at liquid air temperatures, offering the possibility of high-resolution spectroscopy. Other specimens have detected 1-MeV. γ-radiation and 4-MeV. alpha-rays at room temperature, with a signal to noise ratio suitable for monitoring purposes. The current pulses have duration of a few μsec. There is a certain amount of indirect evidence that the thermal cycling programme inherent in the boron diffusion process is modifying the carrier life-time and the compensation of the material[2-4]. This possibility, together with the effect of surface states, is being investigated as essential for production of reproducible devices.

We wish to thank Mr. J. A. Raines for his advice on the diffusion techniques, and Mr. T. James for assistance in fabricating the counters. Permission to publish this communication has been granted by the Admiralty.

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ENGINEERING

Operation of the Backward-Wave Oscillator

WE have recently made some measurements of the voltage distribution along the slow-wave circuit of our 'travelling-wave-tube analogue', operated as a backward-wave oscillator, which are of interest in helping to decide between the various theoretical models which have been proposed to describe backward-wave oscillator operation.

The travelling-wave-tube analogue was described in detail in a recent paper[1], and is based on the lumped circuit travelling-wave tube first described by Matthews[2]. Briefly it consists of a series of drift tubes inside a vacuum envelope interconnected with a series of inductance coils which are outside the vacuum envelope (Fig. 1). The coil-drift tube system simulates an LC delay line the parameters of which can be adjusted to represent those of a normal, practical slow-wave structure. The advantage of the system is that the slow-wave structure properties can be varied, by changing the coils, without breaking the vacuum as would be necessary in the case of a conventional tube. The structure is matched at the opposite end from the gun by means of a high-frequency carbon resistor of appropriate value, while signal is fed on to, or coupled off from, the gun end (according to whether operation is in the forward or backward mode) via a simple T-section network.

Whether the system operates as a forward-wave amplifier, or a backward-wave amplifier or backward-wave oscillator, depends on the electron gun voltage, that is, on choosing the electron velocity so that the electron beam travels in synchronism with the appropriate harmonic. With the particular delay line used, backward-wave operation was obtained for gun voltages ranging between about 200 and 700 volts corresponding to currents of the order of a few milliamperes. No additional attenuation was added to the slow-wave structure—the intrinsic attenuation being sufficient to inhibit operation in spurious modes. The start-oscillation current was found to be about 1·7 mA. and the oscillation frequency about 300 Mc./s., while the coupling impedance of the first backward mode was about 200 ohms, corresponding to an effective *C* value (Pierce's travelling-wave tube gain parameter) of about 0·06 at start-oscillation.

The voltage along the slow-wave structure was measured by means of a coaxial diode probe mounted on a sliding carriage inside the focusing solenoid, enabling it to be connected to each section in turn. Curves of the voltage distribution obtained are shown in Fig. 2. While the mean trend of the points from collector to gun end is exponential, the falling off of voltage in the half-section at the gun end, the minimum occurring in the region of section 3 and the maximum in the neighbourhood of section 7, are all significant and accord very well with the results of the non-linear theory published by Rowe[3]. Comparison of these curves with those of Rowe show a striking similarity, allowing for the fact that our measurements could only be made at discrete points along the structure.

It is quite clear that at least a 3-mode theory is necessary to explain the operation and that a 2-mode theory of the type discussed by Gould[4], although it indicates the right value of starting current, does not predict the correct voltage distribution on the line. It is also important to consider non-linear terms in the

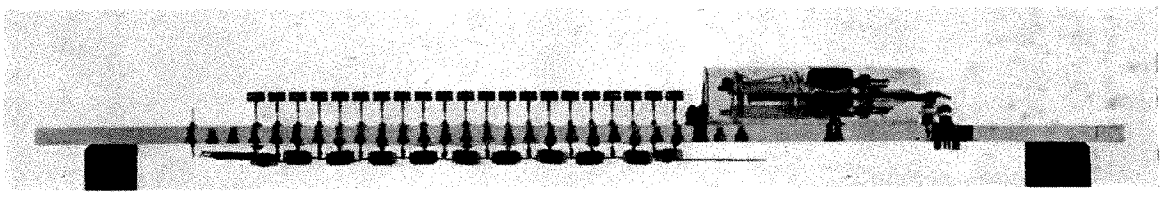

Fig. 1. The lumped circuit backward-wave oscillator analogue

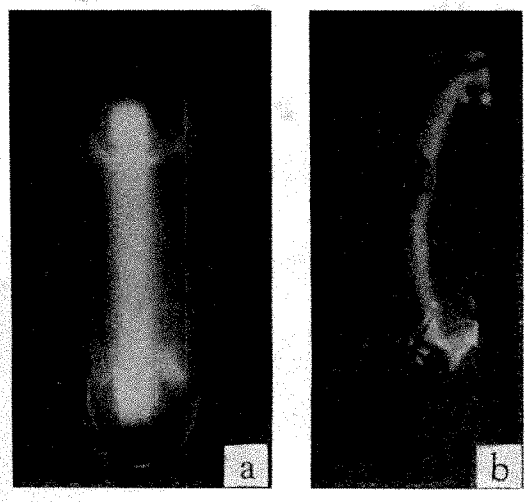

Fig. 2

typical pictures : (*a*) is taken in the symmetry plane of the torus with helium gas at 50 torr pressure when the plasma current has reached its peak value at 25 k.amp. At higher pressure it is necessary to pre-ionize the gas by running a pulsed discharge current of 100 amp. between a number of internal electrodes placed around the torus. Fig. 2*b* shows half of a circular discharge at 400 torr. The picture is taken at an angle to the symmetry plane at the peak value 17 k.amp. of the circulating current. Streak camera pictures indicate that when the gas pressure is high, the plasma looks more regular and stable than at low pressures. Further experiments are in preparation.

We thank Prof. N. Herlofson and Mr. C.-G. Fälthammar for many discussions. Mr. R. Johansson has taken part in the experiments.

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Motion of Molecules in Very Thin Films between Sliding Surfaces

C. L. GAINES[1] has recently discussed the motion which long-chain polar molecules in mono-molecular layers on solid surfaces may undergo. His work leads to considerations of lubrication phenomena which he reports in progress.

Some results which may be related to the study have occurred in sliding studies of optically flat lapped steel surfaces, where the film thickness of stearic acid was that of only several molecular layers.

Information on the structure of the film for room temperatures (well below disorientation temperature) was obtained from observations on the magnitude of the changes in the tangential force at the commencement of, and during, sliding with 'stick-slip' type action. Automatic recording[2] of thirty tangential force-time diagrams for the sliding surfaces was used as in earlier surface sliding work[3], and the results processed to obtain the frequency polygon of all changes in the tangential force, F_T. The magnitudes of the changes in F_T tended to be grouped around multiples of a definite value '*a*', as indicated in the frequency polygon of Fig. 1. This could suggest that sliding can occur at definite strata-levels, and perhaps overturning of the molecules at these levels. Changes in the shearing strength of the film are registered as changes in F_T. In some, but not all, cases, there was micro-interferometric evidence of surface damage and this could not be correlated with the force measurements. It would seem that, although the changes in the shearing strength of any cold-welded metal asperites had contributed to the change in F_T, the final frequency polygon indicates that the changes were mainly due to different shearing strengths of the film at different levels, corresponding to integral multiples of the value at '*a*'.

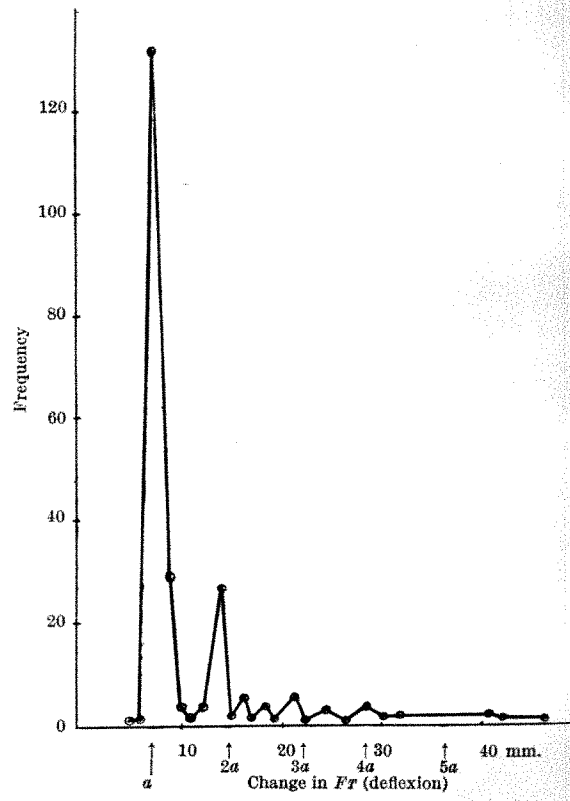

Fig. 1

It would seem that sliding had occurred at selected planes of slip (with overturning ?) which exist by virtue of the molecular surface orientation forces ; there would be a low probability of a slip occurring at a molecular plane very close to the metal surface where orientation forces are strongest, but the probability increases for molecular planes further removed from the surface.

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LETTERS TO THE EDITORS

PHYSICS

Gas-Insulation of a Hot Plasma

THE attempts to heat a plasma to thermonuclear temperatures have all started from the idea that the plasma should be separated from the walls of the vessel by magnetic fields in vacuum. The purpose of this communication is to discuss another possibility, namely, to insulate the plasma from the walls by means of a magnetized gas at high pressure. As the thermal conductivity increases with temperature, a hot gas seems to be a poor insulator; but at high temperatures, where the gas becomes ionized, the thermal conductivity can be decreased very much by a magnetic field. Its variation with the temperature is shown qualitatively in Fig. 1. The first maximum is due to the dissociation and the second to ionization, whereas the third is produced by the electron conductivity and the fourth by the ion conductivity. At high temperature the ion conductivity dominates and its asymptotic temperature variation is as $T^{-5/2}$.

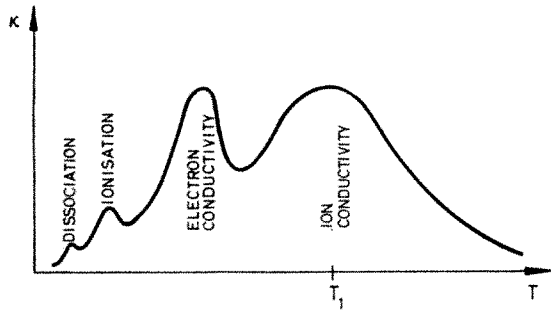

Fig. 1

If in a cylindrical vessel, $r = r_0$, filled with gas, a central region, $r = r_1 < r_0$, is heated with the power Q per unit length but the wall is kept at a low temperature, we have (neglecting radiation losses):

$$Q = -2\pi r \varkappa \frac{dT}{dr} \tag{1}$$

$$Q = \frac{2\pi}{\ln r_0/r_1} \int_0^T \varkappa \, dT \tag{2}$$

Because the integral $\int_0^\infty \varkappa \, dT$ is finite, we can expect a 'burn-out', resulting in a very high central temperature if the power exceeds a certain value Q_b. As the largest part of the integral is due to the ion-gas contribution to $\varkappa$, we can in an approximate calculation use the thermal conductivity of the ion gas only. This is according to Braginskii[1] (see also Rosenbluth[2]).

$$\varkappa = \frac{3}{4\sqrt{\pi}} \frac{k(kT)^{5/2}}{\sqrt{m_i}\, e^4 \lambda} \frac{2 \cdot 645 + 2(\omega_i \tau_i)^2}{0 \cdot 677 + 2 \cdot 70(\omega_i \tau_i)^2 + (\omega_i \tau_i)^4} \tag{3}$$

$$\text{where } \omega_i \tau_i = \frac{eH}{m_i c} \frac{3\sqrt{m_i}\,(kT)^{3/2}}{4\sqrt{\pi}\,\lambda e^4 n_i} \tag{4}$$

If the pressure $p = nkT = 2n_i kT$ (5)

is constant, (3) and (4) give for deuterium:

$$\varkappa = KT^{5/2} \frac{1 + 0 \cdot 756\,(T/T_1)^5}{1 + 3 \cdot 99\,(T/T_1)^5 + 1 \cdot 48\,(T/T_1)^{10}} \tag{6}$$

$$\text{with } K = 0 \cdot 53 \times 10^{-14} \text{ W. cm.}^{-1} \text{ deg.}^{-7/2} \tag{7}$$

$$T_1 = 4 \cdot 0 \times 10^4 \left(\frac{p}{H}\right)^{2/5} \tag{8}$$

T_1 is approximately the temperature that corresponds to maximum ion conductivity.

Introducing the expressions 6–8 into 2, we can write the critical power as:

$$Q_b = \beta K T_1^{7/2} \tag{9}$$

$$\text{where } \beta = \frac{2\pi}{\ln (r_0/r_1)} \int_0^\infty \frac{x^{5/2}\,(1 + 0 \cdot 756\, x^5)}{1 + 3 \cdot 99\, x^5 + 1 \cdot 48\, x^{10}} \, dx \tag{10}$$

is a constant of order unity. If the ratio r_0/r_1 is of the order of 10, β is approximately 3. Putting $\beta = 3$, we get:

$$Q_b = 200 \left(\frac{p}{H}\right)^{1 \cdot 4} \text{ W. cm.}^{-1} \tag{11}$$

If in a thermonuclear reactor we want $T = 2 \times 10^8$ degrees and $n = 10^{14}$ cm.$^{-3}$, the pressure should be $p = nkT \approx 3 \times 10^6$ dynes/cm.^{2}. Then we find:

$H = 10^4$ gauss	$H = 10^5$ gauss
$T_1 \approx 4 \times 10^5$ degrees	$T_1 \approx 1 \cdot 6 \times 10^5$ degrees
$Q_b \approx 600$ kW. cm.$^{-1}$	$Q_b \approx 24$ kW. cm.$^{-1}$

In a thermonuclear reactor, according to this principle the gas may be heated by a high-pressure arc. Maecker[3] reports for an arc in water vapour at atmospheric pressure that a temperature of 5×10^4 degrees is reached already with a current of 1,400 amp. The temperatures which, according to calculations, are necessary for a 'burn-out', are not very much higher.

In comparison with a vacuum-insulated plasma, the gas-insulated device may have some advantage: (1) it is not subject to the same types of instabilities—but possibly to other types; (2) it should be easy to produce a clean plasma, because the hot region is protected from wall dirt by a thick layer of gas at high pressure.

In order to study the behaviour of a high-density plasma surrounded by neutral gas, an experimental programme has been initiated. To avoid the influence of electrode surfaces an electrodeless discharge is used. In a preliminary experiment a circular discharge has been produced in helium at pressures varying from 1 up to 600 torr in a glass torus of 10 cm. diameter placed between two one-turn coils through which a condenser bank $C = 2\ \mu F.$, 30 kV. is discharged in a damped oscillation with a period of 4 μsec. Kerr cell photographs show that an electrodeless circular arc discharge takes place. The current starts in a very narrow channel, which expands as the current increases. Fig. 2 shows two

ζ of the escape layer above the level at which mixing stops is fixed by:

$$\zeta' = H \ln (\pi \sigma^2 Q + 1) \quad (3)$$

where H is the mean scale height in the region below the critical layer and down to the level at which diffusion sets in, and Q is the number of particles in a vertical column of unit cross-section between these two levels. The values of h, ρ, and n appearing in succeeding columns of Table 1 were obtained by interpolation with respect to altitude from the data of King-Hele and Walker. Apart from the effect of the assumptions on M, the standard deviation of the results is perhaps ± 20 per cent.

Table 1. PHYSICAL PARAMETERS OF THE ATMOSPHERE AT THE CRITICAL LEVEL

Time	ζ (km.)	h (km.)	ρ (gm./c.c.)	n (particle/c.c.)	T (° K.)
Day	670	130	6.6×10^{-16}	2.5×10^{7}	2,000
Night	480	61	1.4×10^{-15}	5.3×10^{7}	1,000

Since the observations of satellite orbits yield the scale height h directly, the corresponding absolute temperature T follows from:

$$T = Mgh/R \quad (4)$$

where R is the gas constant and g is the gravitational acceleration. Curves of T for day and night conditions are shown as a function of altitude in Fig. 1, as determined under the stated assumptions on M from the data of King-Hele and Walker. These authors quote values for the temperature somewhat higher than correspond to the curves of Fig. 1, since the inverse-square variation of g in equation (4) was taken into account in the present work. The last column of Table 1 shows values of the absolute temperature T at the escape-level for day and night conditions. As a check on the figures, one can note my result[6] that the pressure p at the critical level is simply the mean weight of a molecule distributed over the mean collision area, or:

$$p = (M/N)g\,(\pi \sigma^2)^{-1} \quad (5)$$

which is independent of temperature. On the other hand, p is given also by

$$p = (n/N)RT \quad (6)$$

for an ideal gas. The figures of Table 1 yield approximately the same result for p of equation (6) for the two cases of day and night conditions, and the average value $p = 7.1 \times 10^{-13}$ bar is closely that given by equation (5).

In general, the values of ζ in Table 1 exceed estimates made previously; Urey[2] assumed a range of 300–525 km. depending on the exosphere temperature, while Nicolet[1] obtained 450 km. from a model atmosphere. Both day and night values of the temperature at the critical level are considerably less than the value (of the order of 3,000° K. or higher) inferred by Nicolet[7] and Urey[2] to account for the dissipation of helium-4 from the Earth's atmosphere. Spitzer[5] gives a lower value (1,500° K.), but I have shown[6] that the difference arises from his employment of superseded data in computing the lifetime of helium-4; when his computations are corrected by use of Johnson's revision[8] of the data of the Rocket Panel, no significant difference from the results of Nicolet and Urey appears.

The quoted values of the temperature of the escape layer as inferred from the loss of helium-4 presuppose a steady rate of dissipation. The discrepancy (of some 1,000° K. or more) from the values of Table 1 may arise because the dissipation is in fact intermittent, as first suggested by Spitzer. Certainly, the general conclusions obtained from observations of satellite orbits are in harmony with this suggestion, since they imply that solar disturbances (yielding corpuscular radiation, ultra-violet rays, and soft X-rays) largely control the variations of short term in the atmospheric density at moderate heights (200–300 km.)[9–12]. By virtue of equation (3), such variations must be reflected in the height and consequently in the temperature of the escape layer. Accordingly, it is possible that transient solar disturbances of duration too short to be revealed by the satellite observations (lasting for times less than perhaps 10 satellite revolutions) may play a dominant part in the dissipation of helium-4 from the terrestrial atmosphere.

One suspects that more refined data would show a variation with time of day, season of year, and latitude in addition to the gross variation from day to night exhibited by Table 1. Thus, no one set of physical parameters of the escape layer can be universally valid.

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Stress Effects on Thermoremanent Magnetization

IT has recently been reported[1,2] that the effect of stress on a rock acquiring a thermoremanent moment is completely reversible. Experiments carried out here have shown this is not true for all rocks. Tests have been made on a number of rocks containing different minerals, and in every case a rotation of moment induced by pressure, together with a reduction of moment, has been observed.

Uniaxial stress experiments were carried out using a non-magnetic pressure vessel designed by one of us (R. N. N.). This consists of a thick-walled hollow dural cylinder with a lid of the same material. Pressure is applied by means of a cylindrical nimonic piston, which compresses a cubical rock specimen against a nimonic cylinder attached to the inside of the lid of the pressure vessel. The rock specimen is heated to its Curie point by means of an a.c. current passing through a nichrome wire element embedded in a fire cement annulus which fits closely around the specimen. The current through this heater is switched off while the specimen is cooling in a magnetizing field of 1·5 oersted supplied by a Helmholtz coil system.

The apparatus is capable of heating a specimen to 600° C. and cooling it again to room temperature in a period of about 2 hr., while a hydraulic system allows constant pressures between zero and 1,500 kgm./cm.^{2} to be obtained.

Experiments with a particular pressure and field direction were carried out on groups of four specimens. Each specimen was heated four times in all, the sequence being the first and third heatings without pressure, and the second and fourth with pressure. All measurements of inclination and intensity of moment were made using a spinning magnetometer[3] which was modified to be capable of consistently detecting angular differences of 0·3°.

A very detailed study has been carried out on material obtained from a Tertiary dolerite dyke in Skye, Scotland. Initial experiments on material from this dyke showed that the application of uniaxial pressure during the acquisition of a thermoremanent moment caused a rotation of the moment away from the stress axis, together with a reduction in the intensity of the moment. Further experiments were made on the dyke material, which, after one heating, was shown to contain a pure magnetite and an impure maghemite, and the variation of the angular rotation of moment with the following parameters was examined: (i) pressure; (ii) the angle, θ, between the magnetizing field and the pressure axis; (iii) the intensity of the magnetizing field; (iv) the grain size of the magnetic constituents of the rock (composition remaining constant).

All the experiments carried out showed clearly that the application of pressure during magnetization produced a measurable effect. It was found that the observed rotation of moment was dependent on (i), (ii) and (iv), but was apparently independent of the intensity of the magnetizing field in the range 0·5–3·0 œrsted. Figs. 1–3 show the results of these investigations.

Further positive experiments have been carried out on rocks containing pyrrhotite, an ilmenite–hæmatite solid solution and a magnetite–ilmenite solid solution. In addition, shear stress has been shown to produce a measurable rotation of moment.

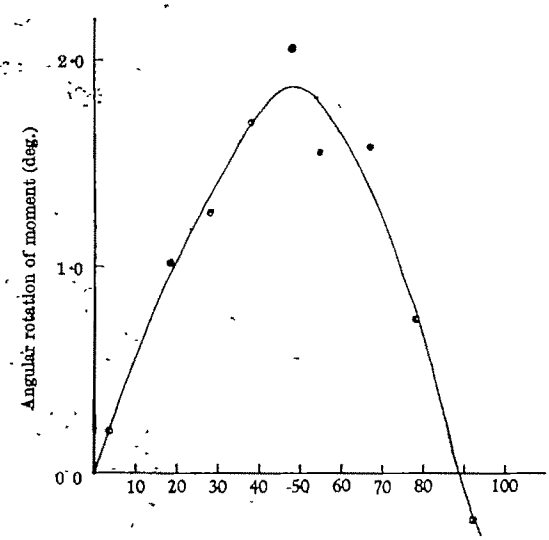

Fig. 1. Dolerite dyke centre material (100μ magnetite grain diameter). Pressure, 550 kgm./cm.^{2}, H, 1·5 œ.

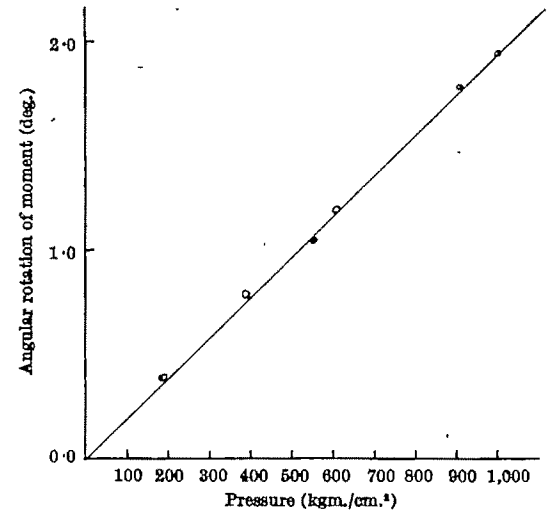

Fig. 2. Dolerite dyke centre material. θ, 45°; H, 1·5 œ.

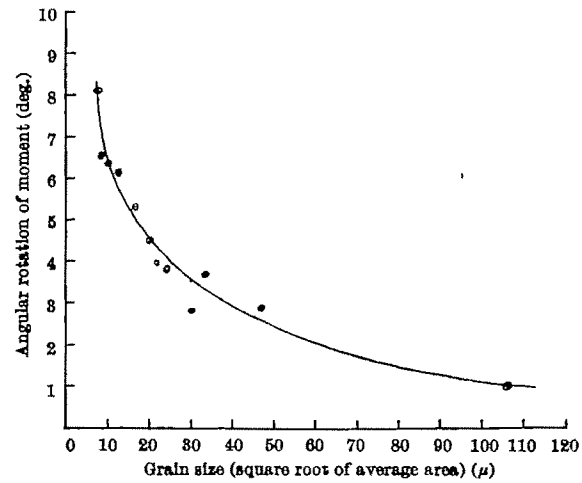

Fig. 3. Dolerite dyke centre and contact material. H, 1·5 œ.; θ, 45°; pressure, 880 kgm./cm.^{2}

In general, the mechanism of the pressure effects described appears to be complex. In the absence of measurements of various relevant parameters in the region near the Curie point where the greater part of the moment is acquired, no quantitative relationship between magnetostriction, etc., and the observed pressure effects can be seen. However, the variation of the thermoremanent moment of this dyke material with pressure is not irreconcilable with the known magnetostrictive properties of magnetite reported for room temperatures[4] if it is assumed that magnetostriction decreases regularly to a zero value at the Curie point.

There is a close similarity between the variation of rotation of moment with grain size and the reported variation of coercive force with grain size[5]. It has been suggested that the latter variation results from a change in the mechanism of magnetization, and, if this is so, it is obviously an important factor in the production of angular pressure effects.

It has been found during our experiments that each specimen has a slight intrinsic anisotropy which may cause it to acquire on successive non-pressure heatings

(*Continued on page* 843)

Supplement to NATURE

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PROSPECTS OF SCIENTIFIC AND TECHNOLOGICAL ADVANCEMENT

Science and Resources

Prospects and Implications of Technological Advance. Edited by Henry Jarrett. Pp. xiii+250. (Baltimore, Md.: The Johns Hopkins Press; London: Oxford University Press, 1959. Published for Resources for the Future, Inc.) 40*s*. net.

THIS is a most unusual kind of book even although it is a collection of essays. It is the result of a plan by Resources for the Future Incorporated. This is an organization in the United States the job of which it is as a non-profit-making organization to look to the future in the field of research and education so far as it affects the development, conservation and use of natural resources.

The book as a whole provides a look into the future in a number of directions. It originated as a series of lectures which were arranged in a rather original sort of way. First, a leading scientist was invited in his own particular field to give his ideas and views as to future developments and requirements in that field. Naturally, the extent to which the lecturer could look into the future depended very much on the subject under discussion. Secondly, two non-scientific commentators were then invited to discuss and examine the first lecture and to put their points of view forward almost as an informed lay person would do. This gives unusual character to the book and makes it especially profitable in that it can be read by scientists and non-scientists alike. Those familiar with the fields under discussion may no doubt disagree with some of the predictions, for that is inevitable; but the purpose of the book is undoubtedly to stimulate thoughts on problems which affect almost every country. Even although speculation is difficult, there is every reason to engage in it so that even in the immediate future misuse and waste of natural resources may be avoided and that those that are known to exist are utilized to the best possible advantage.

The list of authors of the introductory lectures demonstrates at once that the book is absolutely authoritative: "Genetics", by J. W. Beadle; "Weather Modification", by H. R. Byres; "Exploring for Minerals", by J. A. S. Adams; "Chemical Technology", by E. P. Stevenson; "Nuclear Energy", by W. F. Libby; "New Knowledge from Outer Space", by L. A. DuBridge.

The commentators of these essays come from a wide range of professional disciplines and even from politics. This gives a very stimulating series of additional articles often with a very clearly defined personal point of view but none the less interesting in spite of that. It is clear that the editor has not wielded his pen too strongly and has allowed the authors to give free rein to their thoughts and opinions. This may make the treatment of the topics in the book somewhat uneven; but this is not a text-book or a monograph but eighteen essays devoted to the problems of the future in the fields covered.

H. W. MELVILLE

MAN AND HIS ANCESTORS

Mankind in the Making

The Story of Human Evolution. By Dr. William Howells. Pp. 382+8 plates. (Garden City, New York: Doubleday and Company, Inc., 1959.) 4.95 dollars.

An Introduction to Physical Anthropology

By Prof. M. F. Ashley Montagu. Third edition. Pp. xvi+771. (Springfield, Ill.: Charles C. Thomas; Oxford: Blackwell Scientific Publications 1960.) 116*s*.

DR. HOWELLS has set himself the task of giving a full and detailed account of our knowledge of human evolution, and of telling the story in an informal and light-hearted style. The result is something of a clash between instruction and entertainment. The theme is interlarded with whimsicalities and with technicalities smoothed over by a jocular familiarity ("Man, the hero of the tale" . . . "Proconsul . . . bless his heart!" "Miss Middle Pleistocene" and "Fräulein Steinheim") all done with the best pedagogic intentions. That this exercise in popular writing may not be to everyone's taste should not be allowed to detract from the soundness and competence of Howells's interpretation. The evidence is well marshalled, controversies of the past and present are fairly presented and his judgments appear consistently reasonable. This is particularly evident in his treatment of the rather complex problem of the specific and subspecific relations within the genus *Homo*, involving the allocation of fossil specimens of a diversity ranging from the late but 'fully' Neanderthaloid to the early but more *sapiens*-like varieties, notably Swanscombe man. His handling of the still-vexed problem of *Oreopithecus* (which he regards as a primitive hominoid possibly near the hominid stem) is judicious. So also is his analysis of the status of *Australopithecus* and of *Atlanthropus*. The latter he sees as related to Pekin and Java man, but unworthy of a generic status. The evolutionary chapters are preceded by informative sketches of the living primates and of their vertebrate and mammalian background. Dr. Howells concludes with a description of present-day races which is rather disappointing. There is no serious attempt to utilize the great body of available genetic data in an analysis of the dynamics of human

polytypy as evidenced in the operation of, for example, isolation, mixing and selection as factors responsible for the observed distribution of anthropological characters.

Prof. Ashley Montagu's text-book, in its enlarged and revised third edition, represents a serious endeavour to put the student in touch with many of those issues which Dr. Howells allows to slip by.

Thus after the first chapters (in which a sufficient abundance of the taxonomic and morphological facts of primatology and palæoanthropology are provided) there is an interesting dissertation on the possible evolutionary processes underlying the genesis of the Hominidae and modern man, and particularly on 'neoteny' as a major factor. There follows a chapter of conventional classification and categorization of human racial stocks—an exercise which Montagu, justifiably, finds too limited and arbitrary. He places much more emphasis on the evidence of blood groups and other genetically understood characters as indicators of group affinities.

This section is well documented (though many of the text figure references are not to be found in the bibliography). Population (or as he prefers 'ethnic') differentiation is next considered in relation to mutation, isolation and selective agencies of various kinds —climatic, social, sexual and disease. The interaction of heredity and environment, the usefulness and limitation of the twin method, the determinants of 'constitutional' variation, and a chapter on body composition (by Prof. Brožek) all make up useful sections. An appendix contains an over-compressed guide to techniques of use in physical anthropology.

The book has its merits, but the material is presented in a disconcertingly uneven fashion. In some sections very detailed tables are given with only the slightest relevance to the text, yet the long arguments on 'race' and 'ethnic' differentiation consist in large part of generalities scarcely reinforced by specific evidence. The student could be better served by detailed and quantitative illustration and analysis of, for example, balanced polymorphism, gene-flow between hybridizing populations, mutation-rates or genetic drift. Even the calculation of gene frequencies is dealt with in a somewhat perfunctory way.

There are a number of obvious lapses which careful revision of the manuscript should have put right. For example, in Fig. 44, *Australopithecus* is shown as the crown of the Pongid family whereas in the text (for example, p. 288) its hominid status and particularly that of *Zinjanthropus* is repeatedly conceded. In the same figure the semi-mythical *Africanthropus* is included while Rhodesian man is omitted. There is confusion between orthogenetic and ortholinear evolution (p. 157). The 'early' Kafuan stone industry has for some time been regarded as inadmissible. In matters of dating, the Pleistocene stages are not clearly defined and the Villafranchian, so important for the beginnings of the hominids, is left unexplained. The measurement of human skin colour by reflectance spectrophotometry, the only objective and reliable method, receives no mention in the section on methods.

Despite its blemishes and unevenness, Montagu's is a serviceable text-book; it has the paramount virtue of displaying clearly the full scope of physical anthropology and of conveying in a stimulating way the live issues of the subject.

J. S. WEINER

THE CENTRAL NERVOUS SYSTEM

Evolution of Nervous Control from Primitive Organisms to Man

A Symposium organized by the Section on Medical Sciences of the American Association for the Advancement of Science, and presented at the New York Meeting on December 29–30, 1956. Edited by Allan D. Bass. Pp. vii+231. (Washington, D.C.: American Association for the Advancement of Science; London: Bailey Bros. and Swinfen, Ltd, 1959.) 52*s*.

THE title of this symposium is somewhat misleading though this need in no way detract from the value of an excellent collection of monographs contained in the book. The papers here presented do indeed represent, as Mr. Brodie claims, a variety of points of view, written as they are by a botanist, an embryologist, a neurologist, a physiologist, a psychologist and a psychiatrist; but, with the exception of a sketchy contribution by E. W. Sinott on "A Common Basis for Development and Behaviour in Organisms", they contain practically nothing that deals specifically with any theory of evolutionary development of nervous control. They provide, on the other hand, in the main an excellent phenomenological study of the physiological activity of the central nervous system, and there is no evidence that the various contributors envisaged any other purpose.

A highly suggestive note is struck by M. C. Niu in his chapter on chemical inducers. It must be regretfully noted, however, that so far as the nervous system is concerned there is as yet not a single observation that can be said to point to the occurrence of any such inductive process, whether attributable to ribonucleic acid or other body in either the production of mutations or the control of normal development.

The essay by Niu has undoubtedly enhanced the value of the book by reminding neurophysiologists of the important part that may possibly be played by chemical induction, but as yet it remains a possibility only. It is a possibility that can only be fruitful if specificity of inductor elements somewhat in the form of Iscovesco's specific organ inductors should, after all, prove to be a reality. C. I. Prosser suggests that the primitive electrical response of excitable tissue may be of the local graded sort rather than all or none propagated impulses. Together with some analogous speculations contained in the same essay it must very reluctantly be admitted that methods and apparatus for their verification are not yet in sight. H. Grundfest in his contribution entitled "The Evolution of Conduction" gives an excellent critical review of our knowledge of bioelectrogenesis in the nervous system. Defining an excitable cell as one capable of responding to a stimulus by electrogenesis, he distinguishes as distinct functions: the grading in proportion to the strength of the stimulus, and maintained so long as the stimulus lasts, which can be of two types, depolarizing and hyperpolarizing, each of which is produced by a specific transducer action of the electrogenic membrane; and a second generalized function due to the electrically excitable spike generating cell mechanism which can be activated by depolarizing electrical activity of the input and is adapted to conducting a coded message. Grundfest acknowledges that we have as yet no knowledge as to the means by which conducted messages are capable of

releasing specific excitants for the input of the next postjunction cell.

The essay by G. S. Koelle on neurohumeral agents, while giving an excellent account of the present state of our knowledge of the part played by such agents on synaptic transmission, would be enhanced by fuller reference to such facts as are known with reference to the all-important subject of the specific action of local hormones on the central nervous system. J. V. Brady, on the effect of drugs on animal behaviour, has made a gallant attempt to develop an animal laboratory approach to behaviour problems in neuropsychiatry. The urgent need for appreciation of the basic situation of the organism, both as regards the internal and external environment during and preceding any pharmacological experiment, here receives attention which is only too often absent in the evaluation of the neuropharmacological activity of various substances.

The review of brain chemistry by Irvine H. Page is somewhat too ambitious for the twenty pages allotted to it. H. J. Teuber gives his views on alterations of behaviour after brain injury. One could wish that he showed some greater appreciation of the existence of two major difficulties that tend to vitiate the conclusions that psychologists are prone to arrive at in their evaluation of behaviour changes after trauma. First, that anatomical and functional disturbance in the vicinity of the lesion is apt to be of far greater extent that its localization might suggest, and secondly, that the cerebral system is capable of very great lability in its power of compensating lost functions. Further, that without a preliminary knowledge of the pretraumatic mode of function in any given case, such as the habitual type of imagery, assessment of behaviour becomes a matter of utmost difficulty. The essay of I. A. Mirsky on psychoanalysis and human behaviour is obviously out of place in a book of this nature which is not addressed to the clinical psychiatrist.

The volume may be recommended as containing a number of interesting papers, but would certainly benefit greatly if the various contributors had been afforded more space and worked to a more definite scheme of co-operation. F. GOLLA

ANTIBIOTICS REVIEWED

Antibiotics Annual, 1958–1959

Pp. vii + 1107. (New York: Medical Encyclopedia, Inc.: London: Interscience Publishers, Ltd., 1959.) 90*s*.

Antibiotics Annual, 1959–1960

Pp. xvii + 1034. (New York: Antibiotica, Inc.; London: Interscience Publishers, Ltd., 1960.) 15 dollars. Both volumes edited by Dr. Henry Welch and Dr. Felix Marti-Ibañez.

THE 1958–1959 and 1959–1960 volumes of "Antibiotics Annual" are really an account of the proceedings of the sixth and seventh annual symposia on "Antibiotics", and follow on the whole the pattern established by their predecessors. Both are enormous volumes of more than a thousand pages; both cover almost every conceivable aspect of the antibiotics, and there is a wide variation in standard and in the style of the papers presented.

In the first volume, after opening remarks by Dr. H. Welch and Dr. F. Marti-Ibañez, Sir Howard Florey deals with penicillin in perspective, a paper all the more interesting in view of recent work on synthetic penicillins, some aspects of which are dealt with in the second volume. This article is followed by Dr. S. A. Waksman on the antibiotics of actinomycetes, by Dr. C. S. Keefer on the impact of antibiotics on medicine in the United States, and by Dr. H. F. Dowling on the history of the broad-spectrum antibiotics. The more-detailed papers which follow deal with some long-acting sulphonamides, nitrofurans, phenoxymethyl penicillin (penicillin V), spiramycin, new uses and forms of administration of tetracyclines, oleandomycin and triacetyloleandomycin, tetracycline and oleandomycin combinations, erythromycin propionate, novobiocin, ristocetin (spontin), actinobolin (a new broad-spectrum antibiotic showing some effect against experimental tumours and mouse leukæmias), streptovitacin (another 'anti-tumour' antibiotic), vancomycin, kanamycin and others (this list does not include a number of single articles dealing with isolated topics). The later part of the volume deals mainly with technical methods, such as standardization of antibiotic sensitivity disks and other methods of determining antibiotic sensitivities, epidemiological investigations of the frequency of staphylococci of various types in various communities, and finally some experimental work on the growth-promoting effects of antibiotics in animals.

The volume closes with two panel discussions, first on the current status of erythromycin and kanamycin, novobiocin, oleandomycin, ristocetin and vancomycin, with particular reference to their use in staphylococcal disease, and secondly the causation, prevention and control of staphylococcal disease in hospitals.

In the second volume, again following introductory remarks by Dr. Welch and Dr. Ibañez, there are general articles on the challenge of new drugs to the pharmaceutical industry, to the clinical investigator, to the food and drug administration and to the practising physician. Some of the subjects covered in the special articles are phenoxyethyl penicillin (known as 'Broxil' in the United Kingdom and as 'Syncillin' in the United States), some papers on the effect of various substances on the inhibition of penicillinase in staphylococci, then a series of papers on some new antibiotics with increasingly outlandish names—aspartocin, fervenulin, streptozotocin, rifomycin, paromomycin, and so on. A good many papers are devoted to tetracycline analogues, including the new demethylchlortetracycline. The relative merits of the four tetracyclines are dealt with in one of the few papers from Britain by Prof. L. P. Garrod and Dr. Pamela M. Waterworth, as is the use of injectable tetracycline preparations and the treatment of gonococcal infections by Dr. R. R. Willcox. There are several articles on the incidence of reactions to penicillin and a series of papers on laboratory techniques and methods of testing antibiotic sensitivities. Several papers deal with the anti-fungal antibiotic, griseofulvin, and there is a collection of papers giving clinical and epidemiological investigation of the effects of different antibiotics and antibiotic combinations in a variety of infections.

The second volume ends with two panel discussions, one on the present status and problems involved in human sensitization to antibiotics, and one on the chemotherapy of acute and chronic pædiatric and geriatric infections.

The contents of both volumes are arranged in a rather haphazard way, and it is not always possible

to discern any logical sequence of papers except where a group of papers deals with one antibiotic.

Undoubtedly the most interesting papers in either of these two volumes are those dealing with the new synthetic penicillins. Hints are given of new penicillins to come and it is to be hoped that the next volume will give some interesting information about further developments in this field. R. KNOX

BIOCHEMICAL RESPONSE TO INJURY

The Biochemical Response to Injury

Edited by H. B. Stoner, with the assistance of C. J. Threlfall. (A Symposium organized by the Council for International Organizations of Medical Sciences, established under the joint auspices of Unesco and WHO.) Pp. xi+467. (Oxford: Blackwell Scientific Publications; Springfield, Ill.: Charles C. Thomas, 1960.) 57*s*. 6*d*.

THE proceedings of this symposium will be of interest to others besides those concerned practically with the effects of injury and the indefinable syndrome of shock. The book contains seventeen papers which between them consider the effects, measured in a variety of ways, of almost all forms of trauma except irradiation. Each paper gives a comprehensive account of the research of the particular author and of related work by others, so that, with a bibliography of a thousand references with titles and an adequate index, the book is most informative on the tenor and outcome of work over the past decade. Its value is enhanced by a well-edited report of the discussions including a thoughtful account of the strategy, tactics and integration of future work which may be particularly recommended to those who contemplate such work.

Though primarily there may be a specific biochemical lesion, and consequently many inter-related changes at a biochemical level, the response of the animal to injury is a complicated physiological affair in which the nature and extent of biochemical effects is dependent on the constitution of the animal. It is therefore extremely difficult to gauge the significance of any particular biochemical change, and the participants in the symposium were agreed that few general conclusions can yet be drawn. The effect of injury on the vascular system is the core of the problem, but though from time to time a particular substance affecting capillary permeability has been incriminated, it is clear that no single mediator can sustain the role of prime villain in the development of shock. Moreover, the divergence of response to similar injuries in different species complicates the assessment of the general validity of conclusions drawn from certain animal experiments, for example, the importance of the absorption of bacterial endotoxins from the gut in hæmorrhagic shock.

The human response to injury, however, seems to be dominated by an effect on renal function which is rarely apparent in experimental animals, and many of the chapters are of particular interest and importance to clinicians. These include accounts of the disturbance in protein metabolism (Cuthbertson), in water retention and electrolyte loss (Wynn) and in the pituitary–adrenocortical system (Pekkarinen) after surgical trauma or physical injury, the clinical trial of saline therapy (Rosenthal), rouleaux formation (Fåhraeus), and the effect of limb ischæmia on adrenal secretion and body temperature (Stonor and Threlfall).

Other chapters in which the lesions in structure or function produced by specific substances are explored, offer a stimulating challenge to the experimental pathologist, the cytologist and the biochemist; they include the effects of histamine and other endogenous substances (Miles and Wilhelm) and of bacterial toxins (Smith) on vascular permeability, and the early effects of toxic chemicals on mitochondrial structure and function (Fonnesu). The interpretation of these phenomena is still too often handicapped by our ignorance of the physico-chemical nature and interplay of the cell structures involved in the injury, and it is to be hoped that the problems poised in this book will promote further attack in this fundamental field. M. G. MACFARLANE

PHYSIOLOGICAL CARCINOLOGY

The Physiology of Crustacea

Edited by Talbot H. Waterman. Vol. 1: Metabolism and Growth. Pp. xvii+670. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1960.) 22 dollars.

THIS is the first of two volumes which are intended to give a general survey of our present knowledge of the physiology of Crustacea. There are seventeen chapters, the first of which is an introduction to crustacean biology. This chapter seems to have suffered from over-compression, and contains some curious suggestions regarding the evolutionary relationships of the various crustacean sub-groups. For example, it is suggested that the Ostracoda and Conchostraca have a common origin, without giving any reasons. This is a difficult suggestion for anyone familiar with the two groups to accept, or to understand why it should be made. To offer it, unsupported, to the physiologist looking for an introductory account of the probable evolutionary relationships of crustaceans can only be misleading.

The remaining sixteen chapters deal with a variety of topics, ranging from respiration, circulation and heart function to autotomy and regeneration. These chapters are all written by separate authors, and the book reflects the advantages and disadvantages of such a system. The great advantage is that one gets a variety of outlooks, and each chapter is written by an expert who has contributed original work to the particular field. Most of the chapters not only present useful summaries, but also make suggestions as to where there is need for further work, and where new advances might be expected to be made. The main disadvantage lies in the lack of the rounded overall view that one gets from a single author; but the time has passed when one person could be expected to be equally well informed on the variety of topics covered in this book.

The problems of nomenclature and synonymy have been dealt with very sensibly by providing a systematic index which includes synonyms. This allows the consistent use of one name throughout the text while retaining the possibility of referring back to original accounts which used an older name. As a further aid, particularly to the more advanced worker, each chapter is followed by about a hundred (some by more than two hundred) references, so that apart from

providing a great deal of information this book also provides a detailed guide to the original literature.

Anyone interested in the Crustacea as experimental animals will find this book indispensable, and there is much in it that the ecologist too can benefit from reading.

J. GREEN

DIDACTIC PLANT PHYSIOLOGY

Pflanzenphysiologie

Von Prof. Henrik Lundegårdh. Pp. xv+717. (Jena: Gustav Fischer Verlag, 1960.) 48.70 D.M.

NOBODY having the least acquaintance with Prof. Lundegårdh, either personally or through his published work alone, will expect any book written by him to be tamely conventional. It is perhaps proper therefore to make it clear at the start that, although highly individual, this still sets out to be a general text-book and succeeds. Moreover it attempts, what is admittedly one of the most desirable and yet most difficult achievements in didactic plant physiology, its comprehensive treatment from a single pen. It is characteristic of the author that no concessions whatever have been made to the difficulties he has challenged either by limiting their scope or by shirking them as they arise. On the contrary, the book's limits have been set even wider than might be considered essential; there is, for example, a much fuller treatment of the straight anatomy of the higher plants than is generally considered needful in the context. Less surprisingly, though equally important, the roots of metabolic physiology in chemistry and enzymology receive fully adequate treatment; and the frontiers of physiology with genetics are not forgotten, nor those ecological connexions through which Prof. Lundegårdh himself made his first approaches to physiology.

His unfolding of the subject follows natural lines, proceeding from the organization of the cell and the general properties of protoplasm, through metabolism, nutrition and water balance, to growth and plant movement.

Prof. Lundegårdh has himself made important contributions in many of these fields during the course of his long and distinguished career as a research botanist, and the fact is not hidden from the reader. His adventurous mind has led plant physiologists along more than one exciting trail during the past generation, and this book is sure to make a striking impact on the minds of those students into whose hands it comes. They must surely be stimulated, if they have it in them, to creative thought on their own account. When Prof. Lundegårdh states a case you are left in no doubt about the nature of the problem or his own personal solution of it. You may be stimulated to more or less violent disagreement; but, even if you are of one mind with the author, you are very likely to feel that the matter has been illuminated for you from a new angle. It is probably not possible to write an account of the present state of plant physiology which would satisfy all, or even most, specialists and, if it were, the result would inevitably be much duller than the book Prof. Lundegårdh has written. It appeared first in 1950 in the Swedish language and the version now published in German has been considerably enlarged and partially rewritten. It would be pleasant if it were possible to think that in the next few years an English edition would also be appearing so that it might exercise its influence on the undergraduates of our own botany departments.

W. O. JAMES

BACTERIOLOGY OF THE MOUTH

The Microbial Flora of the Mouth

By Dr. K. A. Bisset and Dr. G. H. G. Davis. Pp. 100+8 plates. (London: Heywood and Co., Ltd., 1960.) 22*s*. 6*d*. net.

THE normal oral cavity supports a very large and varied population of bacteria, fungi and protozoa. These organisms appear shortly after birth, being derived in the first instance from the maternal genital tract and later from the air, clothes, feeding utensils and other environmental objects, and persons, that come into contact with the infant. This microbial flora remains throughout life, undergoing changes that are probably mainly quantitative in the presence of oral infection. Apart from lesions due to specific micro-organisms, such as syphilis or tuberculosis, most infective conditions of the mouth, including the commonest of all, dental caries, are due to, or associated with, the organisms that are normally present. For this and other reasons the role in pathogenesis of the oral flora is not easy to clarify, and much more work on this aspect of oral disease requires to be done. A first essential, of course, is an accurate knowledge of the characteristics of the normal flora and a more or less agreed taxonomy and classification. It is indeed remarkable that such has not yet been achieved, for even the earliest bacteriologists had directed their attention to the organisms of the mouth. No doubt the fact that oral infections are rarely life-destroying has accounted for the lack of sustained interest in this field.

This short book is a very welcome contribution to the study of oral bacterial disease, for it is a succinct account of the oral flora from a systematic point of view, and it gives valuable practical advice. Though it is offered by the authors to dental, medical and bacteriological students as well as to their teachers and to research workers, it is unlikely that it will prove of great interest to undergraduates. Teachers and investigators, however, will find it of considerable value, perhaps not least for the practical information given in the appendixes that follow most of the chapters. There, detailed information on the composition and use of media and on various procedures for isolation is given, with appropriate references to the literature. Information of this sort is not readily available in collected form elsewhere.

R. B. LUCAS

MICROBIAL GENETICS

Microbial Genetics

Tenth Symposium of the Society for General Microbiology held at the Royal Institution, London, April 1960. Edited by W. Hayes and R. C. Clowes. Pp. x+300. (London: Cambridge University Press, 1960. Published for the Society for General Microbiology.) 42*s*. net.

THIS is the first time that a symposium of the Society for General Microbiology has taken the genetics of micro-organisms as its theme. This cautious treading is easy to understand. Microbial

genetics, at present the most rapidly advancing frontier in microbiology, and already crowned by Nobel prizes, practically did not exist before 1940. In twenty years it has leaped by a series of major steps: the techniques for the isolation and use of nutritional mutants in 1940; the identification of deoxyribonucleic acid as the substance responsible for transformation in *Pneumococcus* in 1944; gene recombination in bacteria and in bacterial viruses in 1946; bacteriophage-mediated transduction in 1952; 'parasexuality' in fungi in 1953; unidirectional and partial transfer of genetic material in bacteria in 1953, and many others later.

All these advances have made it clear that micro-organisms present such a variety of processes of genetic recombination that higher organisms seem dull in comparison.

While making possible this spectacular progress in the knowledge of micro-organisms themselves, microbial genetics has opened, and contributed decisively to, the general field of molecular genetics, that is, the description of the processes of heredity and variation at the molecular level. This was the consequence of two main reasons: the enormously increased resolving power of genetic analysis when in one experiment millions, rather than hundreds, of individuals can be handled, and the ease with which chemical techniques can be used with micro-organisms.

This volume, for which the Society and the editors, Drs. Hayes and Clowes, should be congratulated, is the collection of thirteen papers and an introduction presented at the symposium. The standard is very high almost throughout and most of the papers are also presented in an intelligible form. The contributors include some of the best people in the various sections of the subject. It is a volume that no microbiologist can ignore and that all geneticists—especially those without direct acquaintance with microbial genetics—will profit by reading.

[G. PONTECORVO

THE FATHER OF MICROSCOPY

Measuring the Invisible World

The Life and Works of Antoni van Leeuwenhoek, F.R.S. By Dr. A. Schierbeek. With a biographical chapter by Dr. Maria Rooseboom. (The Life of Science Library, Vol. 37.) Pp. 223 (28 plates). (London and New York: Abelard-Schuman, Ltd., 1959.) 25*s*. net.

ANTONY VAN LEEUWENHOEK is the most astonishing figure in the history of biology. Unaided, he discovered bacteria, described spermatozoa, and observed a nucleus in a blood-corpuscle. Not for more than 150 years was progress in microscopy resumed at the resolution which Leeuwenhoek could command with his home-made lenses. His discoveries extended over fifty years and were described in a series of some 165 letters to the Royal Society. The last, in 1723, was dictated from his death-bed.

Yet our knowledge of this amazing man has remained strangely incomplete until the present time. Some thirty years ago, a committee of Dutch scientists began the task of assembling a series of volumes in which each of Leeuwenhoek's letters is followed by dern description of the objects concerned. Since 1942, Dr. A. Schierbeek has been editor-in-chief of this undertaking. In 1950, he published in Dutch a two-volume work on Leeuwenhoek, to which he has now added the present book in the English language. It opens with a valuable biographical chapter by Dr. Maria Rooseboom, who tells us much about the social history of the Netherlands in Leeuwenhoek's day. She makes the point that Leeuwenhoek was first introduced to the Royal Society of London at a time when the two countries were at war.

We are here given a view of the father of microscopy in the round. It would be hard to over-estimate the importance of the service to science which these authors have rendered. Here is a book which all biologists must read, and which every student of the history of the sciences will need to study. One of the most interesting topics which are discussed is Leeuwenhoek's relations with the Royal Society. Though he never met them, these men were his colleagues. Their confirmation in 1677, after repeated trials, of the presence of animalcules in 'pepper water' is a vivid chapter in the history of science. Only fourteen years later, however, Robert Hooke lamented that Leeuwenhoek already stood alone in the use of the microscope. Yet for a further thirty years the Society continued to receive the letters from Delft.

Dr. Schierbeek's book is accompanied by a number of plates reproduced mainly from the original publications of Leeuwenhoek. I would suggest that in further editions the references should be given to the year and page in the *Philosophical Transactions*.

ARTHUR HUGHES

APPLIED MICROBIOLOGY

Advances in Applied Microbiology

Vol. 2. Edited by Wayne W. Umbreit. Pp. xii + 384. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1960.) 12 dollars.

ON the whole, the second volume in this series fulfils the promise of the first. The book contains eight fairly comprehensive reviews and eight short articles that were presented during a symposium on "Engineering Advances in Fermentation Practice" before the Division of Agricultural and Food Chemistry at the American Chemical Society meetings in September 1959. Five of the reviews are concerned with the use of micro-organisms in fermentation processes: recent work on the oxidative fermentation of industrial wastes, with particular reference to the disposal of dairy waste, is discussed in a posthumous article by N. Porges; G. J. Haas points out the importance of microbial control during brewing, and details the methods used during the brewing of lager beer; R. J. Allgeier and F. M. Hildebrandt describe the development of the use of deep-fermentation equipment for the manufacture of vinegar; T. H. Soudt contributes an account of the transformations of steroids that can be accomplished with micro-organisms—such interconversions are important adjuncts to chemical synthesis; and W. J. Oswald and C. G. Golueke give an interesting, though at present somewhat hypothetical, discussion of the possibility of biologically transforming solar energy into electrical power. Two reviews deal with the collection and counting of micro-organisms: H. W. Batchelor considers the techniques available for

collecting and measuring particulate matter suspended in air, and R. Ehrlich discusses the properties and applications of membrane filters. In the remaining article, F. Kavanagh contributes a thoughtful essay on the theory, practice and pitfalls of microbiological assays.

As in the first volume, the wide variety of topics covered illustrates the broad scope of the applications of microbiology, but it is perhaps unfortunate that much of the international flavour so desirable in publications of this type has been lost. All the authors are drawn from laboratories in the United States, and several of the chapters, although giving full credit to work done outside the United States, are frankly concerned primarily with American practice in the field discussed.

J. W. G. PORTER

OYSTERS: THEIR BIOLOGY AND GASTRONOMY

The Glorious Oyster

Edited by Hector Bolitho. Pp. 174+17 plates. (London: Sidgwick and Jackson, Ltd., 1960.) 25*s*. net.

Oysters

By Prof. C. M. Yonge. (New Naturalist Special Volume.) Pp. xiv+209+17 plates. (London: William Collins, Sons and Co., Ltd., 1960.) 21*s*. net.

THESE two books provide an interesting contrast. Hector Bolitho is frankly concerned with the pleasures of oyster eating and is supported by W. A. Bentley, in whose restaurant he has no doubt extended his practical experience. Maurice Burton contributes chapters on reproduction and growth, enemies, anatomy and physiology and culture. C. M. Yonge, however, sets out to provide an up-to-date, fully illustrated, scientific account of the structure, biology and cultivation of the European oyster, but includes also references to similar work on other species from the United States, Japan and Australia.

"The Glorious Oyster" first appeared in 1929 but became out of print. This revised and extended edition is well presented and is illustrated by photographs of still-life paintings from collections in Europe and the United States. Some of these, as, for example, that by Jan Steen, which also appears as a frontispiece in Prof. Yonge's book, are well known, but others, such as those by Braque and Manet from private collections, are unfamiliar but very appropriate.

In the section on the history of the oyster, Hector Bolitho has clearly drawn his information mainly from Philpots's monumental work of 1890, and this is acknowledged. The description of oyster dredging at Whitstable, taken from "All the Year Round", of November 26, 1859, is worth every inch of the space it occupies; it will be recognized as authentic by anyone who has worked in the creeks and estuaries of the east coast of Britain. There is an interesting anthology containing not only Sam Weller's "two very remarkable facts" concerning the oyster, but much less-familiar material from Pepys, John Evelyn, Robert Boyle and others.

Maurice Burton's scientific contributions fit easily into the scheme of the book, dwelling rather more on the curious and bizarre features of the oyster's biology than is permissible in a scientific monograph. It is a pity that he repeats the clearly disproved suggestion that the dumping of trinitrotoluene and other explosives was responsible for the catastrophic losses among oysters in Britain in 1920.

Of Prof. Yonge's book it is only necessary to say that, while it upholds the high technical standard of the New Naturalist Special Volumes, it is more readable and of wider interest than some of the earlier books in this series. Clearly his main difficulty has been to compress adequate references to all the major studies on oysters into a monograph of 200 pages. It may be suggested that the description of the extremely scientific oyster culture of Holland should not have been limited to less than a page, but the extraordinary system used in the Norwegian polls has also (necessarily) to be described in a couple of paragraphs. However, all the important references are here for anyone with a desire for further knowledge. The author begins: "This is a small book on a very big subject", and, towards the end, he writes of the consciousness of lack of knowledge about commercially valuable oysters even though they have been more closely studied than any other marine animals. He may rest assured that his latest contribution will help us considerably to appreciate where effort should be applied.

H. A. COLE

LIVESTOCK IN AFRICA

The Indigenous Livestock of Eastern and Southern Africa

By I. L. Mason and J. P. Maule. (Technical Communication No. 14 of the Commonwealth Bureau of Animal Breeding and Genetics, Edinburgh.) Pp. xv+151+179 plates. (Farnham Royal, Bucks: Commonwealth Agricultural Bureaux, 1960.) 45*s*.

AS might be expected, the indigenous livestock of Africa, with few exceptions, have not been improved, even for work purposes, to the extent of those in Asia where ancient civilizations existed. As Norman Wright points out in his foreword, it will probably be easier to increase the production of native breeds adapted to their particular environmental conditions than to import improved breeds unsuited to the local hazards of environment and disease. However, perhaps one might add, except where by suitable crossing and selection the production of the one is combined with the adaptability of the other as in the case of Bonsmara cattle and Dorper sheep.

The book attempts to classify the different types of livestock by various morphological characters—cattle by the position and size of the hump and horns: sheep by their tails, thin, fat or fat rumped; and goats by the length of their ears. Where available, facts are given concerning their size, weight and milk production together with a large number of excellent photographs; references to original descriptions are quoted. For most types estimated numbers and their distribution in different countries are given, but one misses, except in a few cases, an account of the ecological conditions of temperature, altitude, rainfall and type of vegetation with which each type is associated. Nomenclature forms a problem throughout and in the absence of well-recognized

names the authors have adopted the tribal name. With camels, for example, the different tribes often use them for different purposes—pack, riding or milk as well as meat.

As might be expected, the distribution of the different species varies widely; the horse and ass are mainly confined to the north and south of the area, while cattle take their place in the intermediate zone. With cattle too, the zebu type with a large thoracic hump and short horns tends to follow the coastal areas, whereas the sanga type with its small, muscular cervico-thoracic hump and large horns tends to occupy inland areas. One interesting sidelight is that in many breeds individuals either polled or with loose hanging horns exist, showing the widespread incidence of this mutation. The genes for all-the-year-round breeding which occur in some types of sheep and goats might well be introduced into Britain. Indigenous breeds of pigs seem to be absent from Africa, for most of the types appear to conform to the breeds of the countries which first colonized the areas and even the small Bantu pig shows evidence of Asiatic origin.

The information given in this book should form a guide as to which of the various types it will be worth while to concentrate on for improvements in production, for Africa is a continent with a great potential for increased food supplies.

JOHN HAMMOND

PEOPLE AND PARROTS

Verbal Behaviour

By Prof. B. F. Skinner. Pp. x+478. (London: Methuen and Co., Ltd., 1959.) 42*s*. net.

AS a psychologist, Prof. Skinner has tackled the basic problem of verbal behaviour: he has not speculated about primeval grunts or the metaphysics of the word and the world, he has simply asked how the individual acquires his verbal skills. This makes such good sense that one wonders why one had not thought of it before: "We are specially reinforced by speakers and writers who say what we are *almost* ready to say ourselves—who take the words 'off the tip of our tongue' . . . The listener may refuse credit and exclaim *Why didn't I think of that* ?, but he must have 'thought of it' to some extent if he accepted it immediately as an effective metaphor or a really apt remark" (p. 272).

The book does not attempt a quantitative or experimental analysis of verbal behaviour: "The emphasis is on an orderly arrangement of well-known facts, in accordance with a formulation of behaviour derived from an experimental analysis of a more rigorous sort" (p. 11). The concepts applied are those of 'operant conditioning', discussed by the same author in his book, "Science and Human Behaviour" (New York, 1954). Given a repertoire of loosely organized instinctual behaviour patterns or responses acquired in other situations, the animal extends its control of the environment by discriminating those of its activities which pay off. The baby gradually converts his babbling to words by progressively accurate discrimination and reproduction of the responses which his parents reward and which he can practise to himself since he both speaks and hears. "At this stage the child resembles a parrot, which is automatically reinforced whenever its vocal productions match something heard in the environment" (p. 164).

Prof. Skinner sets off from this position and gives us a conducted tour of verbal behaviour. This is fascinating: we catch glimpses of magical thinking, psychotherapy, symbols, metaphors, puns, non-Freudian slips, spoonerisms, 'Finnegan's Wake', speech disorders, generalization gradients, universals, linguistic philosophy, stylistic devices, and ways of making people say what we want without actually beating. These are, of course, only glimpses—the value of the book is that it penetrates the clouds in so many places, for example, p. 314, "It is because our behaviour is important to others that it eventually becomes important to us", and p. 7, "We have no more reason to say that a man 'uses the word *water*' in asking for a drink, than to say that he 'uses a reach' in taking the offered glass".

From his analysis the author derives several new concepts—the mand, the tact, the autoclitic—and this is a considerable contribution in addition to the stimulation and insight he gives on the way.

Although one would like to recommend this book to everyone interested in any aspect of language, this might not be fair. This is a psychologist's book, and there is not much exposition of the basic concepts of operant conditioning theory in it. For those who have no acquaintance with the field the book would be harder reading: it would nevertheless be rewarding, and the reader could always refresh himself with forward glances at the later parts from time to time.

P. R. F. CLARKE

THE HARVEY LECTURES

The Harvey Lectures

Series 53, 1957–1958. By Dr. John H. Dingle, Dr. Frank Fenner, Dr. H. Fraenkel-Conrat, Dr. Joshua Lederberg, Dr. Arthur Kornberg, Dr. Albert H. Coons, Dr. Daniel Mazia, Dr. J. Gough, Dr. John H. Gibbon, jun. (Delivered under the auspices of the Harvey Society of New York.) Pp. xiv+254. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1959) 7.50 dollars.

THE Harvey Society has again amply fulfilled its constitutional aim of "the diffusion of scientific knowledge of the medical sciences". The lectures here published are too different to be adequately summarized, but their interest and variety shows the extent to which medical science now draws on general biology, and, in turn, fertilizes the latter. For example, Dr. F. Fenner's work on myxomatosis is of interest to the anthropologist and student of evolution as well as to the virologist. He points out that few of the viruses we know to-day could survive in scattered populations such as those of Palæolithic man. How then have they arisen? The myxoma virus, from producing a benign tumour disease in the Brazilian rabbit *Sylvilagus*, has become in a short time a virulent general disease of the dense populations of *Oryctolagus*, which have spread from the Mediterranean and especially to Australia. Fenner shows how this spread has been made to provide information about the evolution of viruses, inevitably a difficult study since "viruses exist only to-day, what happened yesterday is already rumour".

Dr. H. Fraenkel-Conrat discusses the tobacco mosaic virus as a "treasure-trove of chemical surprises", especially about the aggregation of protein and nucleic acid *in vitro* to form active virus. He emphasizes the difficulties due to the lack of methods for investigating the fine structure of polynucleotides.

Dr. J. Lederberg provides a fascinating account of sexual processes in bacteria by the movement of a chromosome from one cell to another of a pair. Since this happens progressively the chromosome can be broken at varying stages and the linkage relations studied. "The power and scope of these methods was illustrated . . . by the fact that the simple operation of mixing two mutant cultures on a few selective agar plates can generate information on 10^9 incidents of re-combination—an easy match for the reproductive potentiality of the entire human species".

Other lectures by Dr. D. Mazia on cell division, Dr. A. H. Coons on lymphoid tissue, Dr. A. Kornberg on deoxyribonucleic acid are no less interesting, and the whole volume, though not designed as a unity, provides a striking demonstration of the depth and breadth of medical science.

J. Z. YOUNG

REGENERATION IN ANIMALS

Asexual Propagation and Regeneration

By M. A. Vorontsova and L. D. Liosner. Translated from the Russian by P. M. Allen. Edited by F. Billett. Pp. xxiv+489. (London and New York: Pergamon Press, 1960.) 70*s*. net.

THE study of regeneration in animals has been pursued sporadically since antiquity, was caught and made scientific by Spallanzani, and received the blessing of philosophy from Voltaire. More to the point, its modern history offers us a perfect blend of the marvels of Nature with intellectual challenge, and adds more than a prospect of clinical relevance. Yet few books in English have been devoted to it, and of them only A. E. Needham's most useful, but brief, review is of service in introducing the present-day student to an enormous literature.

The appearance of Marie Vorontsova's book in translation is therefore an important event. It proves to be a happy one in some ways, a disappointing one in others. One cause of disappointment is likely to be all too apparent to the casual reader, and it may be well to mention it at once.

It is rightly felt that complaints about misprints and such-like minor errors argue for intellectual poverty in a reviewer. The price must sometimes be paid, and the making of this book cannot be allowed to pass without protest. The chief offence is in the re-transliteration of the names of Western authors. Dreisch, Abelo, Wolf, Gertwig, Navil', Bronsted and Shul'ts will present little difficulty to regeneration workers. But who is Dzhidzh? Luckily he worked with Rose and can for that reason be traced as Gidge. There are also some slips of substance in the text, most of which are so obvious as to be more irritating than dangerous.

Of the book itself one can speak with qualified pleasure. The authors begin with a brief survey of the modes of asexual reproduction in animals and their incidence. Spore formation and parthenogenesis are quite reasonably excluded, but the absence of reference to polyembryony is odd. In the few insects and mammals which habitually resort to it, the process is biologically important and full of interest, but it has, of course, little kinship with adult regeneration and is presumably ignored on that account.

The second main section of the book is a treatment of physiological regeneration, that is, of processes of tissue replacement inseparable from normal life. Here the authors are content to discriminate between this and reparative regeneration (that is, replacement following traumatic loss) and to give examples demonstrating the ubiquity of tissue replacement in the animal kingdom.

The last section, constituting more than three-quarters of the whole, is devoted to reparative regeneration, a field in which both authors have themselves done distinguished work.

Here we are given an excellent introductory account of 'true' regeneration in all groups of animals in which it has been demonstrated. The emphasis is, of course, on experimental work designed to reveal the cellular genealogy of regenerates, the causal relations during regenerative morphogenesis, and the factors controlling the incidence of the capacity to regenerate. There are a few important omissions of which nerve regeneration is an example. In partial recompense the large Russian literature is properly represented without depriving non-Russian authors (of works published up to 1955) of their due attention. A final chapter discusses such generalizations as have been proposed to describe regenerative phenomena, or to relate them to asexual reproduction.

The authors are occasionally severe. This is a merit when one happens to agree with them, a blemish when one does not. The concept of regeneration 'fields', for example, is so treated that the reader senses a lack of normal human sympathy for an admittedly inadequate attempt to describe important and puzzling phenomena. They are sceptical about the role of neoblasts in planarian regeneration, and frankly hostile to the claims for a unique role for interstitial cells in hydrozoans. In these, and other matters, their attitude is not so much unreasonable as unduly dogmatic and tinged with a little self-righteousness. Nevertheless, on most of the difficult and long-standing problems of regeneration their views will command agreement or, at very least, respect from the majority of their colleagues. It is certainly of great value to have them so clearly stated.

D. R. NEWTH

NUTRITION AND DIETETICS

World Review of Nutrition and Dietetics

Edited by Prof. Geoffrey H. Bourne. Pp. viii+272+7 plates. (London: Pitman Medical Publishing Co., Ltd., 1959.) 60*s*. net.

THIS volume is the first in an annual series. In the preface the editor refers to the "avalanche" of papers which now envelops students of nutrition and makes it difficult for them to keep in touch with advances in the different branches of the subject. He claims that there is ample scope for a new publication which will provide "more lengthy and discursive reviews than those published in conventional

journals", adding that the reviews will provide critical evaluation and bear the imprint of their authors, whose views and theorizing will be welcomed.

The first number contains ten reviews of a wide variety of subjects, including the effects of androgens and œstrogens on the metabolism of proteins and the growth of tissues, the biosynthesis of vitamin C, basal metabolism in the Japanese population, nutritional factors in anæmia, the use of isotopes in nutrition research, and the nutritional requirements of embryos. The reviews originate in five countries, and the authors are recognized authorities in the fields covered. The volume opens appropriately with a scholarly article on "The History of Nutrition" by E. V. McCollum—almost the last survivor of the founders of modern nutritional science—which contains a good deal of information not generally known. For example, McCollum states that J. B. A. Dumas, the French chemist, was "the first man to suggest that a diet which supplied only protein, fat and carbohydrate was inadequate for the support of life", a conclusion based on experience in the siege of Paris in 1871, when efforts to devise synthetic 'milk substitutes' for infants failed. McCollum records that when he himself was engaged in pioneer research on vitamins in the first decade of the century, he did not know of the fundamental discoveries of Eijkman and Grijns in Java on rice and beriberi, made during the years 1896–1901, because these "were all published in journals devoted to hygiene and medicine not usually read by chemists". It was not until 1913 that he learnt about them, through books written by Vedder and Funk. Apparently keeping abreast of the literature presented problems in those days also, though not the same problems that confront the modern scientific worker.

The other reviews are generally of high quality, clearly summarizing existing knowledge. They differ, however, in their value to the average nutrition research worker. "The Biosynthesis of Vitamin C", by C. J. King and R. R. Becker, deals with a very specialized field and the same may be said of "Neoplasia and Nutrition", by T. A. McCoy. The articles "Treatment and Prevention of Kwashiorkor" by a group of workers at the Institute of Nutrition for Central America and Panama, and "Nutritional Factors in Anæmia", by G. R. Wadsworth, are of wider general interest. "Basal Metabolism in the Japanese Population", by Shinjiro Suzuki, brings out the fact that the body size of the Japanese has steadily increased since 1900, with an interruption associated with war and post-war food shortages; this review is agreeably but rather unnecessarily enlivened by a photograph of two attractive Japanese women divers. The last review in the volume, by A. Giroud, on the nutritional requirements of embryos, is unusual and informative; in spite of 350 references the author succeeds in giving a lucid account of a recently developed field of research likely to be of considerable practical significance.

It is difficult to assess the contribution which this "World Review" is likely to make to nutrition research and applied nutrition and to judge whether it will fulfil a real need. The editor has undertaken a formidable task and faces much competition in the shape of other review journals of longer standing. The first volume sets a high standard which may not be easy to maintain.

W. R. AYKROYD

PLASMA PROTEINS

The Plasma Proteins

Edited by Frank W. Putnam. Vol. 1: Isolation, Characterization and Function. Pp. xv+420. Vol. 2: Biosynthesis, Metabolism, Alterations in Disease. Pp. xv + 518. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1960.) Vol. 1, 12.50 dollars; Vol. 2, 14.50 dollars.

THE objective of this treatise was to provide an account of the physical and chemical properties of the plasma proteins, their function, biosynthesis, metabolism and alteration in disease. To attempt to produce an authoritative and up-to-date work on such a vast subject is a tremendous undertaking requiring the utmost co-operation between editor, authors and publishers.

We are told by the editor in his preface that the entire treatise was completed within eighteen months of the first invitation to the authors, and that Volume 1 was published within one year of the first deadline for manuscripts. This is probably true also for Volume 2 which followed only a few months afterwards. Those of us who have had to wait two years and often much longer for our articles to appear in print in collective volumes will be enviously impressed.

There is no doubt that this publication has succeeded admirably in its objective. It is impossible to do justice to it in a short review; but a glance at the chapter headings and the names of the authors, all of whom are experts in the fields they write about, will give some idea of the extent and authority of treatment. The first three chapters are on methodology, and deal with fractionation and isolation by precipitation techniques (R. B. Pennell), electrophoretic and ultracentrifugal methods (G. R. Cooper) and ion-exchange chromatography (E. A. Peterson and H. A. Sober). Molecular parameters of purified plasma proteins are then discussed by R. A. Phelps and F. W. Putnam. Then follow detailed discussions of individual and particular groups of plasma proteins (albumin, by J. F. Foster; γ-globulin and antibodies, by R. R. Porter; macroglobulins and antibodies, by H. G. Kunkel; glycoproteins, by R. J. Winzler; metal binding proteins, by C. B. Laurell; lipoproteins, by F. T. Lindgren and A. V. Nicholls; plasma enzymes, by W. H. Fishman, and circulating hormones, by H. N. Antoniades). R. G. MacFarlane contributes an article on the very complex blood coagulation system. Emphasis throughout the treatise is on human plasma proteins, but there is a chapter by R. L. Engle and K. R. Woods on comparative biochemistry and embryology, wherein data for many species are presented. Biosynthesis is covered by H. S. Anker. Alteration in disease occupies two chapters; M. L. Peterman describes altered patterns and F. W. Putnam surveys the properties and biosynthesis of abnormal globulins. Finally, genetic alterations in human plasma proteins are described by D. Gitlin and C. A. Janeway.

All this mass of material is brought together for the first time in English, and treated from the modern experimental point of view. Despite the large number of contributors there is no serious duplication and there are frequent cross references from one chapter to another. The subject-matter is presented in a logical way, and continuity is preserved.

Despite recent and rapid advances in some of the fields discussed, the comprehensive treatment, wealth

of tabular data and the many references give this treatise a lasting value. Not unimportant is the clarity of style; most of, if not all, the chapters can be read with pleasure as well as for instruction. All this is a tribute not only to the authors but above all to the editor.

This treatise will be of the greatest value to all who have anything to do with plasma proteins; it is undoubtedly a major contribution to the literature on proteins.

R. CONSDEN

The black-and-white figures in this volume leave something to be desired: the characteristic pattern of the leaves of *Coriaria* (Fig. 24) has been quite lost, and the upright shoot of *Halesia* (Fig. 45) gives no idea of the gracefully pendent flowers; *Taxus baccata* var. *adpressa* (Fig. 65) looks far more like a species of *Pernettya*. It is not, however, the minor defects of this series which one regrets: it is the faint atmosphere of stagnation. Current interest in wild and cultivated plants is more lively and inquiring than the authors seem to realize.

B. L. BURTT

FERNS, MOSSES, SHRUBS AND TREES

British Ferns and Mosses

By Peter Taylor. (The Kew Series.) Pp. 231+15 plates. (London: Eyre and Spottiswoode (Publishers), Ltd., 1960.) 25*s*. net.

Garden Shrubs and Trees

By S. G. Harrison. (The Kew Series.) Pp. 318+15 plates. (London: Eyre and Spottiswoode (Publishers), Ltd., 1960.) 25*s*. net.

THESE new volumes in the Kew Series on British plant life are uniform in format and outlook with the two already published, and maintain the same rather humdrum level. At just one point the atmosphere changes. Mr. Taylor's account of the horsetails occupies some 32 pages, and one is immediately aware of his personal enthusiasm for this much neglected group. Backed up as it is by Miss Webster's admirably clear illustrations, this is surely the best account available and is one that every British botanist and field naturalist will wish to have at hand. The ferns themselves are displayed competently but unexcitingly. There is a resolute determination in this series not to frighten any reader by too much modern science. It is a misguided attitude. Sir Joseph Hooker knew better, and in the preface to his "Student's Flora" referred to "those physiological and morphological observations on British plants which have of late given so great an impulse and zest to botanical pursuits". He regretted that he could not fulfil his original intention of giving details of such work. The incorporation of the results of Prof. I. Manton's magnificent experimental studies on British ferns in a popular book of this kind is just what is needed to give a fillip to field botany.

Any selection of material invites criticism, and Mr. Harrison's choice in "Garden Trees and Shrubs" cannot escape it. How could he include *Erica carnea* and omit *Calluna*? Or mention six species of *Magnolia* and not one of the beautiful *M. sieboldii*–*M. wilsonii* group? Also, why no single yellow rose (such as *R. hugonis* or *R. xanthina*) to stand beside the red *R. moyesii*? These are strange omissions in the presence of *Decaisnea fargesii* and *Griselinia littoralis*. The chosen plants are, however, neatly and lucidly described, and the book, with its pleasant coloured illustrations, will yield some informative browsing for botanically minded gardeners. It is not really a book for identification purposes, for the key will often work only for the actual species described, and a different one may come down to the wrong genus. *Ledum* (keyed out on p. 37) has free petals and should be placed next to *Skimmia* and *Cotoneaster* on the previous page.

MICROSCOPIC STAINS

Encyclopaedia of Microscopic Stains

By Edward Gurr. Pp. xii+498. (London: Leonard Hill (Books), Ltd., 1960.) 95*s*. net.

THIS book is to be regarded as an F_1 hybrid (Conn × Colour Index). It retains the characteristics of both parents, being intermediate in size between the slimmer Conn and the stout Colour Index (first edition), and deriving its style and format largely from the former.

Most of the book (420 out of 498 pages on very thick paper) takes the form of an alphabetical list of dyes, together with synonyms, molecular weights, empirical and structural formulæ, and solubility data. These last, giving solubilities in water, ethanol, 'Cellosolve', ethylene glycol and xylene, are particularly useful in practical histology.

Each dye is listed with a number and trade mark ('Michrome') so that, although no price is mentioned, an aura of the catalogue overhangs the whole work. In his preface the author defends his own system of numbering on account of its stability by comparison with alternative systems (the second edition of the Colour Index differs widely from the old one). If the constancy of the dyes listed is as good as that of the numbering system there is much to be said in its favour.

The descriptive notes which accompany each listed dye give numerous references to possible and actual uses, but, in a disconcertingly large number of cases, the author has been unable to find any histological or histochemical use to justify the inclusion of the dye in his lists. In some cases dyes with identical formulæ, molecular weight and solubilities are recorded as separate items, without the appropriate synonym (brilliant croceine; croceine scarlet).

The author makes a case for regarding the molecular weight of a dye as an important indicator of its properties. He therefore presents, at the end of the book, a table of molecular weights as an aid in "selecting dyes for particular purposes".

Two other sections, perhaps added as an afterthought, briefly concern the diazonium salts used in histochemistry and the tetrazolium salts similarly employed. In the case of the former the quoted molecular weight is relatively useless unless the concentration of vehicle and stabilizer in the commercial product is known.

Histological departments and students of histology may like to have this book on their shelves; it contains a large volume of interesting and necessary information.

SYNTHESIS OF APPLIED PALÆONTOLOGY

Paléontologie Stratigraphique

Par Prof. H. Termier et G. Termier. Pp. ix+515. (3,425 figures). (Paris: Masson et Cie., 1960.) 148 N.F.

Atlas de Paléogéographie

Par Prof. Henri Termier et Geneviève Termier. Pp. 100, avec 36 figures en couleurs et 8 figures. (London: Masson et Cie., 1960.) 16 N.F.

THERE is in geology a great need for the publication of comprehensive works which draw together and synthesize the vast quantities of observational detail which have been rapidly accumulating in the past decades all over the world. Similarly there is a need for the critical comparison and co-ordination of the innumerable ideas and speculations that have been published in original papers in a great many different fields. We ought to be truly grateful to those who are prepared to step out of the fray (where glory is won), survey the field and report on the state of the battle. The task they perform is seldom rewarding to themselves, while the works they write involve a great deal of labour. Unfortunately the need for such works and their rarity make us very critical, for so often when they are published we are disappointed to find they are not those for which we were waiting.

Thus we ought to be delighted with these two excellently produced volumes by the indefatigable team of Prof. and Mme. Termier. However, there is no doubt that in spite of the really excellent drawings of the "Paléontologie Stratigraphique" and the equally beautifully executed maps of the "Atlas de Paléogéographie" a feeling of disappointment is not to be avoided.

The "Paléontologie Stratigraphique" is neither palæontology nor stratigraphy. It consists chiefly of a collection of figures of fossils arranged chronologically, and it attempts to survey the whole faunas and floras of each System, the larger Systems being broken down into Lower and Upper, or Lower, Middle and Upper. The matter is to some extent further organized by an introductory article on each System, or division of a System, dealing with the faunas or floras characterizing particular major facies developments. Tables of zones are provided at the end of each section. It is of course not possible to be truly comprehensive even in 515 pages and with 3,425 figures. The choice of genera for treatment is eclectic. Some are important zoologically, others as zone fossils, and many are merely abundant. In consequence neither the evolutional nor the purely stratigraphical account is as complete as it could have been if it alone had been the object of the book. This is in fact a museum in a book, and for the student who has not access to a really good palæontological collection it can be a really valuable reference book (though he will not be able to afford to buy it for himself). For an encyclopædic work of this kind it is exceptionally accurate and up to date. A weakness, however, is the lack of any indication of the magnification of a large number of figures which differ greatly in size from the originals.

The "Atlas de Paléogéographie" consists of 36 maps—each a Mercator projection of the whole world—which originally appeared in the first volume of the authors' "Traité de Géologie". These maps differentiate, at successive stratigraphical horizons, subsiding and non-subsiding seas (in two tones of blue) and show by means of pictographs the distribution of vulcanicity, mountain ranges, coral reefs, forests and other geographical features as well as particular fossils. Arrows show the direction of migration of faunas and floras. Had the maps merely summarized the broad distribution of the regions of thick sedimentary accumulation in the past, and the known distribution at particular times of other sedimentary phenomena and of particularly significant fossils, they might have had some value. But the maps purport to do much more than this; and to the extent that the reader accepts them as established geographical reconstructions and interpretations of migration routes, so is he misled. Moreover, on account of the small scale of the maps compared with the size of the symbols, together with the fact that the maps do not represent true instants of time, an altogether false impression is presented of the extent of the available data. In the hands of an undergraduate, or of a layman, this can be a dangerous book. The experienced stratigrapher will prefer his own speculations.

S. SIMPSON

METALS IN SURGERY

Metals and Engineering in Bone and Joint Surgery

By Prof. Charles Orville Bechtol, Prof. Albert Barnett Ferguson and Prof. Patrick Gowans Laing. Pp. vii+186. (London: Baillière, Tindall and Cox, Ltd., 1959.) 64s.

SINCE the earliest times the surgeon has been in need of some inert material which he can introduce into the body to unite damaged tissues, or to replace structures that are beyond repair. Over the years, however, implantation of a wide variety of metals gave disappointing results, owing either to the mechanical failure of the implant or to its inflammatory effect on the surrounding tissues. Not until shortly before the Second World War was it realized that this lack of success was due to metallic corrosion, and even later before the part played by such factors as fatigue and fretting was really appreciated. It then became apparent that the orthopædic surgeon had to be not only a master of his own art, but also conversant with the crafts of the physical chemist and the engineer.

It is this extra knowledge, in concise and palatable form, that the authors of this book set out to give him. Starting with a brief survey of the historical aspects of the subject, with adequate references, they pass on to consider the theory of metallic corrosion, at first in general terms, and then as applied to the various metals that have found application in surgery, indicating how such corrosion may be exacerbated by the incorrect choice or treatment of the metal to be implanted. Next they consider the structure and mechanical properties of bone, and show that a thorough understanding of such properties is necessary for the correct design and use of metallic implants. Finally, they discuss the healing process as applied to fractures, and describe in detail the various ways in which metals may be used for the internal fixation of broken bones.

Any attempt to correlate three such different disciplines as surgery, electrochemistry and engineering must of necessity result in a treatment which to a specialist in any of these subjects may appear as superficial. It might possibly be argued that a book of this kind would have been of more value had it been written with the collaboration of a chemist and an engineer. Such collaboration, however, might well have resulted in a treatment too long and detailed to be of practical use to the surgeon for whom, after all, the volume is intended.

The book is well illustrated, with many references to the original literature; and while the reviewer might point to a few minor blemishes such as the misspelling of his own name, such slips in no way detract from a work that should be of real value to those for whom it is written. E. G. C. CLARKE

RHEOLOGY

Rheology

Theory and Applications, Vol. 3. Edited by Frederick R. Eirich. Pp. xvi+680. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1960.) 21 dollars.

"EIRICH" is already a classic in rheological literature, even if it cannot be said to have brought about "a better understanding of the essential unity of rheology"; a hope expressed in the preface to Vol. 1.

The present volume contains little that will unify; rather it consists, like its predecessors, of a number of disconnected essays, differing somewhat widely in merit, on applications of rheology to various systems. It has still not been possible to establish an agreed set of symbols, even for the most widely used terms; but, unlike some of the chapters in previous volumes, each of these essays includes an adequate table of the author's choice of symbols.

Vol. 3 contains less material already published in book form by the same authors than did its predecessors; but there are still many pages of repetition of well-known classical treatments already available in other text-books. This reflects vestiges of the earlier idea, which can scarcely be maintained, that this excellent series of books would prove not only necessary but also sufficient for many rheologists.

Following these general criticisms, it is right to say that many of the essays are really admirable. Especially praiseworthy are the first three chapters: B. H. Zimm's essay on polymer chain models for dilute solutions; S. Oka on principles of rheometry; and B. E. Conway and A. Dobry-Duclaux's description of electroviscous effects.

Chapters 4–10 are concerned with the applications of rheology to different materials: latex, printing ink, pastes and paints, sand– and clay–water mixtures, inorganic glasses, concrete, and cross-linked polymers.

The "Atomistic Approach to the Rheology of Sand–Water and Clay–Water Mixtures", by W. A. Weyl and W. C. Ormsby, reflects the almost compulsive urge of some rheologists to insist on an 'atomic', as distinct from a phenomenological, explanation of all experimental data. Rheology, like all other branches of science, is concerned with generalizing, co-ordinating and relating diverse phenomena. In many cases an 'explanation' in terms of molecular structure is both possible and desirable. Other phenomena, such as those dependent on the conditions of packing of large aggregates, do not readily lend themselves to an 'atomic' approach. The authors of this chapter seem almost ashamed that everything cannot be explained in atomic terms.

Chapter 11, by D. W. Criddle, is concerned with interface rheology, and the remaining five chapters deal with industrial processes in relation to lubrication, adhesion, moulding, spinning and screw extruding.

The volume is very expensive, but the production is excellent, and there appear to be few misprints. It is good to learn that it is likely that this will not be the last volume of "Eirich". So far, scarcely any mention has been made of biological systems. A volume, or at least a part of a volume, devoted to biorheology would now be useful, since it would seem to be about eight years since any text-book has appeared on this subject, and much work has been done meanwhile. G. W. SCOTT BLAIR

CONSTANTS OF BINARY SYSTEMS

The Physico-Chemical Constants of Binary Systems in Concentrated Solutions

By Prof. Jean Timmermans. Vol. 3: Systems with Metallic Compounds. Pp. xiii+1322. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1960.) 270*s*.

THE preparation of this volume was supported by a grant from the Union Minière du Haut-Katanga, which is especially interested in this kind of binary system. Although more than half this book is devoted to tables of the properties of binary systems of which water is one component, no solubility data as such are listed. Presumably the author did not wish to include information already collected elsewhere (for example, in Seidell's tables): but nevertheless solubilities do appear in a disguised form as freezing curves. However, the information on freezing curves is not as useful as it might be because the solid phase in equilibrium with the solution is not often indicated. These omissions are particularly unfortunate since freezing curves represent a large proportion of the data.

The notice to users claims that the same properties are tabulated as in the earlier volumes (see *Nature*, 186, 918; 1960); but in fact scattered information is included on other properties such as activities, lattice constants, Verdet's constant, X-ray absorption, osmotic coefficients and the compositions of isopiestic solutions. For some systems values of these quantities are given, but for others only the name of the author and a date are listed.

The compilation is not a critical one and there are considerable discrepancies among the tabulated values. The author in the preface ascribes these errors to inadequacies in the measuring apparatus as well as to the use of impure specimens. Considering the early date of many of the values included it is not surprising that there is some lack of agreement.

This volume is even more expensive than Volumes 1 and 2, and like them, it will probably not be purchased by many private individuals. Every science

library should possess a copy, however, because when Volume 4 (containing the bibliography and index) is available, the use of this book will save much time in searching the literature.

E. F. G. HERINGTON

FROZEN FREE RADICALS

Frozen Free Radicals

By Dr. G. J. Minkoff. Pp. ix+148. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1960.) 5 dollars; 36*s*.

FREE radicals are highly reactive species, but many radicals can be successfully immobilized in solid matrixes at low temperatures. In the past ten years the development of new techniques has led to a great acceleration of the study of the formation and trapping of radicals. This has been encouraged by the initiation in 1956 of a three-year programme of fundamental research at the National Bureau of Standards, where it was hoped that it would prove possible to utilize the stored energy of a high concentration of free radicals in the production of an efficient rocket fuel. Dr. Minkoff spent a year as a guest scientist at the National Bureau of Standards in connexion with this programme.

Drs. Bass and Broida of the National Bureau of Standards have recently edited a volume of sixteen contributions on the history and modern development of radical trapping, which is at present the most exhaustive review of the subject. In contrast, Dr. Minkoff's monograph can be particularly recommended as a well-co-ordinated introductory survey.

The first four chapters of the book are devoted to the history of radical trapping and a description of the modern techniques. Many of the early studies of the phenomena of light emission from the condensation products of discharges and of the reactions taking place in cold traps have been repeated. The stabilization of free radicals has been increased by the use of liquid helium as refrigerant, and descriptions are given of several Dewar vessels constructed for optical studies at liquid-helium temperature. Several methods for the detection of free radicals are given, with indication of their suitability for use when the radicals are trapped. Electron spin resonance has proved particularly valuable in this respect. Statistical predictions have been made of the maximum concentration of free radicals that may be trapped in various assumed models. However, all but one of these give limits which are much in excess of the experimentally determined maximum of a few tenths of 1 per cent as they do not allow for the nature of the matrix or the energy of recombination of the radicals.

The last three chapters of the book summarize the most important experiments published up to early 1959. Many pages are devoted to the observations on nitrogen atoms, as the repetition and extension of the early work gave much stimulus to the National Bureau of Standards programme. Atoms and small radicals have usually been produced in the gas phase and condensed at liquid-helium temperature. However, larger organic radicals are better stabilized by the irradiation of suitable solid solutions with ultra-violet or ionizing radiation. Liquid nitrogenh as usually sufficed as refrigerant in these experiments, in which the radicals may be the primary products of the irradiation or the results of reactions by the primary products. Free radicals have been found to be trapped in polymers, and are also believed to be important in biological systems. Reduced temperature is not necessary in these cases, and they are only briefly mentioned.

R. N. DIXON

NATURAL HIGH-POLYMER CARBOHYDRATES

The Chemistry of Plant Gums and Mucilages and some related Polysaccharides

By Prof. F. Smith and Prof. R. Montgomery. (American Chemical Society Monograph Series, No. 141.) Pp. x+627. (New York: Reinhold Publishing Corporation; London: Chapman and Hall, Ltd., 1959.) 144*s*. net.

PLANT gums and mucilages are complex carbohydrates and rank among the oldest articles of commerce. They are abundant and their applications are diverse, so that their use and importance are growing. The fairly recent unravelling of major parts of their complex structures provides a fascinating story, so that the appearance of this monograph is opportune.

The senior author, F. Smith, is one of the world's leading experts in the field, and the junior author is a well-known carbohydrate chemist—both of Haworth's Birmingham School—so that much was expected from them. Their labour and care are rewarded, for the book fully justifies the claim of the publishers that it contains everything that is known of these substances.

The first few chapters deal in a human and interesting manner with the function and origin of gums, their classification, isolation, detection and identification. A wealth of detail is provided, some of which, however, except for its historical importance, could perhaps have been omitted. Methods for the separation of polysaccharides generally are concisely described, and their analytical procedures are covered in a very long and exhaustive chapter. The rest of the book is devoted to the detail of the determination of the structure of the many gums, mucilages, exudates, etc., so far examined. The importance of periodic oxidation techniques and of methylation procedures, largely pioneered by the senior author, is brilliantly emphasized, and seeing the picture as a whole one is amazed at the wealth of knowledge we now have of these complex high-polymer carbohydrates.

Of particular value in connexion with structural work in the field is the provision of an appendix giving some of the physical characteristics of all the *O*-methyl derivatives of monosaccharides.

An important innovation is the account of studies of gum structure by means of specific immunological reactions which provide diagnostic micro-methods of growing importance.

The book is full of beautifully drawn formulæ which make it of special value to the non-expert. It contains a most valuable series of references, and it is excellently printed and free from errors.

It will form a valuable addition to the library of every chemist, biochemist and plant physiologist, and can be highly recommended.

M. STACEY

ENZYMES AND METABOLISM

Advances in Enzymology and Related Subjects of Biochemistry

Vol. 21. Edited by F. F. Nord. Pp. v+521. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1959.) 12.50 dollars.

THIS volume of "Advances in Enzymology" contains a very important set of articles on some important lines of metabolism which have only recently been elucidated. The synthesis of purines and pyrimidines is covered by three reviews which supplement each other: "Enzymic Reactions in the Synthesis of Purines", by Drs. Buchanan and Hartman; "The Enzymic Synthesis of Pyrimidines", by Dr. Reichard; and "Folic Acid Coenzymes and One-Carbon Metabolism", by Drs. Huennekens and Osborn. In the past ten years the main lines of synthesis have been cleared up, with an appreciable increase in the number of known enzymes; some new and interesting enzymatic mechanisms are involved, and these are discussed critically in the first-mentioned article.

Other metabolic topics dealt with in the volume are oxidation and phosphorylation (in two reviews, by Dr. W. C. Schneider and Dr. D. E. Green, respectively) and the biosynthesis of carotenoid pigments (by Dr. T. W. Goodwin). Schneider's article reviews work on mitochondrial metabolism up to about 1957. Green's article is primarily concerned with the work of his own school on electron transport, which is discussed in terms of the special terminology which they have developed to express their view of the structural organization of enzymes in mitochondria. The enzymology of carotenoid metabolism is not as yet far developed, and Goodwin's contribution is necessarily mainly concerned with the chemistry of these plant products.

Two articles are concerned with the role of metals in enzymatic systems. Drs. Malmström and Rosenberg discuss (in English) the mechanism of metal ion activation of enzymes; Prof. Bamann and Dr. Trapmann are concerned (in the only article in German in this volume) with reactions in which metal ion catalysis may be regarded as a model of the enzymatic catalysis. They give an excellent picture of the field, but leave the impression that much remains to be done.

This volume will clearly remain for some time to come a standard reference for the topics discussed therein.

EDWIN C. WEBB

CONDUCTION IN SOLIDS

Electrons and Phonons

The Theory of Transport Phenomena in Solids. By Dr. J. M. Ziman. (The International Series of Monographs on Physics.) Pp. xiv+554. (Oxford: Clarendon Press; London: Oxford University Press, 1960.) 84s. net.

LITTLE more than four years elapsed after the discovery of wave mechanics before the basic principles of electrical and thermal conduction in metals were established, and such was the speed of the advance that within another four years, up to the end of 1934, the properties of individual metals, and even alloys, were being successfully analysed in terms of the new theory. The War brought progress in this field almost to a standstill, but at its end a new generation of physicists with new techniques and new ideas took up the pursuit once more, and the past fifteen years have seen a vast accumulation of detailed information on the properties of solids of many kinds. Although during this time there has been little change in the underlying principles or even in the mathematical methods employed in the electron theory of solids, yet so great a refinement of treatment has been introduced and so many more experimental effects discovered that, as the author of the book under review states in his preface, it is now probably beyond the capacity of any one man to write alone a satisfactory account of the whole theory.

In his book Dr. Ziman has confined himself to an account of the transport properties of metals, semiconductors and insulators; a subject of which he is undoubtedly a master. The title of the book at once indicates the quantal aspects of the conduction processes. By analogy with the quantized electromagnetic field it has become fashionable in recent years to refer to quantized elastic waves in crystals as phonons, and the whole mechanism of conduction is visualized as the mutual interaction between the phonons themselves and between phonons and electrons. This is an attractive picture, but it can all too easily suggest an over-simplification to the incautious reader: unlike a photon, the nature of a phonon in an elastically anisotropic crystal depends on the direction of its motion. The scattering of an elastic wave in a crystal is a more complicated process than that suggested by the deflexion of a single entity described as a phonon.

In an interesting analogy the author likens the writing of a scientific text-book to the process of purification by recrystallization. The imperfections of original papers are filtered away and the precipitate forms as a crystal in which each atom seems inevitably to be in its right place. This is a flattering description, and many of those with experience of either reading or writing text-books would hesitate to compare them with the perfect crystal. Dr. Ziman's is an excellent book but it will no doubt share the common lot and in the fulness of time will require extensive modification and revision. To the present generation of students—of all classes—the book will surely prove invaluable. It develops a theory in a clear and logical manner; dealing first with the properties of phonons, then with the properties of electrons in a periodic field, and eventually with the interactions between these systems. In this way is unfolded the theory of thermal conduction in insulators, the theory of thermal and electrical conduction in metals, the effect of an external magnetic field on the resistivity, the de Haas–van Alphen and the anomalous skin effects, and much besides.

The mathematics of the book is kept within reasonable bounds although always sufficiently detailed to enable the diligent reader to follow the argument completely. Physical concepts are emphasized, and the book abounds with discussions of significant experiments. The style is graceful, and erudite quotations at chapter headings are provided for the diversion of the reader. The publishers, for their part, have done a good job: the type is clear and the diagrams beautifully reproduced. Altogether this is an excellent book and deserves to be widely read.

H. JONES

GAS DISCHARGES REJUVENATED

Plasma Physics

By J. G. Linhart. (Series in Physics.) Pp. xi+278. (Amsterdam: North-Holland Publishing Company; New York: Interscience Publishers, Inc., 1960.) 50*s*.

Basic Data of Plasma Physics

By Prof. Sanborn C. Brown. (Technology Press Books in Science and Engineering.) Pp. viii+336. (Cambridge, Mass.: The Technology Press of the Massachusetts Institute of Technology; New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1959.) 52*s*. net.

THERE cannot be many examples in the history of physics of an almost moribund branch reviving and blossoming with such vigour as happened in the past ten years to what used to be called 'conduction of electricity through gases' or 'electric gas discharges'. The resurrected science is called 'plasma physics', adopting the name which Irving Langmuir gave almost forty years ago to the tough 'substance' of gas discharges, the highly ionized, highly conducting gas. The revival was due in the first place to the hope of controlled fusion, and led in a few years to giant devices such as *Zeta*, *Stellarator* and *Ogra* which dwarfed not only the modest discharge tubes in which J. J. Thomson and Langmuir made their classical discoveries, but also the largest rectifiers ever made for power stations. It is now common knowledge how successful the plasma was in repelling these first attempts for heating it up to millions of degrees, how it managed to dissipate the energy by processes nobody had thought of. This led to a general sobering and a determination to study the plasma before trying to force it to do what it so evidently dislikes doing. There may be some legitimate doubt whether it will be ever possible to 'study the plasma' except by feeding energy into it in special configurations of electromagnetic fields, and whether such knowledge will ever add up to a general mastery; but the intention is certainly laudable.

It can be said with confidence that at the present there exists no better introduction to this complex subject than Dr. Linhart's book. The author has the three rare qualifications of experience, mathematical facility and inventive imagination. He also possesses didactic ability, but this will be appreciated only by those readers who share with him the advantages of mathematical ability and of an active mind. It is not a book which can be imbibed passively, or uncritically.

The first three chapters on motion of electrons and ions, fluid description of plasmas and equilibrium configurations are more or less conventional and will make fairly easy reading for postgraduate physicists. The author comes into his own in the far more difficult chapters on waves and instabilities, shock waves and relaxation processes. Unfortunately, the derivation of the Fokker–Planck equation is almost incomprehensible, which is particularly regrettable in a subject in which Einstein and Debye have created masterpieces of simple exposition. This, however, is a rare exception in Linhart's book. The final chapters on research on controlled fusion and other applications, though perhaps somewhat too brief, make excellent reading.

Prof. Sanborn Brown's book on "Basic Data of Plasma Physics" is not only an excellent text-book on the more orthodox chapters of gas discharges, but also a reference book which one cannot afford not to have on the shelf. Many of the most valuable data in his book (on high-frequency breakdown, on diffusion and recombination) are the results of the researches of its author and of his collaborator, Manfred Biondi. While much of the material on elementary processes is covered also by Massey and Burhop's "Impact Phenomena", about one-half of the book which deals with breakdown conditions and with discharges is a happy complement to that other excellent work. The arrangement is so clear, with full description of the experimental methods and with all the relevant theory required to explain the data, that the book can be equally recommended to the student and to the expert research worker. D. GABOR

HYPERSONIC FLOW PHENOMENA

Hypersonic Flow Theory

By Wallace D. Hayes and Ronald F. Probstein. (Applied Mathematics and Mechanics, Vol. 5. Series of Monographs prepared under the auspices of the Applied Physics Laboratory, The Johns Hopkins University.) Pp. xiv+464. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1959.) 11.50 dollars.

THIS book will prove invaluable to the increasing number of students and research workers who are becoming interested in hypersonic flow phenomena. Although it is mainly theoretical, it is not such that it requires the reader to have very advanced mathematical knowledge. It should appeal to the engineer who has to tackle the practical problem of hypersonic flight just as much as to the physicist who wishes to acquire a physical understanding of hypersonic flow phenomena. Both authors have over the years made important contributions to hypersonic flow theory and are by experience fully qualified to write authoritatively on this subject, and thus to convey some of the knowledge they have gained in this important field of research, to interested readers of their book. Much of the material presented has not been published elsewhere and reference is also made to many Russian papers on hypersonic flow problems. Some of these are discussed in detail in the text.

The scope of the book is fairly wide, but it does not include any material on high-temperature gas dynamics and magnetogasdynamics. Throughout the text emphasis is laid on fundamental aspects of hypersonic flow and on the development of a soundly based theory. Semi-empirical theories are generally avoided except those which contribute in some way to the understanding of hypersonic flow phenomena. Theories which are based on wrong assumptions are not discussed though they may give good agreement with experiment.

In more detail, Chapter 1 is devoted to the consideration of the general features of hypersonic flow and some of the basic concepts used in the development of the theory. Chapter 2 is concerned with what is referred to as the 'small disturbance theory', as distinct from linearized theory, in relation to flow past slender bodies and gives similarity rules for determining the flow. Special reference is made to van Dyke, who first used the expression 'small disturbance theory' in his studies of flows in which the disturbances in velocity and pressure are small

compared with the velocity of the free stream and its dynamic pressure, but are not small compared to the velocity of sound and static pressure respectively, as is generally assumed in the conventional linearized theory. This chapter ends with a brief section on unsteady hypersonic flow and deals particularly with what is now generally known as 'piston theory'.

Chapter 3 is devoted to Newtonian theory and various modifications of it by Busemann, Lees and other writers. The theory is applied to two-dimensional and axi-symmetrical bodies and to the determination of optimum shapes. Shock layer structure and cross-flow phenomena are discussed, and a theory for unsteady Newtonian flow is developed. As first approximations to more general solutions based on the assumption that the shock layer is moderately thin, constant-density solutions are obtained in Chapter 4 which give information beyond that obtained from Newtonian theory. Cases considered include the wedge, the cone, the circular cylinder and Lighthill's solution for the sphere.

Chapters 5, 6 and 7 consider respectively the theory of thin shock-layers, blunt-body flows and shock-expansion theory, while Chapters 8 and 9 discuss hypersonic viscous effects. Chapter 10 deals briefly with free molecule and rarefied gas flows.

I would strongly recommend this book to students and research workers who wish to study hypersonic flow phenomena. W. P. JONES

GEOCHEMISTRY

Methods in Geochemistry

Edited by A. A. Smales and Prof. L. R. Wager. Pp. vii+464. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1960.) 13.50 dollars; 94*s*.

IN V. M. Goldschmidt's definition of geochemistry (1933) are implicit quantitative composition of the Earth and its parts, discovery of laws controlling distribution of elements, and comprehensive analytical data on rocks, meteorites, waters, atmosphere, to include geophysical evidence on the nature of the Earth's interior. This considerably extends the more restricted scope as originally enunciated by F. W. Clarke in his classical "Data of Geochemistry" (1908), where the solid crust of the Earth is the chief object of study. B. Mason, in his "Principles of Geochemistry" (1952), brings evolution of the subject to more recent times, when he defines the tasks of the geochemist as "the determination of the relative and absolute abundances of the elements and of the atomic species (isotopes) in the Earth" and "the study of the distribution and migration of the individual elements in the various parts of the Earth (the atmosphere, hydrosphere, crust, etc.), and in minerals and rocks, with the object of discovering principles governing this distribution and migration". Thus over the years both theoretical and analytical phases of geochemistry have expanded enormously, so, likewise, have the various methods of attack on the problems involved. In the present volume the authors, with collaboration of a team of specialists, describe modern techniques at the disposal of the geochemist which go far beyond traditional chemical and geological approaches to secure desired analytical data. "It is a long way from the geologist's hammer to the mass spectrometer and the nuclear reactor which are now sometimes the tools the analyst uses", as the authors naively remark in their introduction; what follows in this book gives all concerned a clear indication of how that gap is bridged to-day.

Modern geochemical methods include collection and preparation of material for analysis, here contributed by L. R. Wager and G. M. Brown. E. A. Vincent discusses gravimetric and volumetric analysis, flame photometry, colorimetry and related techniques. Spectrochemical analysis is dealt with by S. R. Taylor and L. H. Ahrens; fluorescent X-ray spectrography by H. I. Shalgosky; stable isotope geochemistry and mass spectrographic analysis by K. I. Mayne; mass spectrometric isotope dilution analysis by R. K. Webster; radiochemical methods by S. Moorbath; radioactivation analysis by D. Mapper; polarography by S. Moorbath and modern chemical separation methods by F. W. Cornish.

Of the above techniques, two comparatively recent procedures of remarkably high sensitivity have been added to the geochemist's weapons of attack available in geochemical analysis. One is the mass spectrometer isotope dilution method, which owes much to development of thermal ionization source mass spectrometers, also to present availability of separated isotopes of many elements; the other method is that of radioactivation analysis. Both procedures are adequately described in this book.

"Methods in Geochemistry" is a new departure in this science in that it is not only an up-to-date exposition of what the authors term "an almost embarrassingly wide choice of techniques for any given problem", but also because it brings together in one volume so much current information on geochemical research which chemist, geologist or physicist alike would have to seek in an otherwise voluminous international literature. The book is highly commendable, both in presentation and purpose. H. B. MILNER

MOISTURE IN TEXTILES

Moisture in Textiles

By Dr. J. W. S. Hearle and Prof. R. H. Peters. Pp. ix+203. (Manchester: The Textile Institute; London: Butterworths Scientific Publications; New York: Textile Book Publishers, Inc., 1960.) 40*s*.; 6.50 dollars.

THE adsorption of moisture by fibres is such an unobtrusive phenomenon that it is, perhaps, not generally thought of as being a reaction in the usual sense of the word. The interaction of the two is, however, of very great practical significance, not only because of associated changes in weight, which are economically important, but also because of dimensional changes in yarns and fabrics consequent on fibre swelling. The mechanism of moisture adsorption is complex and the many theories which have been evolved are admirably surveyed in this book, which is based on a series of lectures given at the Manchester College of Science and Technology.

The book is arranged in thirteen chapters, written by seven contributors. Chapter 1 (P. S. H. Henry) deals with water in the atmosphere and the relevant definitions; seasonal and diurnal variations; and the insulating effect of buildings. This is followed by

a brief chapter (J. W. S. Hearle) on the structure of fibres. The measurement and interpretation of sorption isotherms are discussed in Chapter 3 (A. R. Urquhart), the emphasis being on cotton. Factors which affect sorption, particularly mercerization, are included. Chapter 4 (W. H. Rees) concerns heat of absorption, and thermal quantities are defined and interpreted, together with methods of evaluation; again, the effects of physical and chemical modification such as orientation, mercerization and acetylation are discussed. Chapters 5 and 6 (G. King) survey respectively two- and three-phase adsorption theories, and theories of multilayer adsorption. Rate of change of moisture content, the simultaneous diffusion of heat and moisture, and diffusion of moisture and solvents in fibre-forming substances such as sheet films and polymers are discussed in Chapters 7, 8 and 9 (J. Crank). These phenomena are of considerable practical importance in the bulk storage of textiles, and the theoretical treatment is directed to clarifying the basic mechanisms and to showing how the times of moisture transfer into or from any given package can be estimated from measurements on a standard package. In Chapter 10 (J. W. S. Hearle) the electrical properties of fibres are discussed, including the relation between dielectric constant and regain; the generation and dissipation of static electricity; and the electrical measurement of moisture content. Particular attention is paid to ionic theories of conductance. Chapters 11 and 12 (R. Meredith) are concerned respectively with the effects of moisture on the density and optical properties of fibres, and on the mechanical properties such as tensile and torsional strengths, creep, relaxation, and shear strengths. In the final chapter (J. S. W. Hearle) the retention by fibres of liquid water and the theoretical and practical aspects of removing water from fibrous masses by centrifugal and suction methods are surveyed.

The subject-matter is well presented and is accompanied by an excellent bibliography. J. W. BELL

FRENCH WITHOUT TEARS

An Introduction to Machine Translation

By Émile Delavenay. Pp. ix+144. (London: Thames and Hudson, Ltd., 1960.) 25*s*. net.

SEVERAL books on the mechanical translation of language have now appeared, generated in England, the United States, and the U.S.S.R. Hitherto, however, work in this field on the Continent has been singularly lacking, and, although in the past two years groups have started in the field, in France and in Italy, M. Delavenay's book is the first popular exposition of the French point of view which has been translated into English.

To say that the book follows well-trodden lines would be to do it less than justice, because any expository book must tend to do this. What is perhaps more important is that M. Delavenay's racy style has survived translation (by himself and his wife) and enlivens the reading of what can otherwise be somewhat dull matter.

The book starts with a few general remarks about the nature of translation and, in particular, about the impact of information theory on this art. Here, unfortunately, M. Delavenay allows his enthusiasm to get the better of him in suggesting that information theory is of great importance to machine translation. The fact is that information theory considers the statistical aspects of communication, but nowhere, so far as I know, does it make any reference to meaning, and meaning is the essence of translation.

After this somewhat philosophical start the book runs smoothly through aspects of computing machines and their relevance to the translation of language. It states clearly how a computer works, explains the coding into numerical form which is necessary to transform words into arithmetical quantities for processing in a computer, and then it goes on to discuss various aspects of computer processing of language.

After these preliminaries there is a historical approach. M. Delavenay, quite rightly of course, mentions the original Russian patent of Trojanski dated 1933, although he, like all other Western experts in this field, appears to have seen only the title page. He then goes on to trace the history up to 1955, and to indicate the way in which this subject has grown from an unimportant sideline in certain university laboratories to a large-scale activity in which some thousands of scientists are involved.

After this history there is an account of languages and of meta-language, and also an indication of how linguistic analysis can be performed on a machine. Much of this work follows the lines laid down by the Russian school of machine translators. M. Delavenay in this account makes a number of succinct comments on the virtues of the Russian approach to machine translation and seems much impressed by the Russian development of what is effectively a meta-language.

The next subjects to receive attention are syntax and morphology, and here in discussing the question of reducing storage requirements by the use of micro-glossaries, M. Delavenay gives an interesting example of a partial German translation in which only the most frequent words were translated, with the result that no meaning at all comes through, or alternatively in which only the technical words are translated, in which case the meaning is completely clear without any very good notion of what connecting words are present. This is, in a sense, a validation of the early work of Richens and myself, who proposed to ignore sentence structure and grammar completely and to concentrate on evaluating the technical meanings.

Having dealt with syntax, the last aspect of machine translation to be covered is that of lexical problems. Here there is a detailed consideration of different possible storage media, an indication of the way in which code compression can help in saving storage, an account of the processing of idioms, indications of means by which multi-meaning can be resolved and an analysis of the virtues and otherwise of the Thesaurus method. All these topics are of particular interest to specialists in the field, and it is useful to have the opinions of an expert who is not committed to any particular party-line on the relative merits of the different methods.

The book concludes with a look into the future, as M. Delavenay sees it, and finally, and most usefully, a long example of a machine translation from French into English.

There are a number of small errors which will irritate knowledgeable readers of this book. Many of the numerical data which are given are incorrect

for one reason or another. This does not appear to be due to ignorance on the part of the author because reference to the original French edition shows that the correct figures appear there. It is surely proof, if any is needed, of the virtues of a translating machine for technical material. Such a machine would certainly not have produced the lively text that M. Delavenay and his wife have done, but it would have ensured the factual accuracy of the figures which he gives. These blemishes are, however, quite minor, and the book can be unreservedly recommended as an introduction to this important art.

A. D. BOOTH

MATHEMATICS, GAMES AND ECONOMICS

Mathematical Methods and Theory in Games, Programming, and Economics

By Samuel Karlin. Vol. 1: Matrix Games, Programming, and Mathematical Economics. Pp. x+433. Vol. 2: The Theory of Infinite Games. Pp. xi+386. (Addison-Wesley Series in Statistics.) (London: Pergamon Press; Reading, Mass.: Addison-Wesley Publishing Company, 1959.) 75*s*. net. each volume.

THIS work is, in a broad sense, a contribution to the mathematics of decision making. Most of the material included is of recent origin, and the author himself has contributed substantially to the subject. It is concerned mainly with two-person zero-sum games. The subject-matter results largely from the research efforts of teams organized, or supported, by Stanford University, the California Institute of Technology, the Rand Corporation and the Office of Naval Research. As a result, mathematicians interested in this field, mathematical economists, and operational research workers will find the work almost indispensable, at least as a reference book, if they wish to be up to date.

Part 1 of the two-volume work is concerned with the theory of matrix games. Games are defined, the min-max theorem is presented, and the nature of optimal strategies for matrix games is considered. Various discrete games are solved, and these include an example from advertising where two political parties are engaged in an election campaign. Part 2, which completes Volume 1, is a comprehensive account of programming, both linear and non-linear. Computational methods are discussed, but not practical details, such as some of the problems which arise when an electronic computer is used; attention is given rather to the theory of the computational method. In the chapter on linear programming there are sections, as one would expect, on transportation and assignment, and on the warehouse problem and the caterer's problem. There are two chapters on mathematical methods applicable to economic models. One is concerned with theories of production, consumption and equilibrium, the other with welfare economics, models of balanced growth, and the stability of the equilibrium of price vector systems.

The second volume is concerned with infinite games, and after an introductory chapter on the nature and structure of such games, considers games with convex kernels. Then there are two chapters on "Games of Timing", a name coined in 1950 for games of tactical duels. The study of the latter commenced in 1948 when the Rand Corporation "collected a team of mathematicians, statisticians, economists and social scientists to analyse the meaning and structure of 'the uncertainties of war' and to construct a blueprint for the optimal future operation of the economies of attack and defence in war". By now a great number of games of timing have been analysed, and something of a general theory has emerged. The volume concludes with chapters on infinite classical games and on poker and general parlour games. There is a very interesting analysis of the Le Her game, and it is evident that in various cases solutions are only now appearing of games of some antiquity.

Some general remarks may not be out of place. The work will be essential for anyone carrying out research in game theory or mathematical economics. But it will also be useful for students, especially new graduates entering this field. There is a comprehensive bibliography of more than 250 references and there are problems set at the end of each chapter together with solutions worked out in detail. One unusual feature is that Volume 2 repeats Chapter 1 of Volume 1, and also all the appendixes. These amount to more than one-fifth of Volume 2 and must increase appreciably the price of the volume. The reviewer can find little justification for this repetition, even though it is stated as having been done so that the volume may be read independently of Volume 1.

L. S. GODDARD

WATER SUPPLIES FOR SMALL COMMUNITIES

Water Supply for Rural Areas and Small Communities

By Edmund G. Wagner and J. N. Lanoix. (Monograph Series, No. 42.) Pp. 337. (Geneva: World Health Organization; London: H.M. Stationery Office, 1959.) 20 Swiss francs; 35*s*.; 6.75 dollars.

THOSE of us who live in highly organized communities in the humid regions tend to take water so much for granted that we sometimes overlook how vital a commodity it is to our existence. Without water there would be no life of any kind on the Earth, and without water readily available in adequate quantity and free of pathogenic organisms human development is tremendously hindered. Sir Harold Hartley recently listed eight 'limiting factors' which might handicap the economic progress of mankind, and at the head of his list he placed shortage of water. From the time when early man first settled by a natural spring or permanent stream, down to the modern atomic power station consuming some 3,600,000 tons of coolant a day, water has been vital.

One urgent world-wide problem which faces mankind to-day is the organization of pure water for small communities in rural areas, backward countries and under-developed localities. Although no precise figures are available, it is quite certain that millions of man-days of labour are lost annually and much distress is caused because of illness and death from water-borne diseases. This tremendous problem can only be met by the organization of pure water supplies in adequate quantity and by proper sanitary measures.

It is the aim of this forty-second monograph of the World Health Organization to provide the basic information for government officials and health administrators who face this challenge. The monograph is essentially a practical handbook for civil and sanitary engineers, medical officers of health and public health administrators, and it describes in a clear and concise manner the ways and means of organizing rural water-supply in order to satisfy basic personal hygiene. Methods of installing various types of water-supply systems from both underground and surface water sources are detailed, together with a consideration of treatment under rural conditions and problems of distribution and use. The monograph concludes with a section on the management of water-supply schemes and a lengthy list of appendixes dealing with a wide variety of topics of value to the engineer working in remote areas.

It seems fairly clear from experience already gained that in most small communities in under-developed areas more health benefits can be gained from money spent on a water-supply programme than in any other way. The supply, however, must be adequate in both quantity and quality and not prohibitive in cost if the hygienic standard of the community is to be raised to a new level. There is, in fact, a remarkable degree of correlation in many communities between standards of living and consumption of water *per caput* per day. This new monograph should help materially in raising the water consumption, hygienic conditions and standards of living of many small communities at present held back by poverty-stricken conditions, high incidence of disease and death, and lack of knowledge.

W. G. V. BALCHIN

REACTIVE METALS

Reactive Metals

Edited by W. R. Clough. (Metallurgical Society Conference, Vol. 2.) Pp. xiv+610. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1959.) 113*s*.

THIS book presents the papers and discussion from the third Reactive Metals Conference of the American Institute of Mechanical Engineers in 1958. We have grown accustomed to the reporting of conferences in the United States, and this one follows standard practice. There is no visible sign of any theme or thread of continuity in the papers, except the commonly accepted classification of reactive metals, which here includes the transition metals of Groups IV, V and VI *A* of the Periodic System, together with uranium. The papers are grouped under properties and applications, titanium alloys, nuclear, consolidation, powder techniques, melting and refining; physical metallurgy, temperature effects, phase relationships, interstitial effects; metal processing and fabrication. As a summary of recent American work in very specific fields, such a collection may be of interest to large research and development organizations, but is more likely to be a reference book for the library than resident on the shelves of an individual.

A light-hearted discourse characterizes some of the papers, and, as so frequently happens, the bibliography does not include appropriate European work. The odd references to British papers are occasionally obscure ones (for example, U.K. Atomic Energy Authority Technical Notes) considering that the same work has often been published in the journal of a learned society. Two contributions on vanadium alloys, by Karl F. Smith and R. J. Van Thyne, discuss the requirements of fuel cladding materials in fast fission reactors. The argument follows very closely that published in Britain some three years ago, and seems to contradict the previous American point of view expressed at the Geneva conference later in 1958.

The most interesting work described is that on titanium alloys and the physical metallurgy of molybdenum, vanadium and niobium. It is a great pity that the Americans still persist in referring to 'columbium' in spite of international agreement to the contrary. There is also a strange reference on p. 7, in the keynote address by D. J. McPherson, to the use of 'columbium' in one U.S. reactor and its planned use in one British reactor. So far as I am aware the use of niobium in the Dounreay fast reactor was first suggested in 1953 and was fixed by early 1956, some years before the Conference to which this book relates.

C. R. TOTTLE

PLUTONIUM AND ITS ALLOYS

Extractive and Physical Metallurgy of Plutonium and Its Alloys

Edited by W. D. Wilkinson. (Based on a Symposium held in San Francisco, California, February 16–17, 1959.) Pp. x+314. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1960.) 79*s*.

ANY information on plutonium is welcome, and the freedom of discussion noticeable since the first Geneva Conference on the Peaceful Uses of Atomic Energy has led to many more symposia of the type presented in this book.

The contents are classified as the title suggests; but an introductory first chapter summarizes, very neatly, the properties of the six allotropic forms, the necessary safety precautions in handling, and discusses the solid state of the plutonium atom.

Six papers on extraction metallurgy cover a wide field, from conversion of salts to metal to removal of fission products by liquation. One American paper reports work between 1943 and 1946, and, in contrast, a French contribution refers to 1956. Detailed results are quoted for extraction coefficients in the distribution of plutonium and impurity elements between nitrate solutions and tri-butyl phosphate. This section on extraction processes will be of value to the chemical engineer working in this field, although one imagines that perhaps some of the information is already well known to those receiving security guarded reports.

The physical metallurgy papers are extremely interesting for metallurgists. A general treatment of the alloying potential of the metal is followed by articles on plutonium alloys containing cerium and zinc. The metallographic techniques required and the transformation characteristics are also referred to with respect to the metal and its alloys. References are given at the end of each paper, and an annotated bibliography and subject-index at the end of the book.

Illustrations and diagrams are well presented, and in spite of the comparatively high price, the nature of the subject matter will ensure a demand for it. Anyone concerned with nuclear energy topics should find this a valuable source of information, additional to, and in a more manageable size, than the proceedings of the Geneva conferences. C. R. TOTTLE

INSTRUMENTATION, DATA PROCESSING AND AUTOMATIC CONTROL

Progress in Automation

Vol. 1. Edited by Dr. Andrew D. Booth. Pp. viii+231. (London: Butterworths Scientific Publications, 1960.) 42*s*.

THE editor of this volume defines automation as that field of endeavour which "seeks to duplicate the activities of living creatures, including humans, by non-living but energy consuming means". He goes on to give an excellent historical survey, beginning with the water clock of Vitruvius in 245 B.C. and including many examples of early applications of automatic control. This broad definition is inevitably followed by a wide selection of topics, and the title of the volume is singularly uninformative about their content. In fact, the ten contributors to the volume cover some aspects of British progress in instrumentation, data processing and automatic control.

Articles on instrumentation are contributed by T. B. Rowley and A. E. M. Hodgson. Both are devoted to nucleonic measurement techniques using radioactive isotopes. The first deals with thickness and level measurements and the second with fluid-density measurements, and the combination gives a clear account of these important methods.

Data reduction gives rise to the need for converters to transform the varying analogue quantities in the plant or process into digital form for use by the logger or computer. An excellent contribution by G. J. Herring reviews current practice in analogue to digital conversion and considers in detail a converter designed for use in high-speed data reduction.

The contribution on steel strip mills by G. Syke is a general review of the problems of instrumentation and control in the production of continuous strip. For the chemical industry, J. M. Keating discusses the automatic control of chemical plants and indicates the necessary properties for a digital computer used as a master controller for such a plant. The problems of data processing in an oil refinery are also considered and future developments indicated.

Automatic inspection techniques are discussed by J. A. Sargrove, who considers the possibility of performing statistical analysis on the samples tested and automatically feeding back information to the production line to correct unwanted trends and faults.

There are four articles on machine tool control which form a useful record and are in many ways complementary. K. J. Coppin describes a simple method of machine tool control designed for existing machines. The desired work dimensions are set in by an operator at the start of each traverse and positional measurement is from potentiometers geared to the lead screw. Two fully automatic numerical control systems are described in articles by D. T. N. Williamson, of Ferranti, Ltd., and F. W. Hartley, of E.M.I., Ltd. The Ferranti system uses optical diffraction gratings with moiré fringe counting to achieve positional measurement and is non-interpolating. The E.M.I. system, on the other hand, uses a continuous analogue measure of tool position and interpolates parabolically between points in the stored programme of successive tool positions. Hartley's paper also contains a comparison of several British and American systems and discusses the economics of numerical machine tool control.

H. J. Finden considers in his paper a numerical control system for a machine tool in which a linear inductosyn gives a precise analogue position measurement independent of the lead screw.

The articles are well written and authoritative, and the choice of topics gives a fair cross-section of British efforts in this vast field.

The volume fills a gap in existing literature between the specialist papers in professional journals and the more popular articles on automation. In this respect it will be of value to many engineers, research workers and administrators who require a sound account of progress in a given topic without searching the literature. It is very well produced, but further volumes may be better matched to their purpose as progress reviews if made in a less costly form.

P. H. HAMMOND

SIGNALS AND STATISTICS

Statistical Theory of Signal Detection

By Dr. Carl W. Helstrom. (International Series of Monographs on Electronics and Instrumentation, Vol. 9.) Pp. viii+364. (London and New York: Pergamon Press, 1960.) 63*s*. net.

DR. HELSTROM is primarily interested in the reception of radar signals. He formulates his problems explicitly as problems in statistical inference: to detect a signal in the presence of noise (that is, to decide whether a signal of known form, or perhaps only of known statistical properties, is present or not), to estimate parameters of the signal, such as arrival time and carrier frequency, and to resolve signals, that is, to decide which of a number of known signals are present simultaneously.

After some general material on signals, filters and noise, the author gives a clear description of the Bayes, minimax and Neyman-Pearson decision criteria. Later in the book he describes the use of ratios of maximized likelihoods, and some of the properties of Bayes and maximum likelihood estimates.

The rest of the work consists largely of a detailed application of these methods to the decision problems mentioned above, for situations of varying degrees of complexity: for example, detection when one has nuisance parameters such as signal amplitude, phase and arrival time, or when repeated observations are made on the signal. An aspect of the problem novel to many statisticians is that observations are taken in continuous time, so that the idea of 'sample size' is to some extent replaced by that of 'signal to noise ratio', and the data must be transformed canonically if one is to have an enumerable set of variates.

The solutions to many of the problems are formal, in the sense that they are given in terms of the solution or the eigen values of an untreated integral equation. The author certainly gives a more explicit treatment for several specific cases, and often provides a qualitative appreciation of the results, but it is plain that there is work to be done here. The 'mechanization' of the recommended decision and estimation procedures is touched on only lightly, although, on the other hand, the author claims no more than that he is calculating a "standard of performance against which present systems can be measured", and regarding the optimum systems as guides to design.

The literature references are, perhaps understandably, not always those that a statistician would make. In common with most communications engineers, Dr. Helstrom attributes Cramér's result concerning the spectral representation of a stationary process to Rice, while the Cramér-Rao inequality is credited to Fisher.

These are matters of detail, however, well outweighed by the book's merits, of which the main ones are its clarity, thoroughness and consistent appeal to first principles. P. WHITTLE

PHOTOGRAMMETRY

Photogrammetry

Basic Principles and General Survey. By Prof. Bertil Hallert. (McGraw-Hill Civil Engineering Series.) Pp. ix+340. (New York: McGraw-Hill Book Company, Inc.; London: McGraw-Hill Publishing Co., Ltd., 1960.) 85*s*. 6*d*.

THERE are very few text-books on photogrammetry in English which are sufficiently modern, or which attain a sufficiently high standard of presentation to help the student bridge the very wide mathematical and technical gap between the long-established fundamental principles and modern developments of the subject. The present book goes a long way to remedy this deficiency, and it must rank as an extremely important contribution to the teaching of photogrammetry. There is much new and thought-provoking material, especially in the appendixes (which comprise nearly one-third of the book) and in Prof. Hallert's choice and treatment of worked examples.

Earlier text-books pay some sort of lip-service to the idea of statistical treatment of photogrammetric measurements, but none has examined the theory of errors with special reference to the nature of these measurements and the most convenient methods of adjusting them. The contributions of Prof. Hallert in this field are well known, and it is not therefore surprising that one of the most important innovations of this text is a lucid "Introduction of Photogrammetric Theory of Errors" and frequent use of statistical checks in the worked examples.

The most important criticism which must be made is that there is no proper treatment of analytical aerial triangulation. Five years ago this might have been dismissed as a peculiarly British practice, developed by the Ordnance Survey for a special task. In recent years, however, the suitability of the method has been recognized in many other countries, not only for topographical mapping but also in the applications of photogrammetry to ballistic and satellite research. In this book the part devoted to aerial triangulation deals only with methods of radial triangulation and bridging with plotting machines. The reader is left with the impression that the stereocomparator is only used for terrestrial photogrammetry. The importance of the camera réseau as the only really satisfactory method of correcting film distortion is not described, despite Hallert's condemnation of the use of a register glass in aerial cameras.

Another remarkable omission is the absence of any description of the more refined methods of analogue adjustment to a block of any sort of aerial triangulation. Slotted templates are, of course, described in some detail, but there is no mention of either stereotemplates or the '*ITC*-Jerie' analogue computer. The last is surely one of the most important developments in the whole field of photogrammetry during the post-war period. D. H. MALING

A HOOKE BIBLIOGRAPHY

A Bibliography of Dr. Robert Hooke

By Sir Geoffrey Keynes. Pp. xix+115+12 plates. (Oxford: Clarendon Press; London: Oxford University Press, 1960.) 50*s*. net.

THE recent tercentenary celebrations of the Royal Society have cast our minds back to the early years when that illustrious fellowship was enriched by the inventive genius of Robert Hooke. As curator of experiments, secretary and editor, Hooke was constantly active on the Society's behalf, and he may well have saved it from early extinction. But his colleagues failed to appreciate his true worth; he was injured by the enmity of the pre-eminent Newton, and his fame suffered a posthumous eclipse which persisted for two centuries. Only in our own day, and largely through the advocacy of Prof. E. N. da C. Andrade, has Hooke received something approaching proper recognition as a pioneer in many branches of science and as Wren's trusted associate in the immense task of rebuilding London after the Great Fire.

Hooke's few published works, now rare, afford but little idea of the immense range and fertility of his inventive capacity as it is revealed in the records of the Royal Society over many years. Much of this recorded material became generally accessible some twenty-five years ago through the publication of R. T. Gunther's volumes on Hooke in his "Early Science in Oxford". Light was cast from another angle on Hooke's enigmatic personality by the editing of his "Diaries". But the archives of the Society and other repositories preserve many still unpublished manuscripts and letters by or relating to Hooke, the location and contents of which are not generally known to students and which should be taken into account in any final assessment of the man and his age.

A concise, serviceable bibliography of all this material has now been compiled by Sir Geoffrey Keynes in fulfilment of a plan conceived many years ago in discussions with the late Prof. John Fulton of Yale. It opens with a prefatory account of Hooke's career and of the problems facing his bibliographer, passing thence to a discussion of the continuation of Bacon's

"New Atlantis", by "R. H. Esquire" and dated 1660. Sir Geoffrey inclines to the belief that this was, in fact, Hooke's first published book. Other sections deal with Hooke's early tract on capillary attraction, his controversy with Auzout, the "Micrographia" and its derivatives, the six Cutlerian Lectures, the "Philosophical Collections" which Hooke edited to fill a gap in the sequence of *Philosophical Transactions* caused by Oldenburg's death, Waller's edition of the "Posthumous Works", Hooke's contributions to the *Transactions* and to contemporary books, and, finally, the "Diaries". Following the bibliography proper are four appendixes: these comprise a summary list of Hooke's papers and letters preserved in manuscript, a list of letters from printed sources, a selection of books and articles bearing upon Hooke, and, lastly, Newton's notes on the "Micrographia" which have not been transcribed before.

The book is excellently produced, and its interest is enhanced by the inclusion of reproductions of the title-pages and of a few historic plates from Hooke's works; there are also drawings of the College of Physicians which he designed. Sir Geoffrey Keynes has fashioned a tool which will prove indispensable to students of the life and times of Newton's greatest rival.

A. ARMITAGE

AN INTERPRETER OF WHITEHEAD

Whitehead's Philosophy of Science

By Dr. Robert M. Palter. Pp. xv+248. (Chicago: University of Chicago Press; London: Cambridge University Press, 1960.) 60*s*. net.

THERE are probably several reasons why Whitehead's contributions to philosophy have suffered some neglect, and even a little discredit, with the passage of years. One is the difficulty of his language and symbolism, another his concern with metaphysics. A great mathematician—now no longer living—once told me how shocking it was to write so obscurely as "A. N. W."; yet the same authority declared—just as Whitehead did in so many words—that metaphysics must be firmly based on science for its survival; and furthermore, that it needed to be critical of itself before it applied the lash to others.

Although the present book is not quite the first and only attempt at interpreting Whitehead, it is assuredly the fullest and most understanding yet produced. If, some forty years ago, one could have had Prof. Palter's work at hand when reading "An Enquiry concerning the Principles of Natural Knowledge" and "The Concept of Nature", many hours of frustration might at least have been shortened. In a sense, the later publications were easier to grasp, because their purpose was clearer, and the author's goal more squarely in view.

As things are now, it seems likely that Whitehead's method of extensive abstraction and his philosophy of organism will prove of current interest, and these are well discussed and illustrated in the present volume. Moreover, the latter subject is set fair to offer an epistemological basis for the coming biophysics. In this context, the quotations from Whitehead, copious as they are, fit naturally into the picture, without being tedious or destructive of the author's careful exegesis. An example is the way in which Whitehead is shown to be fully aware that natural science means the observation of things as they are, and that to rely on formal mathematical concepts alone is to perpetuate the errors of the scholastics. In fact, a few lines before this remark, Whitehead states bluntly that "If there be no stuff to appear, there can be no space" ("The Principle of Relativity", p. 39). All this shows that he was no pedant with regard to natural science.

A footnote to p. 5 rescues, from rather out-of-the-way sources, Whitehead's pregnant hint to the effect that some day æsthetics will become founded on symbolic logic. There are straws in the wind that way already.

Finally comes the concept of 'fields'. At the weakest, this means "any theory involving continuous distribution in space of some physical magnitude . . .", and at the strongest, any expression of fundamental laws as partial differential equations. It could scarcely be better said, and subsumes most of the substance of the great period of æther physics.

However complex, nothing can detract from the peculiar beauty of Whitehead's prose. His preface to "The Principles of Natural Knowledge" is pathetically lovely in its restrained sense of poignant sorrow.

I was with "A. N. W." shortly before his death: the mind was clear and the memory nearly perfect, as he looked into the Great Unknown.

F. I. G. RAWLINS

THE NEW FOREST

The New Forest

By Juanita Berlin, Edwin Cohen, Dr. Gordon J. Copley, H. L. Edlin, Oliver Hook, Juliette de Baitach Levy, F. E. W. Venning, H. Widnell, W. R. Myers, and Sir Berkeley Pigott. Pp. x+201+27 plates. (London: Galley Press, Ltd., 1960.) 30*s*. net.

IN view of the wealth of material and scholarship that could have been drawn on, as well as the publicity given to this book, one had reason to expect an authoritative work on the New Forest. Instead, we are presented with an odd and unbalanced assortment of topics that fail to fulfil the claims put forward by the chairman of the Forestry Commission in his foreword.

In an opening chapter entitled "The Background", brief references are made to Stone Age, Bronze Age and Iron Age cultures, and to some of the commoner place names, but there is no attempt to recount or explain the fascinating history of the Forest or the communities who came to settle within its precincts. On the other hand, the chapter on "The New Forest Commoners" deals adequately with the remarkable, if complicated, administration that has evolved through the centuries.

The geology is inadequately dismissed in four pages, and as the contributor admits, much of it is "very briefly and crudely summarized". The distribution of the distinctive Forest soil types is omitted altogether. The same chapter contains a much larger section entitled "Botany", but this deals almost exclusively with pure floristics, and misses completely the opportunity to elaborate the general vegetational pattern in relation to geology and topography. Much later in the book, and separated from the general botanical section, is a rather whimsical, but

nevertheless informative and readable chapter on medicinal herbs.

In the chapter on "Mammals" the part that deals with the history, distribution and hunting of deer is adequate and competent. For the remaining mammals, except the squirrels, there is virtually nothing that relates them to the New Forest as distinct from Britain as a whole. The list of mammals is accurate.

The contribution on "Birds" is awkward in style, and there is an attempt to cram too much information into too short a space—especially when four pages of the thirteen are devoted to one species and the remaining nine pages to 150 species.

One begins to appreciate the atmosphere of the Forest in the chapter on "Perambulation Today", and Edlin's contribution on "Silviculture" is clear, authoritative and interesting.

Some of the remaining chapters and appendixes could have been omitted without loss. There is a strange collection of illustrations; a few of them are well chosen, many contribute little to an appreciation of the New Forest, and quite a number are poorly reproduced. There is no index to the book.

L. E. TAVENER

ADVENTURE, BEAUTY AND SCIENCE IN AFRICA

Serengeti Shall Not Die

By Dr. Bernhard and Michael Grzimek. Pp. 344 (67 plates). (London: Hamish Hamilton, Ltd., 1960.) 30*s*. net.

THIS is the book of the film. Despite the many fine illustrations, the book cannot compete with the film in showing the space of the Serengeti National Park and the beauty of its animals in motion. But the book is complementary to the film in revealing the careful preparation, the hard work and the risks of the task undertaken by Dr. Grzimek and his son, and it gives a moving insight of their relationship.

It is a true adventure story. After the success of their first film "No Room for Wild Animals", the Grzimeks offered part of its revenues for purchase of land to increase the Serengeti National Park, but were persuaded instead to study the animal populations there; that study entailed learning to fly, and that entailed getting permission from their wives.

When these difficulties had been overcome, they made the trip to Tanganyika in their small slow aeroplane, contending with weather and officialdom, gaining sidelights on the countries through which they passed; readers who knew the Sudan before independence will find the account of the Christmas party at Juba very probable and very funny.

The book digresses from the Serengeti and contains much interesting material on the history of East Africa, and of Tanganyika in particular. Some of the opinions about Africa in general may not be shared by those who have worked there; for example, a man who lives in an isolated thatched hut may take a lively interest in world affairs; when visiting a small island on Lake Victoria in 1941, I was asked, "What will happen to France after the war?" Some may doubt the claim of a chapter heading "Knowledge of Men Lessens Philanthropic Feelings, Understanding Animals Heightens Love". Does it always?

There is a sense of urgency about the book, of the futility of proclaiming Nature reserves without the staff to look after them. But there is no occasion for the fatalistic attitude "Africa is dying and will continue to die". The wild and domestic animals and the people recovered quickly from the awful suffering and death when rinderpest swept through Africa in the last century; that was one of a sequence of major catastrophes revealed by the layers of hard and soft soil in some steep river banks, evidence of alternating erosion and recovery.

Erosion in the Serengeti is not due only to the Masai cattle. In tropical countries, wherever continued trampling forms hard tracks, as on the migration routes of the wild animals, there is some erosion, though not so intense as that caused by large herds of cattle. It is stated, "A National Park must remain a piece of primordial wilderness to be effective. No men, not even native ones, should live inside the borders". But later, "During our flights Michael and I also noted the *bomas* of the Masai and counted their herds. We found only a fraction of the number usually given. Unless their numbers rise and their cattle multiply because of modern protective injections, the Masai might not make such bad neighbours of the Park after all".

That opinion is reassuring. The Grzimeks not only carefully counted the wild animals of the Serengeti and found that they amounted to less than 400,000 instead of the supposed million, they also traced their migrations; the animals which graze near Lake Victoria, both inside and outside the National Park, from July until November, are living in the Conservation Area, where the Masai have grazing rights during January–May.

The Grzimeks also studied the plants and found that much of the pasture most palatable to wild animals was growing where the Masai kept their stock. Samples of soil were taken for analysis to discover if its composition could be correlated with the distribution of the better grasses; and that also may be correlated with the intensity of grazing, for climax grasses are too tall to suit small antelopes. But just as it was necessary to make many flights to count the animals on parallel strips, so also the vegetation of the Serengeti could be accurately described only by recording the plants on a series of parallel transects across the National Park.

Such plant recording is one of the many urgent lines of research which might be done from the Michael Grzimek Memorial Laboratory at Seronera, the Park headquarters; for Michael Grzimek, twenty-four years old, was killed when a griffon vulture collided with his aeroplane. His tombstone on the edge of the Ngorogoro crater states "He gave all he possessed for the wild animals of Africa, including his life".

"Serengeti Shall Not Die" is an account of scientific work. Some of it is controversial; none of it is dull; it is enlivened by many beautiful plates in colour and in black and white. It should be widely read, and it is to be hoped that many of the readers will show their appreciation in a practical way, by sending to the Director, Tanganyika National Parks, Arusha, a contribution to the Memorial Laboratory and thus help preservation and improvement of the Serengeti National Park.

A. S. THOMAS

SHORT REVIEWS

Foods and Feeding Habits of the Pedi

With Special Reference to Identification, Classification, Preparation and Nutritive Value of the Respective Foods. By Dr. P. J. Quin. Pp. xvii+278+134 plates. (Johannesburg: Witwatersrand University Press, 1959.) 70*s*.

DR. QUIN provides in this monograph an excellent summary of his work on Bantu nutrition in the Union of South Africa. Although he confines it to the Pedi tribe, most of the data are equally relevant for other Southern Bantu tribes, and social anthropologists, economists, and nutrition experts as well as agriculturists, botanists and entomologists from all parts of Africa will find it a mine of concise and accurate information on the food and feeding habits of the Southern Bantu. The early chapters deal with the plants, animals, reptiles and insects both domestic and wild which enter into Pedi diets. The reader is given not only their local Pedi, English and Afrikaans names but also their scientific names, and in many cases their nutritional composition. Where they happen to form a significant element of Pedi diet this is given in considerable detail; for example, one species of flying ant which the Pedi call dintlhwa and the entomologists *Carebara vidua* contain, when in the flying stage, 25·2 per cent crude protein in the case of the male and 7·4 per cent in the case of the female. These chapters are followed by an examination and analysis of particular Pedi dishes and the work ends with a discussion of the Pedi dietary pattern, of modern tendencies in Southern Bantu dietary habits and of Pedi health. The supporting tables, plates and drawings are first class and there is a useful bibliography. G. I. JONES

Religion in Plato and Cicero

By John E. Rexine. Pp. vii+72. (New York: Philosophical Library, 1959.) 2.75 dollars.

THIS interesting little book bears what amounts to the *imprimatur* of Prof. A. D. Nock, from whom the author has absorbed—and made his own—much of the recent classical tradition of Harvard University. It is an excellent record. These two lawgivers, Plato the philosopher and Cicero the orator, have seldom been studied synoptically, and their aims compared. Plato is metaphysical, and important for us to-day is his attempt to set up the first system of natural theology. Cicero insists on the usefulness of the gods to the State, if they are properly handled. In any such plan, sanctions are always at hand to deal with offenders, whether poets or otherwise.

Historically, the significance for scientific thought is the clear indication that the Deity can be known from the study of natural phenomena. Later centuries were to bring mankind experience of a less optimistic kind, leading to a severe limitation of Platonic religion. In a word, Plato's conception is a preview of the *deus philosophorum* with whom the Christian God cannot be inconsistent, but who is transcendent, and to some extent 'wholly other'. With this in mind, the author's thesis is most illuminating at the present stage of epistemological development in both theology and natural science.

For such a slender volume, there is a generous bibliography, well calculated to help further reading.

The Structure of Scientific Thought

An Introduction to Philosophy of Science. By Dr. Edward H. Madden. Pp. ix+381. (London: Routledge and Kegan Paul, Ltd., 1960.) 35*s*. net.

THIS volume is curiously constructed; it is an anthology the members of which are knit together by a series of introductions to each section. Thus, the value of the whole assemblage depends as much on the quality of these prefatory remarks as it does on the choice of the contributions themselves. The author's aim is to help students to understand the way in which scientific thought has been built up, taking examples from physics, probability, biology, psychology, axiology and so on, and presenting them in their original form. There are full references and an adequate bibliography.

Maybe this method will succeed in the United States: one cannot imagine it doing so in general, if only because the selection is so arbitrary, and somewhat weighted in favour of American sources. This is not necessarily a defect, but it tends to limit the book's appeal. The style of the several introductions is rather tiresome; there is much too much "you", as if the reader needed constant prodding. But the writer's heart is in the right place, he upholds science as a truly humanistic discipline, supreme in its own domain, and never self-conscious about being merely useful or fashionable.

The format of the collection is very attractive, though the large page size, carrying double columns, seems quite needless for a work of this character, and makes it difficult to house in an ordinary bookshelf. F. I. G. RAWLINS

No Stone Unturned

An Almanac of North American Prehistory. By Louis A. Brennan. Pp. xii+370+8 plates. (London: Victor Gollancz, Ltd., 1960.) 25*s*. net.

THIS is a book written to propagate the idea that man first reached America more than 30,000 years ago, and that his development thereafter was completely independent and owed nothing to contacts with Asia. Only with the coming of the higher civilizations of Mexico and Peru does the author allow that something "cryptically oriental" began to "hover" over them, though he will not have anything so simple as long sea-voyages to account for it, but rather a chain of vanished islands which filtered the oriental influences into an attenuated form.

Mr. Brennan is a journalist by profession and his speech agrees thereto, but he is also a keen amateur archæologist and knows the literature. He argues his case with great ingenuity, but not always with judgment. One of the weakest features of the whole thesis

is the doubtful character of the evidence for man in America at dates of the order claimed; the instances cited are well known—Santa Rosa Island, Tule Springs and Lewisville—but Mr. Brennan does not make it clear that they are very far from commanding wide acceptance as evidence of the presence of man. As to subsequent contacts, opinions differ a good deal about their extent, but he is a bold man who will have no contact at all by way of the north Pacific, either in the last stages of the Wisconsin glaciation when the Bering Straits were dry or later in boats. To deny such contacts on negative evidence in a very imperfectly explored area, when one is prepared, as the author is, to entertain the idea of a land bridge to bring the makers of Clovis points across the Atlantic to become the Solutreans, is to show a ridiculous lack of balance.

This is not an archæological text-book. Readers who have knowledge of American archæology may find parts of it stimulating and a good deal exasperating. Those who do not should take it with a large grain of salt. G. H. S. BUSHNELL

The Searching Mind in Medicine

By William A. R. Thomson. Pp. 187+25 plates. (London: Museum Press, Ltd., 1960.) 21*s*. net.

A SERIES of talks, by leading authorities, on the External Series of the British Broadcasting Corporation has been converted into an attractive book by William A. R. Thomson, the editor of *The Practitioner*. Because of the pace with which changes are taking place in modern medicine, however, little remains of the original articles, although Thomson acknowledges the inspiration of the broadcasters and continued help to ensure that his material is accurate and up to date.

The articles are varied and, besides the not unexpected topics of antibiotics, viruses and the effects of radiation on man, the author deals openly and factually with the biochemistry and chemotherapy of cancer. Perhaps too much is made of existing knowledge to show causal relationship between behaviour and physique, but the chapters on memory and learning, the problem of ageing, life at low temperatures and climate and working efficiency will be of interest not only to non-medical readers but also to general practitioners whose reading may have been somewhat circumscribed. The text is concise and carries an air of authority of one who has dug deep for his facts. It is perhaps a little unfortunate, therefore, that Thomson sometimes fails to apply a searching mind to his own beliefs and gets hoist with his own petard. His statement, for example, that "the exceptional handler of men—whether doctor, army officer or teacher—has a shrewd idea of what manner of man an individual is by looking at him" would be accepted by all except those who had subjected their 'shrewd ideas' to the process of statistical investigation. KATHLEEN M. HAWKINS

Understanding Weather

By Sir Graham Sutton. (Pelican Book, No. A469.) Pp. 215+4 plates. (Harmondsworth, Mddx.: Penguin Books, Ltd., 1960.) 3*s*. 6*d*.

IN this welcome book the Director-General of the Meteorological Office makes no claim to have written a comprehensive account of the science of meteorology, and indeed certain aspects of the subject—like air masses and fronts, basic elements of our everyday weather experience—are rather scantily treated. He is not much concerned either with geographical influences, such as the distribution of land and sea and the great mountain ranges, on the global circulation. Also while there is an excellent chapter on micrometeorology (as might be expected), local weather is strangely neglected (although plate 3*b* refers to a "sea-breeze front" which is nowhere mentioned in the text).

These omissions accepted, here nevertheless is an authoritative and up-to-date guide to a great deal of current thinking in meteorological science. Almost half the book is devoted to an account of modern methods of forecasting. This begins with the conventional techniques of synoptic analysis and forecasting, and goes on to Sutcliffe's development theories and Rossby's long waves (for which the way has been well prepared in earlier pages); the author then proceeds to numerical forecasting, from Richardson to the electronic computer (only here does an occasional mathematical equation intrude into an otherwise descriptive treatment), and finally offers a sober assessment of the possibilities of long-range forecasting. As an exposition on a popular level of the professional meteorologist's approach to his subject, this little book is excellent value.

M. PARRY

Comparative Anatomy

By Prof. William Montagna. Pp. x+397. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1959.) 48*s*. net.

THIS is a well-planned book which introduces the student to the important principles of comparative anatomy, organogenesis and embryology. The author first deals with the characteristic features of vertebrates and the development of the body plan and body tissues. Then follows a short chapter on the Chordata, including useful tables. The skin is next considered, then the endoskeleton, the muscular system, the digestive system, the circulatory system, the respiratory system, the excretory system, the reproductive system, the sense organs and the nervous system. Finally, there is a short chapter on the endocrine glands.

In most of the chapters there is a general introduction, then the development of the system is described and thereafter the comparative anatomy in amphioxus, cyclostomes, fishes, amphibians, reptiles, birds and mammals. At the end of each chapter there is a helpful summary and a short bibliography. The author has rightly emphasized embryology more than is the usual practice in a book of this kind, since developmental events give a better understanding of anatomical detail. There is also a useful glossary at the end of the book.

The book is written well, the descriptions are simple and easily understood, and there are numerous well-labelled illustrations and photomicrographs. It is indeed more difficult to write a simple account of important principles than a detailed text-book and in this the author has truly succeeded. He is to be congratulated on producing a useful, easily read, short account of comparative anatomy which should be of great value to the student. The publishers, too, are to be congratulated on their excellent production of this volume. T. NICOL

An Introduction to Embryology

By Prof. B. I. Balinsky. Pp. xiv+562. (Philadelphia and London: W. B. Saunders Company, 1960.) 54*s*.

DR. BALINSKY has produced a most valuable text-book, in which he has, in his own words, "endeavoured to present embryology as a single science, in which the descriptive morphological approach and the experimental physiological approach are integrated. . . . The subject . . . includes such topics as post-embryonic development, regeneration, metamorphosis and asexual reproduction. Lastly, I believe that embryology cannot be presented adequately without establishing some connection with genetics".

In the past few years, two or three similar attempts have been made; for example, the outstanding "Entwicklungsphysiologie" of Alfred Kuhn in 1955, and the collective work "Analysis of Development" edited by Willier, Weiss and Hamburger in the same year. Balinsky's work is, in the choice of subjects, illustrative material and interpretation, much more similar to the only other one-man English book of this kind, Waddington's "Principles of Embryology" of 1956. It is somewhat surprising to find that this work, unlike the other two, is not mentioned in the text or bibliography.

In spite of its very wide field, Balinsky's book gives a quite thorough treatment of the topics selected for discussion. The material is very up-to-date, and plentiful references are given to recent contributions. The book is also well illustrated, with figures and diagrams chosen more for their relevance to recent physiological interests than to serve as mere morphological descriptions in the manner usual in the older embryological texts. The index is unfortunately rather inadequate. This is, however, a minor fault in a work which will be very useful as the most up-to-date general treatment of embryology as a unified science.

Faune de France No. 63

Coléoptères Scarabéides. Par Renaud Paulian. Deuxième édition, revue et augmentée. Pp. ii+298. (Paris: Éditions Paul Lechevalier, 1959.) 5,500 francs.

THIS second edition of the "Faune de France" volume on scarabæoid beetles has been increased in size by some 60 pages. Changes in comparison with the first edition, which was published in 1944, are almost entirely additions. These provide more detailed information on life-histories, variation, distribution and keys for the identification of larvæ, in so far as the larvæ are known. Eight new species and two new subspecies of scarabæoid beetles have been added to the list of French species since 1944, making a total of 261 species. This gives an indication of the wealth of the French fauna, for the corresponding number for the British Isles is 68.

The work contains keys which permit complete identification down to species and varieties, and each species is described in detail with a summary of its biology and distribution so far as these are known. Experience with the first edition has shown that the keys work easily and that the figures are adequate. The indexes to predators and parasites and to host plants are a useful addition.

The author has made an attempt to use the infra-specific categories in a consistent and logical manner and to this end defines species, subspecies, race, form and aberration in the preface. The use of the term 'race' is confusing and as defined here is the equivalent of ecophenotype. Aberrations are defined as accidental variations, often unique. This being so, there seems little value in giving keys to enable them to be identified. These are, however, minor defects in a work which has proved its worth.

E. B. BRITTON

Wild Animals of the British Isles

A Guide to the Mammals, Reptiles and Batrachians of Wayside and Woodland. By Dr. Maurice Burton. (The Wayside and Woodland Series.) Pp. ix+180+111 plates. (London and New York: Frederick Warne and Co., Ltd., 1960.) 17*s*. 6*d*. net.

THIS is another beautifully bound book in the "Wayside and Woodland" Series, containing 48 excellent colour plates from photographs and 63 interesting black and white illustrations. It is the usual compact size, so would be suitable for carrying in the pocket on a ramble. In all, 58 species of amphibians, reptiles and mammals (excluding marine mammals) are included, whether as rare as the red deer, as localized as the wild cat, or as common as the house-mouse. Each is dealt with simply and in a straightforward manner, some at greater length than others. The various animals are described, each under its own name, in the following sections: insect-eaters, flying mammals, gnawing animals, flesh-eaters, hoofed animals, lizards, snakes and amphibians. These sections are preceded by a helpful introduction, and there is an index at the end of the book.

This would be a most useful addition to a school library. It would be invaluable to the young naturalist as the accounts are both clear and accurate, and would greatly assist identification. Many adults would also find this a pleasing book.

B. J. G. MAITLAND

Dangerous Marine Animals

By Bruce W. Halstead. Pp. x+146. (Cambridge, Maryland: Cornell University Press; London: Putnam and Co., Ltd., 1959.) 4 dollars; 30*s*.

IN this semi-popular, well-illustrated handbook, Dr. Halstead gives an account of marine animals that bite, sting or are poisonous to eat. He states that "it is not the purpose of this manual to throw needless scares into the skin-diving populace, but rather to point out some known facts regarding dangerous marine organisms, and to show what to do about the situation, if worse comes to worse".

He describes and illustrates each organism (and where appropriate, the venomous apparatus), including also the latest information on medical aspects, treatment and prevention. He has cast his net wide, from cœlenterates to marine reptiles and seals, and his handbook will be particularly useful to the aqualung diver, the biologist and the medical practitioner as the first compact guide to the subject.

Dr. Halstead appears to have listed all the important vertebrates, but among the invertebrates many dangerous creatures remain to be generally recognized. In the cœlenterates, for example, the author identifies a total of eleven species (out of a total of 25 stingers

listed by me after considerable searching of the literature). His list ranges from such mildly irritating shore anemones as *Actinia equina* and *Anemonia sulcata* to the deadly sea wasp (*Chiropsalmus*) that can kill in 3–8 min. Moderately severe stingers, like the coral reef hydroid *Lytocarpus*, the medusæ *Chrysaora*, *Pelagia*, *Lobonema* and the *Stephanoscyphus* stage of *Nausithoë* are not mentioned.

Likewise, we lack precise information for many other invertebrate groups on how many species are potentially dangerous. This is mentioned here, not in criticism of Dr. Halstead's most useful and up-to-date synopsis, but to indicate that our knowledge in this field is far from complete. W. J. REES

Insects and their World

By Harold Oldroyd. Pp. viii+139 (60 plates). (London: British Museum (Natural History), 1960.) 7*s*. 6*d*. net.

SO MUCH is known about the teeming millions of insects that to write about them both accurately and simply is by no means easy. Mr. Oldroyd is therefore to be congratulated on providing for the general public and for elementary students of insects a very useful introductory text. He touches lightly on their classification, structure, physiology, behaviour, adaptations and their importance to man. The style is always lucid, avoids technical jargon and is pleasantly illuminated by shafts of wit.

The only disappointment was to find in so lavishly illustrated a book that the plates had so little relation to the interesting stories told in the text. Scarcely any of the drawings or photographs show living insects in their natural environment, or attempt to illustrate points in the life-history. Many of the photographs show pinned insects, or dead ones awkwardly posed on rather unsuitable backgrounds. May we hope that in future editions some of the less-suitable photographs will be replaced by appropriate drawings? The drawings already used are good, but rather formal, however; that by Terzi of the blue-bottle makes the photograph facing it appear very crude. The figures and plates should also be numbered in a single series.

The book is well printed on glossy paper and is free from typographical errors. The very few minor errors of fact or interpretation will doubtless be corrected in the future editions which the book deserves. G. C. VARLEY

Advances in Pest Control Research

Vol. 3. Edited by R. L. Metcalf. Pp. vii+448. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1960.) 109*s*.

THIS, the third volume in the series "Advances in Pest Control", consists of nine articles by different authors who each examine a limited aspect of pest control research. There is a surprisingly extensive inter-relationship between individual essays which enhances their value by providing a wider view of the subject. The volume should prove to be a useful one.

Three essays written around groups of chemicals (organic halide nematocides by W. Moje, dithiocarbamate fungicides by R. A. Ludwig and G. D. Thorn, triazine herbicides by H. Gysin and E. Knüsli) differ in emphasis according to the characteristics of the chemicals, pests and crops involved and the reactions between them. The essay on translocation by J. W. Mitchell, B. C. Smale and R. L. Metcalf clearly shows the wider knowledge of plant structure and function than of the properties which determine the penetration and movement of chemicals in plants. The empirical nature of the use of mixtures of biologically active materials is illuminated by P. S. Hewlett, who discusses the varied investigations on the joint action of insecticides with balanced emphasis. The general lack of understanding of the complexities of the interaction between chemicals and organisms can again be seen in the essay on DDT-dehydrochlorinase by H. Lipke and C. W. Kearns, who barely hint at other possibilities of biological detoxication of DDT. F. P. W. Winteringham describes the labelled pool-technique as a way of searching for the effects of an interaction between chemicals and living organisms together with techniques which make the approach possible. The search for chemicals attractive to insects is reviewed by N. Green, M. Beroza and S. A. Hall, who classify attractants according to the type of response elicited (sex, food) and discuss their possibilities for controlling, or obtaining information about, insect pests. Knowledge and imagination are the bases of the procedure, described by R. C. Bushland, of controlling insects by male sterilization.

K. A. LORD

Blakeslee

The Genus *Datura*. By Aamos G. Avery, Sophie Satina and Jacob Rietsema. Pp. xli+289. (New York: The Ronald Press Company, 1959.) 8.75 dollars.

AN unfortunate title, for this is not, as one might imagine, a revision or monograph of the genus *Datura*, but rather a special kind of *Festschrift* compiled in honour of the late Dr. Albert F. Blakeslee, dealing with various aspects of the biology of a number of *Datura* species. Dr. Blakeslee devoted almost forty years to the study of the 'Jimson weed' (*Datura stramonium*) and its near allies, and this book shows just what can be accomplished by such intensive cultivation of a limited field. The results are certainly impressive, at least so far as genetical and cytological researches are concerned, and, for the taxonomist, it is especially interesting to have minute details of the mechanisms of variation explained on the whole lucidly and with some degree of consideration for those who are not professional geneticists. In this connexion the chapters on polyploidy, extra chromosomal types and gene mutations are particularly enlightening: it is surely by such studies of mechanisms rather than by controversy and hypothesis that the secrets of evolution and phylogeny will be revealed. Readers more concerned with practical problems of plant breeding will find much to interest them in the succeeding chapters on seed development, growth, processes in the embryo and seed, and barriers to crossability. The discourses on chimæras and radiation experiments should appeal equally to the theorist and practician. It is perhaps the taxonomist who fares worst in this symposium, for, making all due allowances, it cannot be pretended that the chapters on taxonomy and nomenclature are more than cursory. The section Brugmansia is almost wholly neglected, and we are not given any clear guidance as to the status of this group in relation to other species of *Datura*. The phytogeographers are not much better served; the geographical distribution of *Datura* species raises all

sorts of intriguing but unanswered queries. Are there any grounds, for example, for supposing that *D. stramonium* is indigenous in Europe, Asia or Africa? Is *D. leichardtii*, which is seemingly so nearly related to the Mexican *D. pruinosa*, really a native of Australia? Had a qualified taxonomist been privileged to work with Dr. Blakeslee's team, one feels that these questions and many others might have been answered. Deficiencies are almost certain to be found in such 'occasional' literature; but at least it can be said that "The Genus Datura" will be a most valuable help in the preparation of future monographs of this very interesting genus. R. D. MEIKLE

A Book of Ferns

By Greta Stevenson. Second edition, revised and enlarged. Pp. iv+168. (Hamilton, New Zealand: Paul's Book Arcade, 1959.) 13*s*. 6*d*.

GRETA STEVENSON'S "A Book of Ferns", a revised edition of an earlier work, deals exclusively with the ferns of New Zealand. Although not so comprehensive as Crooke's edition of Dobbie's classic, it is, nevertheless, a well-prepared little guide and it is well illustrated with simple line drawings. Primarily intended for the novice, two-thirds of the recorded species are described. The nomenclature throughout is good, if conservative, although authorities for names are unfortunately omitted. Keys based on position of sorus and on habit of growth should enable the reader to determine his plant with comparative ease. One may question the statement that the "best size for a herbarium sheet is 17 in. by 11 in." since the Kew-size sheet, adopted in many herbaria, is 16½ in. by 10½ in. The use of naphthalene, recommended as an insect deterrent, has lost favour these days, being largely superseded by the more effective *para*dichlorbenzene. Nevertheless, Greta Stevenson's book can be thoroughly recommended as a competent introduction to New Zealand ferns. A good glossary, a list of Maori vernacular names and notes on cultivation complete a work which admirably fulfils its purpose. F. BALLARD

Trees and Bushes in Wood and Hedgerow

By Helge Vedel and Johan Lange. Translated by C. H. R. Hillman. Adapted by H. L. Edlin. Pp. 224. (London: Methuen and Co., Ltd., 1960.) 16*s*. net.

THE similarity between the flora of the two countries has made it possible to adapt this book, compiled by a team of Danish foresters and artists, to suit British forest flora. Its aim is to provide a practical reference book to the character and appearance of all trees and shrubs to be found in the open countryside. Specimens grown only in botanical collections have not been included. Each species has a reference number, which simplifies the linking of the various sections.

The book begins with an introduction to five keys. These keys are for the identification of branches with: (1) needle-like or scale-like leaves; (2) opposite compound leaves; (3) opposite simple leaves; (4) alternate compound leaves; and (5) alternate simple leaves.

Next there is a section of excellent coloured plates of 120 different trees and shrubs, with many subsidiary sketches to assist identification. Then follows the section describing each of the 127 species, with small diagrams to explain botanical details and places of origin. Each is very clearly written.

There are four interesting short sections, namely: "The Tree's Wood"; "The Development of British Forests"; "Forest Tree Breeding"; and "Great Trees".

There are a Latin–English glossary, followed by a glossary of botanical terms and, lastly, an index. B. J. G. MAITLAND

Taxonomy of Flowering Plants

By C. L. Porter. (Series of Biology Texts.) Pp. xii+452 (600 illustrations). (San Francisco and London: W. H. Freeman and Company, 1959.) 44*s*.

THIS is an excellently produced and efficiently written handbook of the taxonomy of flowering plants for North American students. It is not easy to explain in a clear and interesting way the complex matters involved in the principles of taxonomy and nomenclature, but this book comes close to doing so. Within its limitations—it does not pretend to be an advanced text-book, and the plants mentioned as examples or figured are mostly North American—it is hard to find any important fault. The numbers of species assigned to various families and genera seem not infrequently to be on the low side—there are surely more than 5,000 species of Gramineae, but otherwise the text seems excellent. The text-figures and photographs, 600 in all, are unusually numerous and clear and do much in helping to give this book the attractive appearance it has. J. P. M. BRENAN

Die Cactaceae

Handbuch der Kakteenkunde. Von Curt Backeberg. Band 4: Cereoideae (Boreocereeae). Pp. xxxi–xxxviii+1927–2630. (Jena: Gustav Fischer Verlag, 1960.) 91 D.M.

HERR BACKEBERG'S fourth volume is devoted to the sub-tribe Boreocereinae of the semi-tribe Boreocereeae of the tribe Cereae of the sub-family Cereoideae. It thus includes the treatments of such larger genera as *Echinocereus* (73 species), *Pilosocereus* (60), *Cereus* (36) and *Melocactus* (36). Many of the numerous smaller genera have been proposed by the author himself, who defends the recognition of small genera in his foreword. The high standard of the numerous illustrations is maintained. Philatelists will notice (Fig. 2450) the portrayal of *Melocactus communis* on the farthing postage stamp of the Turks and Caicos Islands.

Plant Pathology

An Advanced Treatise. Edited by J. G. Horsfall and A. E. Dimond. Vol. 2: The Pathogen. Pp. xiv+715. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1960.) 22 dollars.

THIS is the second of three volumes intended to provide an advanced treatise on plant pathology. The first dealt with the diseased plant, and this one is concerned with what causes disease. In their prologue the editors indulge in words and definitions, and distinguish between three kinds of pathogen—animate, inanimate and viruses. They are in no doubt that insects are animate pathogens and are under the mistaken impression that insects are

'generally included in plant pathology in Europe', but, nevertheless, they wisely decide in the end to leave them with the entomologist. The opening chapter is a review of the nature, origin, and evolution of parasitism towards commensalism by specialization. Then follow two chapters on the reproduction of viruses, bacteria and fungi. The next six chapters are concerned with the nature of pathogenicity and cover the ability of the pathogen to breach the host by mechanical and chemical means, the importance of toxins, variability in the pathogen, and the inheritance of pathogenicity. There are also important contributions on spore germination and on soil pathogens in relation to the rhizosphere, but these are rather out of place and tend to break the continuity of the central theme.

About three-quarters of the text was prepared in more or less equal proportions by American and English authors. The other four contributions originated in Canada, India and New Zealand. There are comprehensive author and subject indexes and more than seventeen hundred literature references. It can be said now, without waiting for the third volume, that the editors and their advisory board have certainly achieved the task they set themselves in providing research workers and advanced students of applied biology with an exposition on plant pathology which is, in fact, unequalled in the English language.

W. C. Moore

British Pharmaceutical Codex 1959

Pp. xxix+1301. (London: The Pharmaceutical Press, 1959.) 70*s*.

"THE British Pharmacopœia" is mainly used by pharmacists. "The British Pharmaceutical Codex" is of more interest to the doctor; it tells him all he needs to know about the official drugs and their preparations, and adds a useful and authoritative summary of their actions and uses. It also gives specifications for other drugs, both old and new. The new "Codex" contains seventy new general monographs mainly dealing with drugs introduced in the past five years, and about one hundred of the old general monographs have been deleted, so that the new edition is shorter than its predecessor, which was itself shorter than the 1949 edition. This shrinkage is due to the elimination of remedies no longer used. The leech was fully described in the 1954 edition with an account of its actions and uses, and recommendations for storage; that monograph has now been eliminated, and the "Codex" has become less picturesque than it was and more like "The British Pharmacopœia"; the time will probably come when these two standard works will be amalgamated.

J. H. Gaddum

Food Poisoning, Food-borne Infection and Intoxication

Nature, History, and Causation; Measures for Prevention and Control. By Elliot B. Dewberry. Fourth edition. Pp. xvi+411+40 plates. (London: Leonard Hill (Books), Ltd., 1959.) 45*s*. net.

IT is a platitude to say that everything we eat is perishable, and it is therefore very difficult to understand why until relatively recently a large proportion of those entering the laboratories of the food industry were trained only in chemistry. Of these, some near enough to large industrial areas were able to attend classes in general bacteriology, a subject very difficult to teach except to full-time students. The remainder were forced to obtain their knowledge solely from text-books. The establishment of courses in food technology at various technical colleges has eased the situation, but the facilities are not yet adequate for the requirements of a virile industry.

First produced in 1943 at a time when the industry was desperately short of laboratory staff, Dewberry's book was a most useful source of information to those dealing with war-time problems of food handling and processing. The third edition in 1950 was still produced "in complete conformity with the authorized economy standards". The present edition, expanded by some 100 pages to include chapters on food hygiene, canned foods and their inspection, and (briefly) *Cl. welchii* food-poisoning, has changed little in quality of production. It has therefore become somewhat bulky for general use.

Although bacterial food-poisoning takes pride of place, sections are included on poisoning by metals, plants, fungi, fish and shellfish and on food allergy. For additional or confirmatory reading there are many references, making the book a most useful source of information for the food technologist and the seriously minded executive. It is, in fact, good value for money.

F. H. Banfield

Organic Reactions

Vol. 10. Edited by Roger Adams, A. H. Blatt, V. Boekelheide, Arthur C. Cope, David Y. Curtin, Frank C. McGrew and Carl Niemann. Pp. vii+563. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1959.) 96*s*. net.

THIS volume contains a treatment in the usual detail of three reactions capable of wide application in organic chemistry. The first, dealt with by S. M. Parmerter, concerns the coupling of diazonium salts with aliphatic carbon atoms. An explanation of its character is followed by discussions of its mechanism, scope and limitations, and synthetic applications; the experimental conditions and procedures are then considered; and lastly there is a tabular survey, classified in twelve sections, of the kinds of reactions in question. The treatment is limited to reactions in which the two nitrogen atoms of the diazonium salt remain in the new molecule.

The related Japp-Klingemann reaction is surveyed on similar lines by R. R. Phillips. The treatment of the third member of the triad, the celebrated Michael reaction, occupies the greater portion of the book (pp. 179–555) and affords a contribution of outstanding value: the thoroughness of this co-operative study by E. D. Bergmann, D. Ginsburg and R. Pappo, which was begun at the Weizmann Institute of Science, Rehovoth, is indicated by the accompanying list of 1,045 literature references.

At the end of this volume there are an author index and a chapter (subject) index covering Volumes 1–10 of this invaluable series.

John Read

Reports on the Progress of Applied Chemistry

Vol. 42, 1957. Pp. 910. (London: Society of Chemical Industry, 1958.) 100*s*.

THIS very valuable review has grown appreciably in size and price. The separate articles are all concisely written, and it would be difficult to say where, if at all, any limitation could be attempted. The book will mostly be of interest to industrial

concerns or research organizations, where price is not important. It contains summaries of a very large field of literature, much of which will be found only in large and specialized libraries, and maintains its high standard, the articles being by experts.

Fundamentals of Physical Chemistry

By Prof. H. D. Crockford and Prof. Samuel B. Knight. Pp. xvii+463. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1959.) 56*s*. net.

THIS book is based on an earlier one intended for pre-medical and other students with a limited knowledge of mathematics. It continues this plan, although the treatment is enlarged by additional topics, including three chapters on thermodynamics. The equations are deduced so far as possible, and special emphasis is given to units. Each chapter begins with a brief statement of its contents, and sub-headings and sections are titled, so that the reader knows just what is being discussed. Fully worked problems are given in the text and review questions and problems at the end of each chapter. Answers to problems are given. The treatment, especially in the part on electrolytes, is modern. The subjects covered are well selected, and the text is concise, carefully written, and clear, the authors having obviously taken great trouble with it. In future editions the conventions of sign of electrode potentials will doubtless be revised in accordance with recent recommendations, which will make the subject much clearer.

This is an excellent introductory book on physical chemistry which can be recommended to those teaching and learning the subject at this stage.

The Chemical Elements

By Helen Miles Davis. Second edition, revised. Pp. viii+198. (Washington, D.C.: Science Service, Inc.; New York: Ballantine Books, Inc., 1959.) 50 cents.

THIS is a very unusual and interesting little book. It was written by Helen Miles Davis, who died in 1957 when the second edition was in preparation. The revision was completed by Dr. Seaborg, the authority on transuranium elements. There is a survey of each element, including the history of its discovery, the whole based on the Periodic Table, and each group has a table of the atomic structure of the elements contained in it. Much of the information is in the actual words of the discoverers, taken from original papers, and this makes the book particularly interesting. The sources, isotopes and properties of each element are given concisely and some characteristic compounds are mentioned. There is nothing superfluous in the book, and its contents are of high standard.

Chemistry for Engineers

An Introductory Course. By Edward Cartmell. Pp. vii+172. (London: Butterworths Scientific Publications, 1959.) 25*s*.

THIS small book deals with a number of topics of interest to students of engineering which do not usually find a place in the ordinary elementary courses provided for science students. Even if engineering students attend such courses the book will provide a useful supplement to them. Previous knowledge is limited to such as would be available in schools, and the treatment is restricted to a selection of the more important applications of chemistry of interest to engineers. It includes such topics as fuels, metals and corrosion, water treatment, lubrication and nuclear power. The amount of space devoted to atomic and molecular structure and of valency bonds is rather large, but the treatment is intelligible and interesting. There is a good balance between general theory and practical applications, and the book should be very useful to lecturers called on to cater for the requirements of engineers who have only a limited time to devote to chemistry.

J. R. PARTINGTON

Water Treatment Handbook

Compiled by R. Leviel. Second English edition, revised. Pp. 561. (Suresnes (Seine): Degrement Acfi S.A., 1960. Distributed by Hugh K. Elliott, Ltd., 199 Piccadilly, London, W.1.) 60*s*. net; 8.40 dollars.

THE first English edition of this book was published in 1955, and there have been four French editions since 1950. After a section on methods of analysis of water and of materials used in water-works practice, the bulk of the work deals systematically and in considerable detail with the various processes used in treating water for domestic and industrial supply. The author is the technical manager of a French company which supplies water-works equipment, and many of the numerous photographs and diagrams refer to the products marketed by the firm. Thus, although methods of treating water do not differ widely in different countries, the present account is of particular value in describing the methods used in France.

Since the last edition, a new and useful section has been added on French legislation governing water supplies and the discharge to streams of sewage and industrial wastes, and containing also the recently published "International Standards for Drinking Water" put forward by the World Health Organization in 1958. There is a substantial section, more than 100 pages in length, of formulæ, tables of constants, and the like, which are used in the design of distribution networks and in the treatment of water by physical and chemical methods. There is also a chapter on the treatment of sewage and industrial wastes, but the standard of this, both as regards material and translation, is much below that of the rest of the book.

Atmospheric Diffusion and Air Pollution

Proceedings of a Symposium held at Oxford, August 24–29, 1958. Edited by F. N. Frenkiel and P. A. Sheppard. (Advances in Geophysics, Vol. 6.) Pp. xvii+471. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1960.) 12 dollars.

IN order to bring together scientists from the various fields in which atmospheric diffusion is important, an international symposium was arranged jointly by the International Union of Theoretical and Applied Mechanics and the International Union of Geodesy and Geophysics. The symposium was held at Oxford in August 1958, with Dr. F. N. Frenkiel and Prof. P. A. Sheppard as joint secretaries. Seven

sessions dealt respectively with: (1) a genera survey; (2) recent findings on atmospheric turbulence; (3) theory of turbulent diffusion; (4) diffusion of heavy or finite particles; (5) transfer through the troposphere and stratosphere; (6) effects of thermal stratification; (7) pollution patterns from point and area sources. Altogether more than forty papers dealing with different facets of the diffusion problem, and presenting the views of authors with different interests, were discussed. These papers, with notes of the ensuing discussions, are brought together in this volume; a few papers which are published elsewhere are represented by extended summaries.

This collection shows how the balance of contributions has, in recent years, swung from the experimental physicist to the theoretician. Possibly this reflects the wealth of empirical data now available. A notable feature is the increasing emphasis on the spectrum of turbulence.

This volume differs from others in the same series which contain articles summarizing selected topics. It is a collection of new results and new ideas which should do much to stimulate scientists who are interested in diffusion. The production is excellent and the editors should feel well satisfied with this final product of their labours. A. C. BEST

Australian Atomic Energy Symposium, 1958

Proceedings of a Symposium on the Peaceful Uses of Atomic Energy in Australia, held in Sydney from June 2 to 6, 1958. Pp. xi+788. (Melbourne: Melbourne University Press; London: Cambridge University Press, 1960. Published on behalf of the Australian Atomic Energy Commission.) 100*s*. net.

AUSTRALIAN interest in the scientific and technological aspects of atomic energy was demonstrated in a symposium held in Sydney in June, 1958, under the auspices of the Australian Atomic Energy Commission. The full report of this symposium, containing 114 papers together with discussions, is now available in book form. The scope of the symposium was all-embracing and ranges from the geology of Australian uranium ores and the extraction of uranium from them, the prospects for nuclear power, descriptions of *Hifar*, the 10-MW. heavy-water-moderated research reactor of the Australian Atomic Energy Commission at Lucas Heights, cosmic radiation, the use of radioisotopes in physical and biological research, to education and controlled thermonuclear reactions.

Some of the papers were presented by overseas visitors, and these were generally of a review nature, but most were from Australian sources, the Australian Atomic Energy Commission itself, the Commonwealth Scientific and Industrial Research Organization and other Commonwealth and State Departments, universities, medical schools and industry. Some papers were of a topical nature, others described original work. The general impression is that of work of high quality and of a lively interest.

The volume contains such a wide variety of papers that it is fated to become a library reference book, but there can be no doubt that the symposium which it reports was a very successful affair. Not only did it bring together the wide range of Australian interests in the peaceful uses of atomic energy, but also it stimulated public interest, as was one of its intentions.

A. S. WHITE

Classical Dynamics

By R. H. Atkin. Pp. ix+273. (London: William Heinemann, Ltd., 1959.) 30*s*. net.

WITHIN the limits imposed by the author he has produced a useful book. The concise explanations are good even though at times the reader may be dissatisfied with them and wish to learn more; this is especially true of the chapter on small oscillations. Moreover, the large number of worked examples and problems should be of value to students and teacher alike.

In the preface the author, who is now principal of Unischol Tutorial College, says: "I have written this book in the belief that it is possible to learn dynamics and answer examination questions at the same time", and later "It therefore seems sensible to present the subject by first explaining the ideas which are involved, in a suitable algebraic framework, and then illustrating the scope of their applications by solving a large number of typical problems". It is written for physicists and covers most of the classical dynamics in two and three dimensions needed by undergraduates up to, but not including, a reference to Hamilton's equations and variational methods.

Thus "Motion in a Plane" (Chapter 5, Section 3) consists of a clear one-page description of the importance of linear momentum, angular momentum and energy, and of the equations which contain them, together with five well-known examples which between them illustrate problems in trajectories, two particles, the use of conservation laws and rotating axes.

A book of this type is not a text-book but a manual, and the publishers admit this on the cover. No attempt is made to describe the principles of mechanics or to explain how these principles are used in the construction of apparatus and the description of physical phenomena. There is no suggestion that there are difficulties in understanding, for example, angular momentum and gyroscopic motion and that these difficulties have caused scientists to write monographs on these matters. So far as I can discover, modern physics is not even mentioned. In short it in no way resembles my idea of a good text-book on mechanics, either for a mathematician or for an engineer or a physicist.

I think it is fair to ask whether there is any need nowadays for text-books on dynamics except for engineers and for examinations. Since the excellent books by Lamb many more have been published, but few, if any, of them are better. Mechanics is only one of the branches of physics from which admirable problems can be drawn to illustrate the use of the differential and integral calculus. The idea that mechanics and applied mathematics are one and the same thing is Edwardian and can now be quietly forgotten. G. J. KYNCH

Optics

By Dr. C. J. Smith (A Degree Physics, Part 3.) Pp. vii+736. (London: Edward Arnold (Publishers), Ltd., 1960.) 63*s*. net.

THIS volume continues Dr. Smith's series of books designed for students taking the B.Sc. General degree. The early chapters deal with the general properties of waves and vibrations, with the measurement of the velocity of light, and with the wave-theory and Newton's corpuscular theory. Lenses

are followed by a detailed treatment of non-paraxial rays and aberrations, and of the simpler optical instruments. The full and critical discussion of colour and colorimetry and the two chapters on interference in thin films and in thick plates are good and up to date, as chronicles of progress. But it seems strange to find, in a book of this level, accounts of line spectra and photoelectricity that do not mention quanta or photons; a brief mention of the electromagnetic theory in the last chapter so that polarization by reflexion can be explained in terms of the Fresnel equations (quoted); and nearly everything that Michelson is known for except the Michelson–Morley experiment. It is almost as if the book had been censored; in which case a titillating phrase about the special theory of relativity on p. 35 has been missed.

One must of course be reasonable. The author has had to decide where and when in this monumental series he will introduce a given topic, and its very scale must lead to an almost ruthless compartmentalizing and some very difficult decisions. One thing has to be done thoroughly at a time, and the student who has worked through the text of this volume will have gained a very thorough grounding in optics. He should certainly never find himself at sea; so that this compartment really need not have been quite so watertight.

Thermodynamics

By Gordon J. Van Wylen. Pp. xxiii+567. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1959.) 64*s*. net.

PROF. VAN WYLEN'S book is directed to the engineer, and here the comparison would probably be with Roberts and Miller, or with Zemansky. The idea of temperature and the zeroth law of thermodynamics, and the properties of pure substances, are first discussed; entropy is treated as an important and exchangeable physical property of a system; and the concept of irreversibility is thoroughly explored. Practical power and refrigeration cycles, and the operation of turbines, are explained, with many examples. The interesting thing here is the emphasis on general principles and their applications to the real world; the older outlook was perhaps centred on the ideal gas and the reversible cycle and a mathematician's entropy that started as a perfect differential and ended up as the logarithm of a probability. Some of the revered conventional textbook material cannot be found here at all, and some is mentioned only briefly; this has made for a clearer and more attractive presentation of the macroscopic point of view. G. R. NOAKES

Modern Physics

By Prof. H. A. Wilson. Fourth edition. (The Student's Physics.) Pp. xv+473. (London and Glasgow: Blackie and Son, Ltd., 1959.) 40*s*. net.

THERE must always be some doubt about the length of time for which a text-book should be kept alive. The first edition of this book was published in 1928, and it was then up to date and authoritative; now it is sadly behind the times. The author is, of course, an authority on the theoretical aspects of the physics he treats, but he does not seem to be at home in the new sections on semi-conductors (6 pp.), low-temperature physics (11 pp.), and elementary particles (2 pp.). Some of the chapters such as that on X-ray crystallography look old-fashioned, and it is surprising to find a topic such as the J phenomenon still included.

The trouble is that a text-book cannot be kept up to date merely by adding sections "here and there" (the phrase used in the dust cover); there must be pruning and re-distribution as well. The author has sadly failed to live up to the title of "Modern Physics". H. LIPSON

Methods of Experimental Physics

Vol. 1: Classical Methods. Edited by Immanuel Estermann. Pp. xii+596. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1959.) 12.80 dollars.

THE series of volumes of which this is the first covers the whole field of experimental physics, and the term "Classical Methods" is explained in the preface as meaning the kind of experiment that is associated with the conventional subdivisions of macroscopic physics. It deals with the evaluation of measurements; the definitions of fundamental units and the determination of 'best values' of the fundamental constants; the mechanics of solids, of fluids, and of vibrations; heat and thermodynamics; optics; electricity; and magnetism. The authors, while working as a team and preserving a uniformity of style, have enjoyed considerable latitude in treatment; some, as P. M. Marcus on thermodynamics, have gone fairly deeply into the underlying theory; others, as J. R. Holms and G. L. Weissler on optics, have concentrated on a full discussion of experimental details. The result is a concise summary of modern techniques, which is in many places a good deal more readable than the usual kind of reference book. It is intended for the physicist who needs a concise and critical guide on matters outside his own special field, and should prove useful for this purpose. G. R. NOAKES

Nuclear Reactor Materials

By Dr. B. R. T. Frost and Dr. W. B. Waldron. (Nuclear Engineering Monographs.) Pp. vii+79. (London: Temple Press, Ltd., 1959.) 12*s*. 6*d*. net.

THIS monograph is one of a very useful series dealing with the physics and engineering of nuclear reactors. It is intended for the use of university and technical college students, research assistants and qualified technicians who require a broad understanding of those topics of nuclear engineering outside their own particular field of study. Previous volumes in the series have dealt with basic nuclear physics, reactor theory, heat transfer, shielding, and reactor control and instrumentation. The present volume gives an excellent outline of the special physical and mechanical properties required of the structural and fuel materials used in reactors and of the recent metallurgical developments in order to provide these materials. The monograph is based on a series of lectures which was given by members of the staff of the Metallurgy Division, Atomic Energy Research Establishment, Harwell, to students in the Department of Nuclear Engineering, Queen Mary College, London, and both the authors are members of the staff of the Division.

The contents consist of six chapters and a comprehensive bibliography. In Chapter 1 the more important aspects of modern metallurgical theory are surveyed, and the common metallurgical terms are explained. Chapter 2, devoted to structural materials, deals separately with aluminium, magnesium, beryllium, iron and steel, and the refractory metals, zirconium, niobium, tantalum, vanadium and molybdenum. Subsequent chapters deal with the fuel materials (uranium, plutonium and thorium); liquid metals as coolants and as carriers for liquid-metal fuels and blankets; ceramics and metal-ceramic mixtures used as fuels, moderators, or as control and shielding materials; and the final chapter discusses the problem of corrosion of the fuel and canning materials by the various coolants. The text is adequately supplemented by tabulated data and clear line drawings. S. WEINTROUB

Nuclear Reactor Optimization

By P. H. Margen. (Nuclear Engineering Monographs.) Pp. x + 81. (London: Temple Press, Ltd., 1960.) 12*s*. 6*d*. net.

THE book which is under notice is intended to provide students and research assistants with a broad understanding of specific topics in this field. It competently describes a technique, based on fairly elementary formulations of the relevant theory, for varying the parameters of a given power reactor design to reach the lowest overall power cost and gives a detailed discussion of the application of this technique to a heavy-water-moderated, carbon-dioxide-cooled reactor.

Such a discussion requires a brief comment on almost all the factors which affect the design of the reactor, and the author has succeeded in providing a mass of detailed information without obscuring the main lines of the argument.

This presentation may lead the reader to conclude that effective design can therefore always be achieved by appropriate modification of the elementary mathematical procedures described in this book. In practice, validation of a particular design requires the use of markedly more sophisticated computational techniques. These provide a starting point for an optimization study and must again be used to check the optimized design if it departs appreciably from the initial concept.

In fact, a situation in which all main reactor parameters can be fixed merely by a minimization of total power cost is unusual—and the inclusion of constraints such as peak fuel centre temperature or burn-out margin is vital to the analysis. The essential role of such constraints is insufficiently emphasized in the presentation.

These criticisms do not obscure the merits of a clear presentation of an important aspect of reactor design.

J. FELL

University Physics

By Prof. F. C. Champion. Revised, one volume edition. Pp. viii+786. (London and Glasgow: Blackie and Son, Ltd., 1960.) 30*s*. net.

THIS book aims at giving what might be called basic physics—roughly the content of first- and second-year university courses—in one volume. It succeeds in this aim by sternly resisting any temptation to stray on to specialized topics, and it thus gives the impression of being rather dull. There are, however, three chapters at the end that deal with modern physics, but they do not go deeply into any aspects.

Many examples of examination questions, with answers and hints for solutions, are also included. These are not always wisely chosen; often they are purely bookwork questions which do not give the aid to students that quantitative problems would give. Moreover, the practical element sometimes seems to be lacking; in a.c. theory, for example, the emphasis—quite rightly—is on basic principles, but there should also be some attention paid to producing answers in ordinary units.

It might also be mentioned that a Cartesian convention is used for optics, in accordance with general university practice. In electricity and magnetism the C.G.S. system is used, the M.K.S. system being dismissed rather summarily.

To summarize, this is a sound book that will be useful as a reference book for students, but it is unlikely to fire them with an enthusiasm for physics.

H. LIPSON

Analytical and Canonical Formalism in Physics

By Prof. André Mercier. (Series in Physics.) Pp. viii+222. (Amsterdam: North-Holland Publishing Company; New York: Interscience Publishers, Inc., 1959.) 40*s*.

LAGRANGE'S formalization of analytical dynamics by sets of differential operators applied to certain functions characterizing a dynamical system led to Hamilton's variational principle and his canonical equations. The extension of the field of application of Hamilton's principle, from classical dynamics to more general physical systems, may sometimes have seemed to be an exercise in pure mathematics, but relativity and quantum field theory have renewed the interest in structural formalism, so that it is not surprising that one of Prof. Mercier's aims is to show that much of the modern formal field theory is of pre-quantic character. The emphasis is on structure, but here and there illustrations from specific physical domains are given, and a number of problems for the reader are proposed; these are not examination-type questions, but generally ask for the completion or extension of abbreviated detail in the text. The book provides a profound investigation of the role of basic mathematical formalism in physics, from Lagrange to Dirac, and will repay those readers who are prepared to follow a closely argued mathematical essay in anatomy.

T. A. A. BROADBENT

A Course in Applied Mathematics

By Prof. Derek F. Lawden. Pp. xv+655. (London: English Universities Press, Ltd., 1960.) 70*s*. net.

PROF. LAWDEN'S book is chiefly intended for students reading for Part 2 of the London General B.Sc. under the recently revised regulations. It conveniently contains all the applied mathematics required by this syllabus: Lagrange's equations, but not variational principles, in dynamics; the elements of the Faraday–Maxwell electromagnetic theory and foundations of potential theory; stress and strain and simple elastic problems; basic equations for the motion of an ideal fluid, with simple instances of irrotational flow and of vortex motion.

The text is clear and logically organized; a knowledge of vector algebra is assumed, but vectors are used sensibly and appropriately, and no attempt is made to force every argument into a vector mould. The operators 'grad', 'div' and 'curl' arise naturally in field theory, though perhaps a little more stress might have been laid on the fact that these are simply three aspects of the single Hamilton operator ∇. There is a good supply of worked examples and of exercises for the student, carefully selected from degree examinations to illustrate the principles and details of the theory.

This is a very useful text-book, and if it is a little deficient in outlook value, that may be because the author has chosen to work thoroughly in a carefully restricted domain. T. A. A. BROADBENT

How Photography Works

By Dr. H. J. Walls. Pp. 352. (London and New York: Focal Press, Ltd., 1959.) 42*s*. net.

THIS book can be strongly recommended to those making a career in the profession of photography who have already acquired some photographic knowledge. Despite some good attempts by the author to justify his claim in the preface that no scientific knowledge is assumed, it must be stated that the book would prove difficult reading for any person without a good knowledge of general science at Intermediate examination level. While not being a text-book, it would be excellent general reading for such people and, for this reason, it should also appeal to amateur photographers having a similar educational background.

After the first chapter on the formation of an image, which includes many features of lens design, there follow nine chapters on the mechanisms of the photographic process from initial exposure to the completion of processing. Two chapters deal with the subjective aspects of viewing photographs and there are also two chapters on colour photography. After each chapter good references are given for further reading, and the index has been carefully prepared.

R. B. COLLINS

Handbook of Textile Fibres

By Dr. J. Gordon Cook. Pp. xxv+422. (Watford: Merrow Publishing Co., Ltd., 1959.) 15*s*. net.

THIS book well justifies its title. It is most handy for looking up things about textile fibres in use to-day, of every kind apparently, natural and man-made, that one can think of. They comprise natural fibres, vegetable, animal and mineral; regenerated fibres of polysaccharide and protein origin; and synthetic fibres from polyamides, polyesters, polyvinyl derivatives, polyolefines, glass, ceramics, metals—there are, in fact, almost four double-column pages of them in the index. That does not mean, though, that the book is stodgy and chiefly masses of tables—far from it: also presented are the history and economics, production and processing (with special attention to dyeing), structure and properties, the behaviour of the fibre in practical use, and technical notes besides; all set out compactly and systematically yet achieving the double purpose of a reference book for the more experienced technologist and of an instructive general guide for the beginner. It is comprehensive enough as an introduction to textile fibres as a whole, and also provides comprehensive details about them as individuals. It could scarcely be more useful for its size, and is strongly recommended.

W. T. ASTBURY

Siberian Arctic

The Story of the Siberia Company. By Jonas Lied. Pp. 214+31 plates. (London: Methuen and Co., Ltd., 1960.) 30*s*. net.

THE events described in the main part of Mr. Lied's book took place during 1910–1920, though they are prefaced by an admirable *résumé* of the previous history of Siberia and followed by an account of what is known of events under Soviet rule.

In 1910 the only practical transport routes from the vast Siberian plains were along the course of the Rivers Obi and Yenisey; the Obi and its tributaries navigable for some 9,000 miles, and the Yenisey for 2,000. To the south the rivers met the Trans-Siberia Railway, a means of transport to the west, but a prohibitively expensive one for trade purposes; and to the north they flowed into the Kara Sea, a potential cheap waterway to the markets of Europe and America. The possibilities of this route had interested various merchant adventurers, but, until 1910, none of them had possessed the necessary business ability and resources to develop them. Then Alfred Derry, buyer and director of Messrs. Derry and Toms, drapers of Kensington High Street, London, caught a glimpse of the vision during visits to the annual trade fair at Nijhny Novgorod. A chance meeting with an energetic young Norwegian, Jonas Lied, followed, and early in 1912 was formed the Siberian Steamship Manufacturing and Trading Co. Ltd. Lied himself carried out all the investigations and negotiations at the Russian end, and his account of those exciting days is the best part of the book. The first successful season was in 1913 when cargoes of cement and assorted trade goods were exchanged for two camels from Turkestan, two bears, a roebuck and an assortment of more-valuable, if less-colourful, local products. Exports from Siberia included timber, flax, hemp, wheat, hides, butter and potash; imports were machinery, cement and general trade goods. The company, after initial vicissitudes, was advancing towards success when the Russian revolution put an end to its prospects, though it was a long time dying against a somewhat tedious background of internal squabbles. L. M. FORBES

Geology of Norway

Edited by Olaf Holtedahl. Pp. xii+540, with 21 separate maps. (Oslo: Norges Geologiske Undersokelse, No. 208, 1960.) 100 Norwegian crowns.

Geology of Sweden

Description to accompany the Map of the Pre-Quaternary Rocks of Sweden. By N. H. Magnusson and others. Pp. 177, with map (1 : 1,000,000) in three sheets. (Stockholm: Sveriges Geologiska Undersokning, Ser. Ba, No. 16, 1960.) Text 15 Swedish crowns, map 45 Swedish crowns.

MODERN text-books on the geology of Norway and of Sweden have, until now, been available only in the national languages and in Russian translations; and a most welcome outcome of the twenty-first International Geological Congress in Scandinavia is the appearance of these new works in

English, compiled by the respective Geological Surveys. The text on Norway, by 21 authors, carefully summarizes the extensive literature and is particularly valuable for its well-chosen bibliographies. It is accompanied by an attractively coloured 'solid' map of the country on the scale 1 : 1,000,000, a 'drift' map (1 : 2,000,000), and nineteen other maps on various scales illustrative of classical Norwegian districts and of the economic geology. The memoir on Sweden is the work of five authors and, like the maps, relates to the solid geology only; but a comparable monograph by G. Lundqvist on the Quaternary formations (Stockholm: Sveriges Geologiska Undersökning, Ser. Ba, No. 17, 1960), with drift maps, has been published separately at the same price. All these publications will have a long life and should find a place even in the smaller geological library. C. F. DAVIDSON

The Early Lectures of Ralph Waldo Emerson

Vol. 1: 1833–1836. Edited by Stephen E. Whicher and Robert E. Spiller. Pp. xxvii + 545. (Cambridge, Mass.: Harvard University Press; London: Oxford University Press, 1959.) 100*s*. net.

SOON after his resignation from the pastorate of the Unitarian Church at Boston, Emerson considerably extended the cultural activities of the district by a series of lectures for which he has become well known. They were particularly concerned with the elucidation of natural phenomena, the biographies of great men and literature. To each lecture Emerson brought the fruits of keen observation, wide reading and powerful thinking. The result was a many-sided contribution to knowledge and philosophy, which, in this new work, emerges with a freshness which is remarkable for material published one hundred and twenty years ago. Reasons for the study of natural history, man's place in the universe, Emerson's keen analysis of the place of water in Nature; notes on his wanderings in Italy; the life-histories of Luther, Michel Angelo Buonarroti, Mellor, George Fox, Burke; an account of the traits of the "English National Genius", all reveal Emerson as a man whose contributions to cultural life were deep and wide-ranging.

Profs. Whicher and Spiller have worked long and patiently to produce the lectures in a form complete with extensive technical and informative notes which make them invaluable for reading material originally intended for oral communication.

Subject Catalogues

Headings and Structure. Pp. 186. (London: The Library Association, 1960.) 22*s*.; 3.30 dollars.

IN this book Mr. Coates, who has been in charge of the cataloguing side of the "British National Bibliography" almost from its inception, deals with some of the problems which arise when an attempt is made to build subject catalogues, classified or alphabetical, on some systematic basis. It is concerned essentially with first principles, but assumes some background knowledge such as can be acquired from a standard text-book on cataloguing, and it not only directs attention to the shortcomings of some of the classification schemes in general use but also provides a timely warning against excessive reliance on mechanical information retrieval, and a reminder that a machine cannot produce more than has originally been put into its construction. After describing C. A. Catto's contribution to the systematization of alphabetical subject indexing, Mr. Coates reviews the subsequent contributions to subject-heading theory of Keiser, Ranganathan and Faradane. Then, after a chapter on the dictionary catalogue since Cutler, he examines the contribution of classification and outlines the application of Ranganathan's chain procedure to the colon classification and to the decimal classification. Finally, after considering the use of group arrangement in the subject index, Mr. Coates discusses the subject catalogue from the point of view of the user. Comprehensive references to the literature enhance the value of a scholarly book not merely to practising cataloguers and to students of cataloguing but also to those concerned with the further research in classification which is still required.

Britain's Scientific and Technological Manpower

By George Louis Payne. (Prepared for the President's Committee on Scientists and Engineers.) Pp. xiii + 466. (Stanford, Calif.: Stanford University Press; London: Oxford University Press, 1960.) 45*s*. net.

THIS book is based on a review of British official documents dealing with technological man-power undertaken at the request of President Eisenhower's Committee on Scientists and Engineers. Essentially it is an expansion of an annotated bibliography of official documents and publications concerning British scientific and technological man-power and education, and this literature is covered comprehensively up to the time of Lord Hailsham's appointment as Minister for Science. With the exception of the Crowther Report and the second White Paper on Industrial Research and Development Expenditure, 1958, there is very little of importance that is not covered, and the value of the survey both to the American and to the British reader is enhanced by the effort made to present where possible comparable American statistics.

The scope of the survey and the broad view taken are sufficiently indicated by the chapter headings. Introductory notes on terminology, etc., and a chapter on the problem and its background are followed by chapters on technical man-power and its employment in 1956 and on current and expected demand for scientists and engineers. Three chapters follow on the secondary schools, the universities and on non-university channels to a technical education. Next come two chapters on the expansion of educational facilities and on the expansion of educational opportunities, the latter dealing with scholarships, student release by employers and the like; and finally two chapters on research and development and on technological expansion and the social scene. There are some supplementary notes on professional terms and institutions and on the universities in an appendix, and also some notes on American man-power statistics.

What critical comment the book contains is mainly in the last chapter; but the value of the book lies in its comprehensive presentation of published information on the scientific and technological man-power situation in Great Britain since the Second World War in all its varied aspects. It is an admirable reference work, and British as well as American readers should be grateful for the thoroughness with which the information has been collected and the clarity of its presentation. R. BRIGHTMAN

(*Continued from page* 806)

a consistent direction of magnetization up to 4° away from the magnetizing field direction. This natural anisotropy precludes the use of separate specimens for non-pressure and pressure experiments.

This factor, together with the grain-size factor, may have contributed to the experimental results which led Stott and Stacey to suggest that the effect of pressure on a rock acquiring a thermoremanent moment was completely reversible.

It is hoped to publish in the near future a fuller description of the experiments and results of this investigation, which has been carried out with the supervision and encouragement of Prof. J. M. Bruckshaw.

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METEOROLOGY

Autumn Temperatures in the Red Sea Hills

DURING the autumn vacation, we made geomorphological and biological surveys in the Red Sea hills and coastal plain north of Port Sudan. Details of these will be published later. While trekking among uncharted jebels in the area 36·50° E., 21·00° N., high surface temperatures were recorded, especially on wind-blown sand. For example, on September 24, 1960, at 1300h. local time, when the air temperature varied between 40·5 and 43·5° C. (105–110° F.) the surface sand temperature was 83·5° C. (182·5° F.) as measured with an electrical resistance thermometer employing thermistors[1]. The only animal to be seen was a solitary grasshopper. Four hours later, when the temperature had fallen to 32·0° C. (90·0° F.), the sand temperature had dropped 45·5° C. to 38·0° C. (100·5° F.) and some ants were crawling over it.

These results give some idea not only of the enormous temperature fluctuations that occur in desert regions[2,3] but also of the high ground temperatures that are by no means unusual in the Sudan even quite late in the year. They compare with 84° C. (183° F.) recorded on the Loango Coast close to the equator, 78° C. (172° F.) on a sand dune in the Sahara[2], a black bulb temperature and sand surface temperature of 58° C. (136° F.) near Cairo[3]. Very much higher temperatures were obtained in fine wind-blown sand, which must have high insulating properties, than on mixed or coarse sands, gravel or rock surfaces.

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RADIATION CHEMISTRY

Kinetics of Radiation-induced Chemical Reactions

THE development of linear accelerators which can produce electron pulses a few μsec. long with a peak current of several hundred m.amp. and an energy of several MeV. has made possible the study of chemical reactions by techniques similar to those used in flash photolysis. A single pulse from this type of machine will deliver a dose of the order of several thousand rads to a few ml. of liquid and should in many cases produce a chemical change large enough to be easily detectable by optical absorption with a time resolution as low as 0·1 μsec. Experiments of this kind, in which the production of the benzyl radical from benzyl compounds in organic solutions was investigated, have already been described by McCarthy and MacLachlan[1]. I am doing some similar work on various aqueous solutions, and this communication briefly describes my apparatus and some of the preliminary results obtained with it.

Irradiations are carried out at the Linear Accelerator Facility in the Scientific Apparatus Department, Associated Electrical Industries, Ltd., Manchester, which has available a machine producing 2 μsec. pulses of 4-MeV. electrons[2]. The irradiation cell consists of a thin-walled 'Pyrex' tube 20 mm. diameter and 50 mm. long, closed with quartz end-windows. The electron beam enters through the side of this tube, and a beam of light from a high-pressure mercury lamp passes along its axis. The optical system is arranged to focus the transmitted light on to the entrance slit of a monochromator and then on to a photocell. The photocell output passes through an amplifier with a rise time of about 0·1 μsec. and is applied to the vertical deflexion plates of a cathode-ray oscilloscope the horizontal sweep of which is arranged to start a few μsec. before the electron pulse. In this way traces are obtained showing the time variation in optical absorption of the liquid in the irradiation cell at any chosen wave-length. With the monochromator entrance slit closed a spurious signal is obtained and shows as 'noise' on the oscilloscope screen. This noise lasts for 2 μsec., and is caused by electrical interference produced at the same time as the pulse. Its amplitude is equivalent to a few per cent of the full signal obtained from the light source, and this limits the change in light intensity which can be detected during the pulse to a few per cent. This relatively low level of interference has been achieved by suitable electrical shielding and also by locating the monochromator outside the irradiation area to eliminate gamma-ray effects on the photocell and amplifier. Light is transmitted to the monochromator via an optical system of high aperture with a path-length of about 10 m. Traces obtained with the light source off and the monochromator slit open show an emission of light from the solution caused by the Čerenkov effect. The amplitude of this emission is fairly constant for 2 μsec., and the rise and fall times are a few tenths μsec. The optical system was designed to reduce the quantity of this light reaching the photocell to a minimum, and in practice the amount received is of the order of 10 per cent of the light from the lamp. The true absorption of a solution during the pulse is found by comparing traces made with the lamp on and off. The effects of Čerenkov light and electrical interference become

negligible a few tenths μsec. after the pulse, and from this time onward it is possible to detect changes in light intensity of about 0·1 per cent. The lamp output stays constant to better than this for periods of several hundred μsec., and changes in its output only become a limiting factor over longer intervals. Fig. 1 illustrates the performance of the apparatus at high sweep speed and high sensitivity. It was taken at 3100 Å. with once-distilled water containing dissolved air and shows an absorption after the pulse which decays with a short time constant, followed by a longer one. During the pulse the spot was deflected off the screen by the signal from the Čerenkov light. The amplitude of this deflexion was smaller with the lamp on, thus showing the presence of absorption during the pulse.

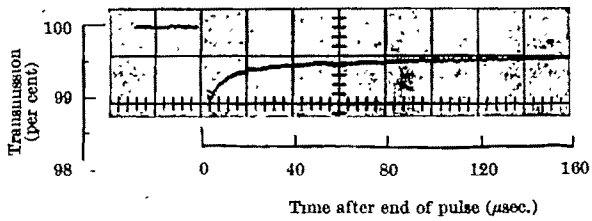

Fig. 1. Optical transmission of water at 3100 Å. ($\Delta\lambda$ 100 Å.) after a 2-μsec. electron pulse

With many solutions, permanent changes in optical absorption are produced by radiation because of the formation of stable products. I have examined the rate at which these changes occur in 5×10^{-5} molar ceric sulphate (in normal sulphuric acid) and also in three different strengths of ferrous ammonium sulphate (in 0 8 normal sulphuric acid containing 10^{-3} molar sodium chloride). Ceric sulphate absorbs light at 3350 Å. and is reduced to the non-absorbing cerous form by radiation. After a single electron-pulse the optical transmission at this wave-length was found to increase with a half-time of approximately 100 μsec. towards a new steady value. Ferrous ammonium sulphate, on the other hand, is transparent in the ultra-violet and is oxidized by radiation to the ferric form which has a broad absorption band with a maximum at 3100 Å. The optical transmission at 3150 Å., after a single electron pulse, was found to decrease towards a new steady value at a rate dependent on the initial concentration of ferrous ion. Fig. 2 shows a trace obtained with a 10^{-3} molar solution. The small dot in the top left-hand corner is the transmission immediately before the pulse and the steady decrease to a nearly constant value of about 85 per cent at 5 msec. is attributed to the production of ferric ion. The sharp transient just after the pulse was also found in sulphuric acid and is

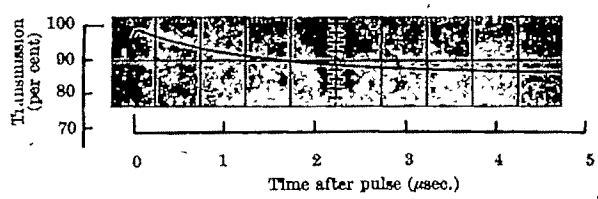

Fig. 2. Optical transmission of ferrous ammonium sulphate solution at 3150 Å. ($\Delta\lambda$ 100 Å.) after a 2-μsec. electron pulse. 10^{-3} molar ferrous solution, 10^{-3} molar sodium chloride, 0 8 normal sulphuric acid

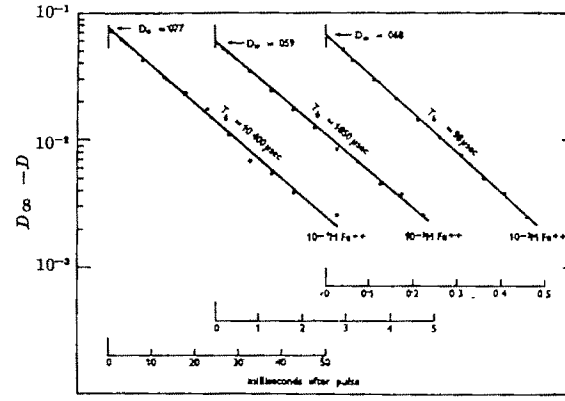

Fig. 3. Rate of appearance of ferric ion in ferrous ammonium sulphate solution after a 2-μsec. electron pulse. D, Optical density at 3150 Å.; D_∞, final steady value of density

thus not likely to be directly concerned with the ferrous–ferric reaction. The optical density D of the solution at any time after the pulse should be proportional to the amount of ferric ion present at that time and can be calculated from curves of this type. D approaches exponentially towards a final steady value D_∞ and in Fig. 3 $D_\infty - D$ is plotted as a function of time for three different concentrations of ferrous ion. The slight variation in D_∞ for the three curves is probably due to the variation of dose among pulses. The half-times ($T_{1/2}$) are inversely proportional to the concentration, and the values obtained indicate that the probability of oxidation of a ferrous ion by a radical is of the order of 10^{-5} per collision. The exponential build-up of ferric ion shown here is perhaps unexpected in view of the complicated mechanism usually postulated for this reaction[3]. However, my results do not at present exclude components with much longer half-times.

These experiments are being continued, and the kinetics of a variety of radiation-induced chemical reactions will be studied in detail. I wish to thank Associated Electrical Industries and the staff of their Irradiation Facility and also the staff of the Biochemistry Department of the Christie Hospital and Holt Radium Institute for their co-operation in this work.

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Reversible Behaviour of the Ultra-violet Irradiated Deoxyribonucleic Acid and its Apurinic Acid

The present communication reports changes produced by ultra-violet irradiation in thymidylic acid (A), deoxycytidylic acid (B), apurinic acid (C), deoxyribonucleic acid (D) and a 1 : 1 mixture of A and B, and also the reversibility of these changes in C and D. The conditions of the irradiation are described in a previous paper[1]. Apurinic acid was prepared according to the method of Tamm, Hoder

Table 1

Optical density decrease (min.)	*A*	*B*	*A* + *B*	*C*	*D*	2 × *D*
0–5	0·034	0·071	0·058	0·235	0·097	0·194
5–10	0·024	0·035	0·023	0·079	0·049	0·098
10–15	0·008	0·019	0·011	0·050	0·022	0·044
15–20	0·008	0·006	0·017	0·024	0·014	0·028
Total decrease	0·083	0·131	0·109	0·388	0·182	0·364

and Chargaff[2]. The concentration of the solutions was such that at *p*H 7 (phosphate buffer) the optical density readings at the maxima were 1.000 ± 2 per cent. The irradiation time was 20 min. for each solution, and the decrease of optical density at 260 mμ was recorded at 5 min. intervals, as shown in Table 1.

These results indicate that the decrease in optical density of the mixture of the two nucleotides (thymidylic and deoxycytidylic acids) is approximately equal to half the sum of the two nucleotides irradiated individually ($\frac{1}{2}$ thymidylic acid + $\frac{1}{2}$ deoxycytidylic acid). However, when these two acids together exist in polymeric form, that is, apurinic acid, the decrease in optical density is more than three times that of the monomeric mixture, apurinic acid > 3 (thymidylic plus deoxycytidylic acids). I suggest that this discrepancy may be due to the unique photochemical behaviour of thymine

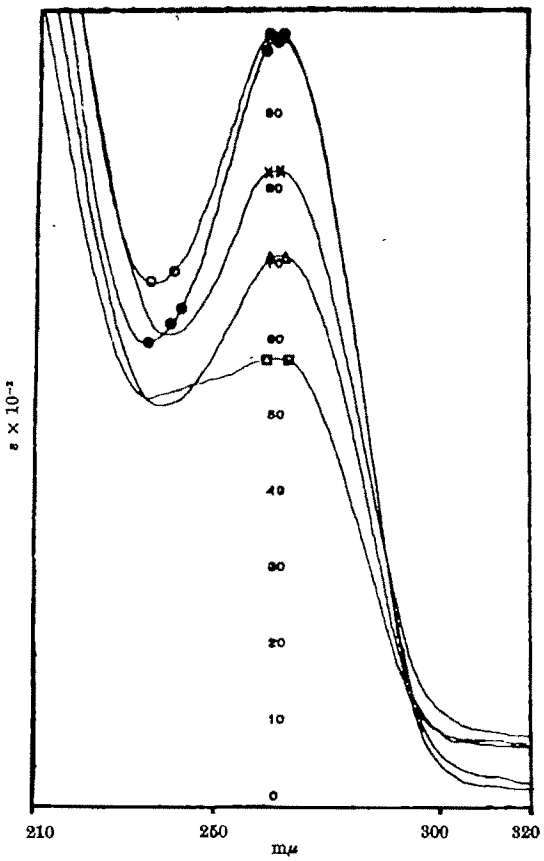

Fig. 1. Irradiation and reconstitution of apurinic acid. ○, Heated before irradiation (standard); ●, before irradiation (standard); ×, heated (6 hr.) after irradiation; △, standing (8 hr.) after irradiation; □, 20 min. irradiation

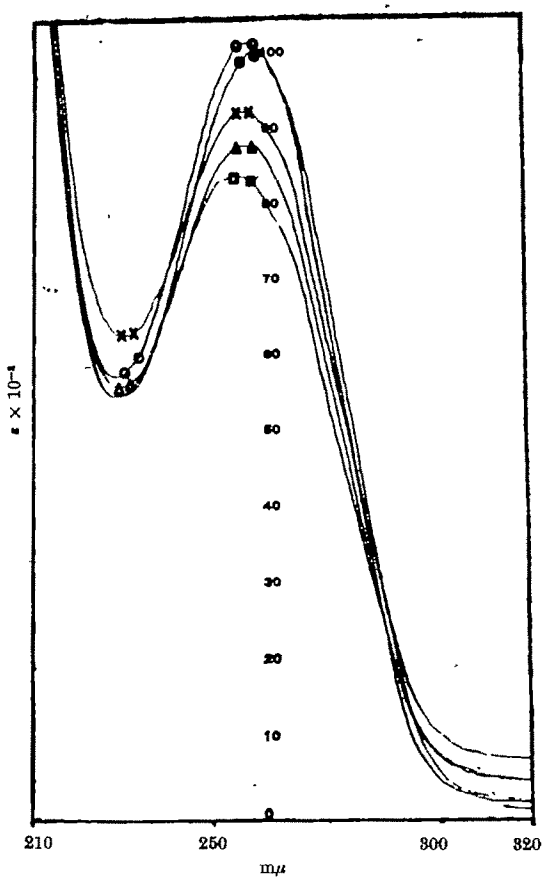

Fig. 2. Irradiation and reconstitution of deoxyribonucleic acid. ○, Heated before irradiation (standard); ●, before irradiation (standard), ×, heated (135 min.) after irradiation; △, standing (180 min.) after irradiation; □, 20 min. irradiation

derivatives[3]. Thus, I have pointed out that in polymeric nucleic acid, an unstable and reversible intermediate, 6-hydroxyhydrothymine derivative, could be formed and thus given an apparent decrease in optical density at 260 mμ. In the monomeric form (that is, thymidylic acid), the unstable intermediate would revert to the starting material during irradiation, while the slow decrease of optical density at 260 mμ would result only from degradation of this intermediate. If the above assumption is correct, the decrease of optical density of the polymer is therefore entirely owing to the irradiation effect on the two pyrimidine bases. Since purine bases are unaffected under these irradiation conditions[4], the decrease of optical density for deoxyribonucleic acid, containing about 50 per cent purines, should be half that for apurinic acid. Therefore, if the observed decrease for deoxyribonucleic acid is doubled it should equal that of apurinic acid, which is a purine-free pyrimidine nucleotide polymer. The experimental data support this hypothesis[5].

The reversibility of irradiated deoxyribonucleic acid and apurinic acid as indicated by ultra-violet spectra was observed by treatment with heat (70°), acid (*p*H ~ 2) or acid and heat and also by standing at room temperature. The spontaneous reconstitution is probably due to the reverse isomerization of irradiated deoxycytidylic acid units to the original[6]. The acid or heat reconstitution probably results from

dehydration of 6-hydroxyhydrothymidylic acid units[3]. The increase in optical density in the spontaneous reconstitution of deoxyribonucleic acid reached 0·005 as its maximum value on standing about 3 hr. For heat reconstitution, the value reached 0·092. When compared with the standard curve (heat before irradiation), the portion that is reconstituted is about 50 per cent. In the case of apurinic acid spontaneous reconstitution reached 0·118 in 8 hr. and heat reconstitution reached 0·240 (ref. 7). This is about 60 per cent reconstitution. In acid or acid and heat reconstitution the values were somewhat lower and the absorption maximum shifted to 262 mμ in both cases.

The irradiation conditions that I used were based on our findings in cytosine derivatives. In deoxyribonucleic acid, the cytosine derivative is deoxycytidylic acid and on irradiation the spontaneously reversible step for the concentration used was completed in about 20 min. This irradiation time was chosen as a standard because it was observed that at the end of 20 min. irradiation time the ultraviolet spectrum started to deviate from the isosbestic point—the criterion for the first reversible step[6]. The total energy input, or number of Einsteins absorbed in solution, was $1 \cdot 88 \times 10^{-5}$ Ein./c.c. in a 20 min. period[5].

Experiments are being continued in the hope that future work will shed some light on the biological aspects of the problem.

R. Beukers, J. Ijlstra and W. Berends[9] have just published their findings on the ultra-violet irradiation of deoxyribonucleic acid. These findings were based on their previous observations[10] on the irradiation of thymine in the frozen state. I would like to report that the irradiation of thymine and 1,3-dimethylthymine in the frozen state resulted in the formation of dimers. These dimers, determined by elementary analyses, molecular weight, ultra-violet spectra and infra-red spectra, were stable in acid, base and heat. However, in solution they would revert to the original compound when irradiated with 2537 Å. light, but are stable with 3600 Å. or light of longer wave-length. The identification of these dimeric products is being pursued in this Laboratory.

I am grateful to M. Mouyos for technical assistance.

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CHEMISTRY

Acidic Dissociation Constants of Alcoholic Hydroxyls of Hydroxycarboxylic Acids: Tartaric Acid

THE hydroxycarboxylic acids form very stable complexes with metal ions. In alkaline solution, both the carboxylic and the alcoholic hydroxyl groups take part in complex formation. For the calculation of stability constants of complexes it is necessary to know the acidic dissociation constants of both groups. Since the alcoholic hydroxyls are very weakly acidic and the molecule contains relatively easily dissociable group(s) also, it is not possible to determine the dissociation constants by the usual methods. For mandelic acid the value of the dissociation constant of alcoholic hydroxyl can be calculated from the change of absorbancy at 244 mμ produced by sodium hydroxide[1]. However, in general the hydroxycarboxylic acids do not absorb even in far ultra-violet. The acidic dissociation constants of optically active substances may be estimated from the change of rotatory power produced by alkali hydroxide. The present communication deals with tartaric acid.

The rotatory power of tartaric acid first increases with increasing *p*H and reaches a limiting value about *p*H 7 (ref. 2). This increase can be attributed to the gradual ionization of the carboxylic groups. Above *p*H 13 the rotatory power decreases on further increasing the concentration of alkali. Fig. 1 shows the change of the optical rotatory power as a function of *p*H at Na_D. We used the *p*H values determined by Schwarzenbach and Sulzberger[3] instead of the concentrations of sodium or potassium hydroxide. It can be seen that in solutions containing sodium hydroxide, the direction of rotation changes at *p*H 15·76 (7·95 *M*/litre sodium hydroxide). The rotatory power also decreases in solutions which contain potassium hydroxide, but the direction of rotation does not change. However, at shorter wave-lengths the optical rotatory dispersion curves were determined between 260 and 583·9 mμ—the change of direction of rotation also takes place in the presence of potassium hydroxide. For example, at 300 mμ the rotation is zero in 9·2 *M* potassium hydroxide (*p*H 16·9) or in 4·9 *M* sodium hydroxide (*p*H 15·1).

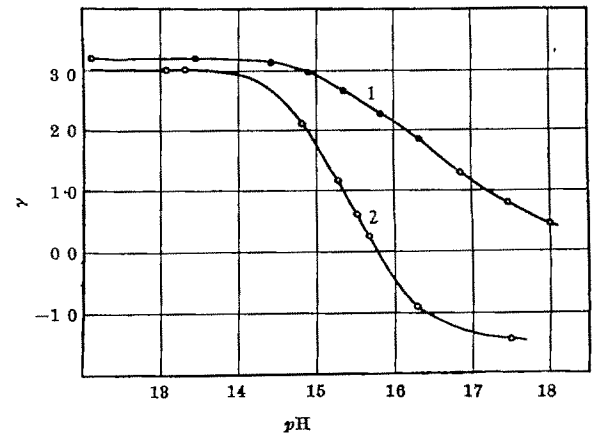

Fig. 1. Rotatory power of tartaric acid as fraction of *p*H. 1, solutions alkalized by KOH; 2, solutions alkalized by NaOH

The main reason for the decrease of rotatory power produced by increase of concentration of alkali is the gradual ionization of alcoholic hydroxyls. The differences accompanying the use of potassium hydroxide and sodium hydroxide for alkalization can be attributed to (i) secondary equilibria, and (ii) the different deformability of sodium and potassium ions. These latter effects were not taken into consideration in making the calculation. The acidic dissociation constants were estimated by Stearn and Wheland's method[4] modified by us. The acidic dissociation constants were defined by the following expressions:

$$K_3 = \frac{[TH^{3-}][H^+]}{[TH_2^{2-}]}\ ;\ K_4 = \frac{[T^{4-}][H^+]}{[TH^{3-}]}$$

Using these expressions, we find that the dissociation constants determined in solution treated with potassium hydroxide are $K_3 = 1 \cdot 13 \times 10^{-14}$ and $K_4 = 2 \cdot 54 \times 10^{-16}$; for solutions treated with sodium hydroxide, $K_3 = 1 \cdot 45 \times 10^{-14}$ and $K_4 = 3 \cdot 23 \times 10^{-16}$.

Details of the experimental work and the method of calculation will be published in *Acta Chim. Hung.*

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Theoretical Basis for Kinetic Effects in Gas-Solid Chromatography

LATERAL diffusion in the gas phase as well as sorption–desorption kinetics may both influence the plate height of gas-solid chromatography. While the complicated nature and alignment of adsorbing surfaces in a column cannot be fully described mathematically, a model is presented here which allows for the fundamental diffusion and reaction processes of gas-solid chromatography. The theory is written in a general form which can be readily extended to more complex phenomena. The adsorption isotherm is assumed linear, a condition recently made practical by highly sensitive detectors.

The fundamental equation for non-equilibrium (kinetic) effects in chromatography is[1-3]:

$$s_i = (v_i - \bar{u})\ \partial m_i^*/\partial z \qquad (1)$$

where s_i is the rate of accumulation due to kinetic effects of solute in the ith form, v_i is the downstream velocity in the ith form, $\bar{u}$ is the average zone velocity, m_i^* is the equilibrium concentration expressed in the appropriate units, and z is the distance. If $i = 1$ represents the gas (fluid) phase, then we may write[3]:

$$s_1 = m_1^* D_1 \nabla^2 \varepsilon_1 \qquad (2)$$

where D_1 is the diffusion coefficient of solute in the gas and ε_1 is the equilibrium departure term for the gas. The surface, $i = 2$, accumulates solute on a unit area at the rate[2], $s_2 = -k_{21}\, m_2^*\, [\varepsilon_2 - (\varepsilon_1)_{\text{interface}}]$, where k_{21} is the first-order rate constant for desorption from the surface. If the sorption–desorption kinetics are very rapid, the term in square brackets equals zero, and the equality $\varepsilon_2 = (\varepsilon_1)_{\text{interface}}$, representing interfacial equilibrium, is a boundary condition[3] on ε_1. In this well-known case, diffusion, only, controls the non-equilibrium. In the general case, however, the above equation for s_2 becomes a boundary condition on ε_1. Using equation (1) in which $v_2 = 0$ (because the surface is stationary), this condition becomes:

$$-Rv\ \partial \ln c/\partial z = -k_{21}\,[\varepsilon_2 - (\varepsilon_1)_{\text{interface}}] \qquad (3)$$

where v is the average gas velocity, R is the ratio $\bar{u}/v$, and c is the total amount of solute in a unit volume of the chromatogram. The latter may be represented by $c = m_1^* A_1 + m_2^* S_2$, where m_1^* is the equilibrium concentration of solute in the gas, A_1 is the fractional volume of gas, m_2^* is the equilibrium amount of solute per unit area of surface, and S_2 the surface area in a unit volume. The value of R in terms of these quantities is $R = c_1^*/(c_1^* + c_2^*) = m_1^* A_1/(m_1^* A_1 + m_2^* S_2)$.

If more than one surface is involved (such as with mixed adsorbents or adsorption at a gas-liquid interface), additional surface elements, S_i, must be introduced and treated in an equivalent way. Complications caused by non-uniform surfaces, etc., have been discussed[2] in a manner readily applicable to the present case.

The elimination of s_1 between equations (1) and (2) yields the following general differential equation from which ε_1 is to be obtained:

$$\nabla^2 \varepsilon_1 = \frac{(1-R)\, v_1}{D_1}\, \frac{\partial \ln c}{\partial z} \qquad (4)$$

A special case is considered here in which parabolic flow occurring between flat plates a distance $2d_1$ apart represents the interstitial flow. The future improvement of this model to represent more accurately the support lattice should permit a significant advance in the theoretical calculation of chromatographic parameters.

Equation (4) is integrated using $v_1 = (3v/2)(1 - x^2/d_1^2)$, where x is the distance from the centre of the channel. Using equation (3) in addition to type 1 and type 5 boundary conditions from reference 3, ε_1 is found to be:

$$\varepsilon_1 = v\, \frac{\partial \ln c}{\partial z} \left[\frac{-R(1-R)}{k_{21}} - \frac{x^4}{8D_1 d_1^2} + \frac{x^2}{2D_1}\left(\frac{3}{2} - R\right) - \frac{d_1^2}{120D_1}\,(40R^2 - 108R + 75) \right] \qquad (5)$$

This expression is identical to the one representing ε_1 when equilibrium is found at the interface, except that the term containing k_{21} does not appear in the latter. The contribution of the preceding non-equilibrium to the plate height is found in the usual way as:

$$H_c = \frac{2R(1-R)v}{k_{21}} + \frac{2}{3}\left(R^2 - \frac{12}{5}R + \frac{51}{35}\right) v\, \frac{d_1^2}{D_1} \qquad (6)$$

Each term in this expression has been obtained individually assuming only one process to be rate controlling. The general conditions under which rate effects are additive are, however, not entirely obvious. The fact that they are not always additive has been shown using a specific model for partition chromatography[3].

While equation (6) is expected to hold at most velocities, it probably fails at higher velocities. This is the result of the interaction of lateral diffusion in the gas phase with eddy diffusion[3,4]. The latter involves shuttling molecules back and forth from rapid to slow streamlines, an effect that acts essentially to increase the lateral diffusion coefficient, D_1. This additional lateral diffusion increases in proportion to flow velocity, and is thus negligible at low velocities.

Equation (6), along with necessary extensions to the present model, should be useful in suggesting ways of changing channel size, temperature, surface area, and other surface properties in a manner that is beneficial to the separability of component zones.

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Dipole Moment Data and Hyperconjugation

IT is being increasingly recognized[1] that the evidence for hyperconjugation from dipole moment data needs to be re-interpreted. Since the electronegativity of an *sp* or sp^2 carbon differs from that of an sp^3 carbon, the primary moments of the C(*sp*)—C(sp^3) and C(sp^2)—C(sp^3) bonds are not zero, and the dipole moments of molecules such as toluene, methylacetylene, etc., may arise solely from this effect.

Recently I have published a method for the calculation of bond moments based on the principle of electronegativity equalization[2], and I have now applied it to many molecules, including toluene, propylene, and butene-1. In these molecules, the atomic and homopolar dipoles cancel each other and the total moments should be given by the resultant of the vectorial sum of the primary bond moments.

From the data by Pritchard and Skinner[3], the electronegativities of sp^3 carbon and sp^2 carbon are 2·63 and 2·88, respectively. Using the screening-constants given by Kohlrausch[4], we can calculate[2] the value of the charge transferred in a C(sp^2)—C(sp^3) bond: $q = 0{\cdot}049$ e.u. Table 1 shows that the calculated primary moments of toluene, propylene, and butene-1, given by the product eqR_0 (column 4), agree extremely well with the experimental values for the dipole moments.

Table 1

Molecule	q (e.u.)	R_0 (Å.)	eqR_0 (D.)	μ_{exp} (D.)
CH_3—C_6H_5	0·049	1·52	0·357	0·36 ± 0·02
CH_3—CH=CH_2	0·049	1·53	0·359	0·35 ± 0·01
CH_3.CH_2—CH=CH_2	0·049	1·54	0·362	0·38 ± 0·30

Bond distances from "Tables of Interatomic Distances", Special Publication No. 11, Chemical Society (London, 1958).
Dipole moments from Mariott, A. A., and Buckley, F., "Table of Dielectric Constants and Dipole Moments of Substances in the Gaseous State", Nat. Bur. Stand. Circ No. 537 (Washington, D.C., 1953).

These results can be valid only if the opposed C(sp^2)—H and C(sp^2)—H bond moments are equal. Now, the calculated C(sp^2)—H bond moment in ethylene is 0·40 D., and the calculated C(sp^2)—H bond moment in methane is 0·21 D., but the positive charge in the sp^3 carbon of the molecules under consideration (due to charge transfer to the sp^2 carbon) increases the C(sp^2)—H bond moment considerably; an iterative calculation shows that the two types of C—H bond moments cannot differ by more than 0·05 D.

It seems that the dipole moment evidence for hyperconjugation is not valid, although, since the bond moment is a ground-state property, hyperconjugation may exist in excited states and accordingly be important for the interpretation of the spectra and reactivity of molecules.

A detailed account of this work is to be submitted elsewhere.

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Reaction of Aromatic Compounds with a Chlorinated Coal and Aluminium Chloride

VAN KREVELEN *et al.*[1] have reported on the coupling of pitch molecules by chloromethylation and subsequent condensation under the influence of a Friedel-Crafts catalyst, while Iyengar, Banerjee and Banerjee[2] have claimed the alkylation of coals with benzyl chloride and aluminium chloride. But in these laboratories a similar type of reaction between a chlorinated low-rank coal (containing about 50 per cent of hydrolysable chlorine) and several aromatic compounds, in the presence of aluminium chloride, has given inconclusive results which suggest that alkylation may not have occurred during the reaction with benzyl chloride.

A chlorinated low-rank coal (Ellington High Main 81·0 per cent carbon, 5·1 per cent hydrogen, dry ash-free, N.C.B. Rank Code No. 802), prepared as previously described[3], was treated with an aromatic compound (Table 1) under suitable conditions. The dry chlorinated coal (7 gm.) was stirred with 100 ml. carbon tetrachloride (nitrobenzene was used as a solvent in the case of aniline) and 0·5–1·0 gm. of anhydrous aluminium chloride. A blue or green colour developed at this stage, suggesting initial formation of a complex with aluminium chloride. No hydrogen chloride was evolved. The aromatic compound (aniline, toluene, chlorobenzene, dimethyl aniline or dimethylbenzylamine) was then added (2–10 gm.) and the mixture refluxed for about 7 hr. After cooling and filtering, the product was washed with carbon tetrachloride and then dried at 100° C. *in vacuo*

The results in Tables 1–2 show that, while the changes in elementary composition correspond with the expected reaction, the results do not definitely confirm the alkylation, since there was no corresponding release of hydrogen chloride. The increase in ash content suggests the presence of aluminium compounds in the products. It is doubtful if the results quoted by Iyengar, Banerjee and Banerjee[2], which do not include ash or chlorine contents,

Table 1

Ref. No.	Aromatic compound	Wt. gain on coal (per cent)	Elementary analysis of chlorinated coal and products Per cent d.a.f.						Per cent ash air dry basis	Comment
			D	H	N	S	O + errors	Cl		
—	—	—	63 0	3·4	1 4	1·8	9·7	20 7	2·2	Chlorinated coal
1	Aniline	36·8	70 9	4·7	5·9	1·7	8·5	8·3	6·0	Product
—	—	—	64 0	3·6	1·5	2·0	13 7	15·2	1·4	Chlorinated coal
2	Toluene	12 3	63 4	3·8	1·4	1·9	12·7	16·8	4 1	Product
3	Chlorobenzene	18 1	62 0	3 7	1·4	1·7	14·1	17·1	5 6	Product
4	Dimethylaniline	19·8	63 7	4·0	2·1	1·8	12·6	15·8	3·6	Product
—	—	—	61 0	3·3	1 3	2 0	13·7	20·0	1·3	Chlorinated coal
5	Dimethylbenzylamine	14 4	59 0	3 6	1 5	1 8	15 2	18 9	3 8	Product

Table 2. CHANGES IN ELEMENTS DURING REACTION
(gm. atoms/100 gm. atoms original carbon)

Ref. No.	Aromatic compound	Change in number of gm atoms				Change in empirical formulæ	
		O	H	N	Cl	Found addition of	Required for addition of compound
1	Aniline	+4·8	+5·2	+8 7	−5 2	$C_6H_{6\cdot 3}N_{1\cdot 1}(Cl_{-0\cdot 7})$	C_6H_5N
2	Toluene	+ 7	+ 6	nil	+1·4	C_7H_6Cl	C_7H_7
3	Chlorobenzene	+1·0	+ 9	nil	+1 0	$C_6H_{5\cdot 4}Cl_{0\cdot 9}$	C_6H_4Cl
4	Dimethylaniline	+1·7	+1·9	+1 2	+1 7	$C_8H_9N_{0\cdot 6}Cl_{0\cdot 8}$	$C_8H_{10}N$
5	Dimethylbenzylamine	+ 8	+1·4	+0 6	+0 6	$C_9H_{11}N_{0\cdot 7}Cl_{0\cdot 7}$	$C_9H_{13}N$

substantiate their claim that alkylation did in fact occur.

I thank P. L. Rogerson for much of the experimental work, and the British Coal Utilisation Research Association for permission to publish this communication.

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BIOCHEMISTRY

Biological Dehydroxylation

THE hydroxylation of aromatic compounds in the animal body to form phenols is a well-established biochemical reaction (see review[1]) and has been known for nearly a hundred years. It was in 1867 that Schultzen and Naunyn[2] first showed that benzene was converted to phenol in man and the dog. The reverse reaction, namely, dehydroxylation, is not well known. The first suggestion that such a reaction occurred *in vivo* was published in 1955 when Booth, Murray, DeEds and Jones[3] noted an enhancement of the *m*-hydroxyphenylacetic acid output in the urine of rabbits that had been dosed with 3,4-dihydroxyphenylacetic acid (homoprotocatechuic acid) or with the flavonoids, rutin and quercetin. It was suggested that the *m*-hydroxyphenylacetic acid arose by loss of the *para*-hydroxyl group of 3,4-dihydroxyphenylacetic acid. The excretion of increased amounts of *m*-hydroxyphenyl acids has since been observed after the administration of 3,4-dihydroxycinnamic acid (caffeic acid) to man, the rabbit and the rat[4,5] and after 3,4-dihydroxyphenylalanine (dopa) to the rabbit and the rat[4]. The ingestion of coffee leads to the excretion of increased amounts of *m*-hydroxyhippuric acid in human urine[6], and this has been ascribed by Booth *et al.*[5] to the breakdown of chlorogenic acid, which is the quinic acid ester of caffeic acid, and which occurs in coffee beans to the extent of 5 per cent on a dry weight basis. According to Armstrong *et al.*[6,7], *m*-hydroxybenzoic, -phenylacetic, -phenylpropionic and probably -phenyllactic acids occur in human urine, but the origin of these *meta*-acids is obscure. However, these acids could arise during metabolism by dehydroxylation of 3,4-dihydroxyphenyl acids (catechol acids). It is thus possible that dehydroxylation is a reaction of considerable metabolic significance.

It should be mentioned also that biological dehydroxylation has been observed in the quinoline series, for 4-hydroxyquinoline-2-carboxylic acid (kynurenic acid) is partly excreted as quinoline-2-carboxylic acid (quinaldic acid) in man and the rat[8], and 4,8-dihydroxyquinoline-2-carboxylic acid (xanthurenic acid) is excreted as 8-hydroxyquinoline-2-carboxylic acid in the rat[9], but 4,8-dihydroxyquinoline is not dehydroxylated[9]. However, the hydroxyl group in the 4 position of quinoline is not strictly phenolic, and the mechanism of its dehydroxylation may not be the same as the removal of the phenolic group in the catechol acids.

In order to put the dehydroxylation of the catechol acids on a sound basis we have synthesized [carboxy-^{14}C] 3,4-dihydroxyphenylacetic acid and administered this compound by mouth to rabbits. The various metabolites of this acid were then determined by isotope dilution and paper chromatographic techniques after acid hydrolysis of the urine. The results are shown in Table 1.

Table 1 shows that in 44 hr. after dosing with the homoprotocatechuic acid labelled with carbon-14 about 85 per cent of the carbon-14 is excreted in the urine, and this can be accounted for as four compounds. The main excretory product is the original acid. However, both *m*- and *p*-hydroxyphenylacetic acids are labelled and so is 4-hydroxy-3-methoxyphenylacetic acid (homovanillic acid). The last acid

Table 1. METABOLITES OF [^{14}C]3,4-DIHYDROXYPHENYLACETIC ACID (DOSE, 100 MGM./KGM.)

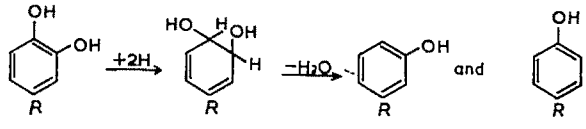
	Percentage of dose* excreted in 44 hr. determined by isotope dilution
3,4-Dihydroxyphenylacetic acid	63
m-Hydroxyphenylacetic acid	14
p-Hydroxyphenylacetic acid	1·4
4-Hydroxy-3-methoxyphenylacetic acid (homovanillic acid)	5 6
Sum of metabolites	84
Radioactivity of urine after 44 hr.	85 5
Radioactivity of urine after 8–9 days	100 3

* Mean value of three animals

is a known metabolite of homoprotocatechuic acid, of dopa[4], and of 3,4-dihydroxyphenylethylamine (3-hydroxytyramine or dopamine)[10]. Its isomer, 3-hydroxy-4-methoxyphenylacetic acid (homo-*iso*-vanillic acid), was looked for in our experiments but it was not found.

Now the isotope dilutions in our experiments were carried out on ether extracts of the acid-hydrolysed urines, and it might be argued that the *m*-hydroxyphenylacetic acid was an artefact. However, the *m*-acid was found in unhydrolysed urines by paper chromatography in non-acidic solvents and by isotope dilution. In fact, the amount found in unhydrolysed urines was no different from that found in acid-hydrolysed urines, and it was concluded that *m*-hydroxyphenylacetic acid was a true urinary metabolite of homoprotocatechuic acid.

The formation of *p*-hydroxyphenylacetic acid is interesting because it shows for the first time that the *m*-hydroxyl group of a catechol acid can also be lost *in vivo*. A mechanism for the dehydroxylation of catechol acids has been suggested by one of us[11]. It is suggested that homoprotocatechuic acid is hydrogenated *in vivo* to 3,4-dihydro-3,4-dihydroxyphenylacetic acid, which could then lose water to yield *m*- or *p*-hydroxyphenylacetic acid or both:



where $R = CH_2COOH$. The nature of the R group is important for it would influence how much *m*- and *p*-dehydroxylation occurred. When $R = CH_2COOH$, more *p*-dehydroxylation than *m*- is to be expected and this is in accord with the figures in Table 1, where the ratio *m*-acid/*p*-acid is 10, which means that there is ten times as much *para*-dehydroxylation of homoprotocatechuic acid as *meta*- in the rabbit.

Dehydroxylation could also be a metabolic reaction of the catechol amines, adrenaline and noradrenaline. *p*-Dehydroxylation of adrenaline would give the known sympathomimetic agent, phenylephrine (or meta-synephrine) base and *m*-dehydroxylation, synephrine base. These two amines could be normal metabolites of the body.

This investigation was supported in part by a research fellowship (to R. R. S.), No. *EF*-8238, from the National Institute of Allergy and Infectious Diseases, United States Public Health Service, and another (J. G. W.) participated during the tenure of a World Health Organization fellowship.

Note added, August 19. Dr. Sidney Udenfriend (National Heart Institute, Bethesda, Md.) has informed us that he has found synephrine in human urine, and an account of this finding is being prepared for publication. He has also directed our attention to a communication by himself and his co-workers (see Sjoerdsma *et al.*, *Science*, 130, 225; 1959) on the finding of *m*-tyramine (*m*-hydroxyphenylethylamine) in the urine of humans dosed with the monoamine oxidase inhibitor, 1-phenyl-2-hydrazinopropane (*JB*-516 or 'Catron'). It is possible that *m*-tyramine is a product of the dehydroxylation of dopamine *in vivo*.

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Ultra-Violet Photography of Fluorescent Spots on Chromatograms of Biological Extracts

THE use of ultra-violet light to detect and photograph chromatographed compounds absorbing in the region of 254 mμ is well known[1]. In the course of investigating a number of unknown compounds found on chromatograms of plasma extracts, a simple technique was developed for photographing spots which fluoresce in ultra-violet light at 360 mμ. This consists of interposing a Kodak 2*A* gelatin filter, which absorbs radiant energy below 405 mμ, between the chromatogram and the contact paper ('Kodabromide *F*5'). The filter is enclosed for protection between 1/16 in. glass plates, bound with tape at the edges. The chromatogram is exposed for approximately 30 sec. to ultra-violet light from a 365-mμ source ('Mineralight' handlamp, Ultraviolet Products, Inc., San Gabriel, Calif.) at a distance of 1 ft. The photograph is then developed in the usual way.

To illustrate the application of the method, Figs. 1*a* and *b* show respectively photographs taken at 254 mμ without a filter (absorbing compounds), and at 365 mμ with the filter (fluorescing compounds), of a chromatogram of plasma extracts from three normal subjects and three patients with uræmia. In Fig. 1*a* it can be seen that the plasma concentration of the ultra-violet-absorbing substances *X* and *Y* increases with increasing levels of blood urea nitrogen. In Fig. 1*b* the increased amounts of the fluorescent substance *X* in the uræmic patients' plasma, compared with that of the normal subjects, is clearly demonstrated. Further work on the identification of both compounds is at present being undertaken.

The technique described dispenses with the need for a camera, and is now used routinely in this laboratory to supplement the information obtained

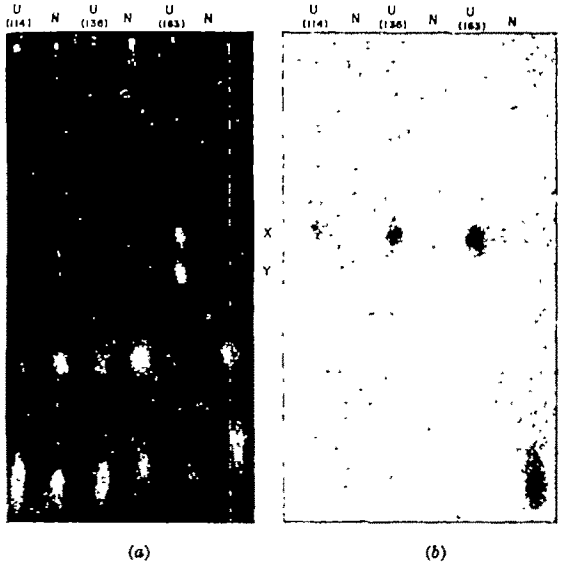

Fig. 1 Ultra-violet photographs of a descending chromatogram in n-butanol/water (86 : 14), taken at 254 mμ (a) and at 360 mμ with filter (b). N, Plasma extract from normal subjects; U, plasma extract from patients with uræmia; X, Y, unknown compounds. Figures in brackets refer to levels of blood urea nitrogen

from 254-mμ photographs. It is particularly useful for substances such as 5-hydroxyanthranilic acid, which are not detected by the latter method. For compounds such as X, which fluoresce in ultra-violet light and also absorb, the fluorescent technique is the more sensitive. It should be applicable to all substances in which visible fluorescence is activated at wave-lengths below 405 mμ, and thus provides a general extension of the method described by Smith and Markham[2], in which a cellulose nitrate filter cutting off wave-lengths below 320 mμ is used.

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Oxidative Activity of a Particulate Fraction from *Rumex* Virus Tumour Tissue

ALTHOUGH the capacity of cytoplasmic particles from plant tissues to oxidize Krebs-cycle intermediates has been clearly demonstrated[1], only one investigation to date has been reported on the oxidative reactions of particulate fractions from plant tissue cultures[2]. Such investigations are of particular interest and importance in that they permit an elucidation of the biochemical differences between normal (callus) and neoplastic plant tissues and between tissue cultures and the parent plant parts. This work is concerned with the oxidative activity of a particulate fraction from virus tumour tissue of Black's original R_1 strain from *Rumex acetosa* L.

The tissue was grown on medium No. 24 of Burkholder and Nickell[3] under the conditions previously described[4]. Approximately 15 gm. of tissue, 4–6 weeks old, was ground in a mortar and pestle with 30 ml. of buffer containing potassium dihydrogen phosphate, 0·1 *M*; sucrose, 0·5 *M*; dipotassium salt of ethylenediamine tetraacetic acid, 0·01 *M*; *p*H 7·3. A small quantity of quartz sand was added to aid in grinding. The macerate was strained through cheese-cloth and centrifuged at 500*g* for 10 min. The resultant supernatant was centrifuged at 20,000*g* for 20 min. and the pellet finally obtained was suspended in 3·0 ml. of buffer containing potassium dihydrogen phosphate, 0·02 *M*; sucrose, 0·4 *M* and magnesium chloride, 0·005 *M*, *p*H 7·2.

All the above operations were carried out at 0–4° C. Manometric measurements were conducted at 30° C. using standard Warburg apparatus. Nitrogen content of the particulate suspensions was determined on 1·0-ml. samples of suspensions which had been diluted 1 : 10 with distilled water. The samples were digested by a micro-Kjeldahl method and nesslerized. Nitrogen was determined colorimetrically in a Klett–Summerson photoelectric colorimeter equipped with a 490-mμ filter.

All reagents used were of the highest quality available commercially.

The particulate suspension was yellow in colour, and microscopic examination with an oil-immersion objective showed that it consisted of oval particles which stained with janus green *B*. These particles were very similar in appearance to particles commonly referred to as mitochondria.

The particulate suspension catalysed the oxidation of citrate, α-ketoglutarate, succinate, fumarate and malate (Table 1). The rate of pyruvate oxidation was very low, but the addition of catalytic amounts of malate resulted in a considerable increase in pyruvate oxidation (Table 2). The use of malate as a 'sparker' in pyruvate oxidation has been previously reported[5]. Of the other Krebs-cycle acids utilized as substrates, succinate was oxidized most rapidly while the rate of fumarate oxidation was repeatedly the lowest obtained. These findings could account for the reported accumulation of fumarate in older tumour tissues[4].

A cytochrome oxidase system is present in *Rumex* tumour tissue[6] although the rate of oxidation of all but two of the substrates utilized, citrate and malate, was not significantly enhanced by the addition of cytochrome *c*. The failure of added cytochrome *c* to

Table 1. OXIDATION OF KREBS-CYCLE ACIDS BY A PARTICULATE FRACTION FROM *Rumex* VIRUS TUMOUR TISSUE

Substrate	Mm.³ O_2/mgm. N/hr.* (−) Cytochrome *c*	(+) Cytochrome *c*
Pyruvate	19	—
Citrate	53	118
α-Ketoglutarate	75	73
Succinate	188	191
Fumarate	41	48
Malate	88	127

Complete reaction mixture: Particulate suspension, 0 5 ml.; substrate, 0·02 *M*; adenosine monophosphate, 0 001 *M*; diphosphopyridine nucleotide, 0 0005 *M*; diphosphothiamine, 0 0001 *M*; coenzyme *A*, 0·000025 *M*; glucose, 0 02 *M*; potassium phosphate (monobasic), 0 02 *M*; sucrose, 0 4 *M*; magnesium chloride, 0 005 *M*; cytochrome *c* (where added), 0·0001 *M*. Total volume, 3 0 ml.; temperature, 30° C.; *p*H, 7·2, gas phase, air. Centre well of each Warburg vessel contained 0 2 ml. 20 per cent potassium hydroxide and a filter paper wick.

* Corrected for low rate of endogenous oxygen uptake.

Table 2. PYRUVATE OXIDATION BY A PARTICULATE FRACTION FROM *Rumex* VIRUS TUMOUR TISSUE

Substrate	Mm.³O_2/mgm.N/hr.*
Pyruvate	23
Pyruvate + malate (0·001 *M*)	103
Pyruvate + cytochrome *c*	23
Pyruvate + malate + cytochrome *c*	123

Reaction mixture same as in Table 1

* Oxygen uptake in presence of malate (0·001 *M*) showed no measurable increase over endogenous rate.

enhance oxidation has been interpreted as indicating that the mitochondrial complex has been isolated in reasonably intact form, and that sufficient cytochrome *c* is bound to the particles[7]. It is possible that in cases where added cytochrome *c* failed to enhance the rate of oxidation of substrate other factors may be limiting[8].

Evidence is presented to demonstrate that *Rumex* virus tumour tissue cultivated *in vitro* contains particles which possess the capacity characteristic of plant mitochondria to oxidize Krebs-cycle acids.

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Enzyme Repression as the Control Mechanism in the Synthesis of Induced β-Galactosidase

IT is known that the mechanism controlling the level (synthesis) of the constitutive enzymes in cells is enzyme repression[1]. An early example for enzyme repression was the inhibition of the synthesis of constitutive β-galactosidase by lactose or galactose[2]. In the present investigation I have examined the regulation of the synthesis of induced β-galactosidase.

The strain *Escherichia coli ML* 30 and the medium *M*–9 (ref. 3) which contains either 2 mgm./ml. maltose—twice recrystallized from 80 per cent ethanol—or glycerol as sole source of carbon were used in this work. The inducer, *iso*propyl-thio-β-D-galactoside[4] or lactose, was added to the exponentially growing culture, containing 30 μgm/ml. bacterial dry weight, at 37° C. on a rotary shaker. At intervals, during the first one and a half division after the addition of inducer, samples were taken for galactosidase and dry-weight assay. For the enzyme assay, 0·5-ml. aliquots of the culture were pipetted into tubes containing 0·5 ml. chloramphenicol solution (50 μgm./ml.) in 0·01 *M* sodium phosphate (*p*H 7). After toluene treatment at 37° C., 4 ml. of a solution of $2{\cdot}5 \times 10^{-3}$ *M* *o*-nitrophenyl-β-D-galactoside in 0·01 *M* sodium phosphate were added and the tubes incubated for a measured time, until the desired intensity of colour had developed. The reaction was stopped by the addition of 5 ml. of 0·4 *M* sodium carbonate. After centrifuging the cells, the optical density was measured at 420 mμ. One unit of enzyme is the amount which, under these conditions, hydrolyses 1 mμmole *o*-nitrophenyl-β-D-galactoside per min. The galactosidase activity, *Z*, in units galactosidase per ml. is plotted against dry-weight of bacteria, *X* in μgm. per ml. The rate of induction is defined as the differential rate of synthesis, $p = \Delta Z/\Delta X$ (ref. 5). Cell density was determined by the aid

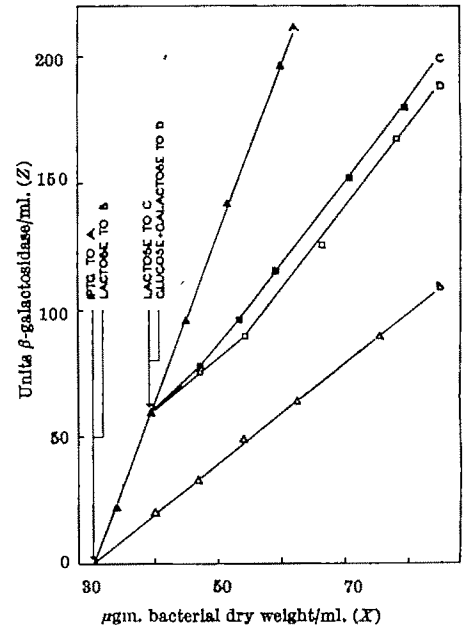

Fig. 1. Effect of lactose and its metabolites (glucose + galactose) on the synthesis of β-galactosidase induced by *iso*propyl-thio-β-D-galactoside. The exponentially growing cells, on maltose as carbon source, was induced with 10^{-4} *M* *iso*propyl-thio-β-D-galactoside (*A*) or with 10^{-3} *M* lactose (*B*). At the points indicated by an arrow, 10^{-3} *M* lactose (*C*) or 5×10^{-4} *M* glucose + 5×10^{-4} *M* galactose (*D*) was added respectively to the induced cells

of a Pulfrich nephelometer. Standard curves were used to convert the readings obtained to dry-weight of bacteria per ml.

As shown in Fig. 1, the rate of synthesis of β-galactosidase induced by *iso*propyl-thio-β-D-galactoside is greater ($P = 6{\cdot}6$) than in the case of lactose of the same concentration ($P = 2{\cdot}0$) if the cells were grown on maltose as carbon source. The addition of lactose to cells induced by *iso*propyl-thio-β-D-galactoside—although lactose is an inducer in itself—inhibits the synthesis of enzyme. From the kinetics of the inhibition, it is not the lactose itself which causes inhibition but its metabolic products, namely, glucose and galactose. This inhibitory effect is very similar to that described previously concerning the inhibition of constitutive β-galactosidase synthesis by enzyme repression[2].

If the result shown in Fig. 1 may be generalized, that is, in the case of a metabolizable inducer the rate of synthesis of the induced enzyme is being regulated not only by the structure and concentration of the inducer but also by its metabolites, then it may be assumed that the same inducer will show a different inductive activity in cells grown with different carbon sources.

As seen in Fig. 2, if glycerol is used as source of carbon, the inductive activity of lactose in small concentrations is nearly the same as that of *iso*propyl-thio-β-D-galactoside. If an increasing concentration of lactose is used, then the enzyme induced by it produces great amounts of hexose. The metabolism of the cell grown on glycerol is not able to utilize this excess of hexose, and in consequence it will inhibit the synthesis of the enzyme. This inhibition will be suppressed only when the excess of hexose is metabolized by the cell.

From a theoretical point of view it is very important that *iso*propyl-thio-β-D-galactoside is a non-metabol-

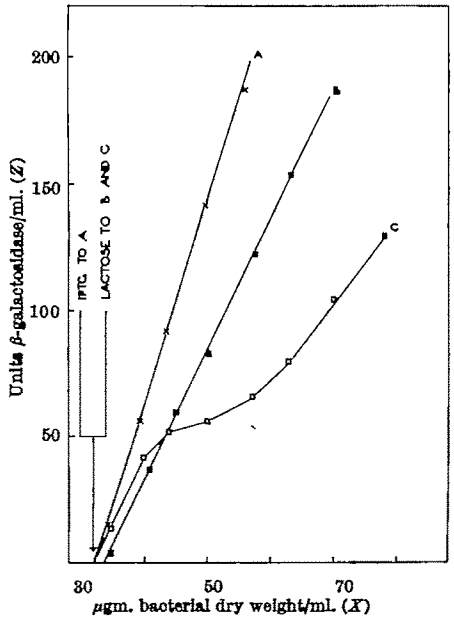

Fig. 2. Synthesis of induced β-galactosidase in cells grown on glycerol as carbon source. At the point indicated by an arrow, the exponentially growing cells were induced with 10^{-3} *M* isopropyl-thio-β-D-galactoside (*A*), or 2×10^{-4} *M* lactose (*B*), or 10^{-3} *M* lactose (*C*)

izable inducer, that is, no metabolite is produced by the induced enzyme that would enter the cell metabolism. Consequently, experiments carried out with such inducers will give no answer to the question whether the mechanism of the induction or its regulation is influenced or not by the metabolites of the inducer.

These investigations show that the rate and level of synthesis of the induced enzyme is determined by the ratio of the concentration of the inducer and of its metabolites, glucose and galactose, causing enzyme repression. Further investigations in this direction are in progress.

I thank Dr. J. Monod for the supply of the strain of *Escherichia coli* used in this work.

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A Method for the Direct Detection of Proteolytic Enzymes after Electrophoresis in Agar Gel

SEVERAL methods have been developed for the detection of different enzymatic reactions in agar gel[1]. The present communication describes a method for the direct detection of proteolytic enzymes following electrophoresis in agar gel.

The principle of the method is the following: after the electrophoretic separation of the enzyme preparation, the agar plate is immersed in a bath containing a protein which is susceptible to degradation by the proteolytic enzyme. After incubation the plate is fixed, dried and coloured in the normal way[2]. The sites on the plate possessing a proteolytic activity toward the chosen substrate are revealed as weakly or non-coloured zones against an evenly coloured background. This coloured background is due to the protein substrate which diffuses into the agar gel during the incubation. In the zone where the proteolytic enzyme is situated all, or a portion of, the substrate is degraded. The coloration in this zone is non-existent or weak because the products of the degradation are not fixed by the acid fixator nor coloured by amido black.

The experimental conditions (buffer, *p*H, ionic strength, etc.) used for the preliminary electrophoretic separation may differ from those employed for the detection of the proteolytic enzyme, as these two operations are completely independent. For optimum results with each enzyme preparation and corresponding substrate, it is necessary to adjust the reaction conditions, that is, the *p*H, the temperature and time of incubation, the substrate concentration and the quantity of enzyme employed.

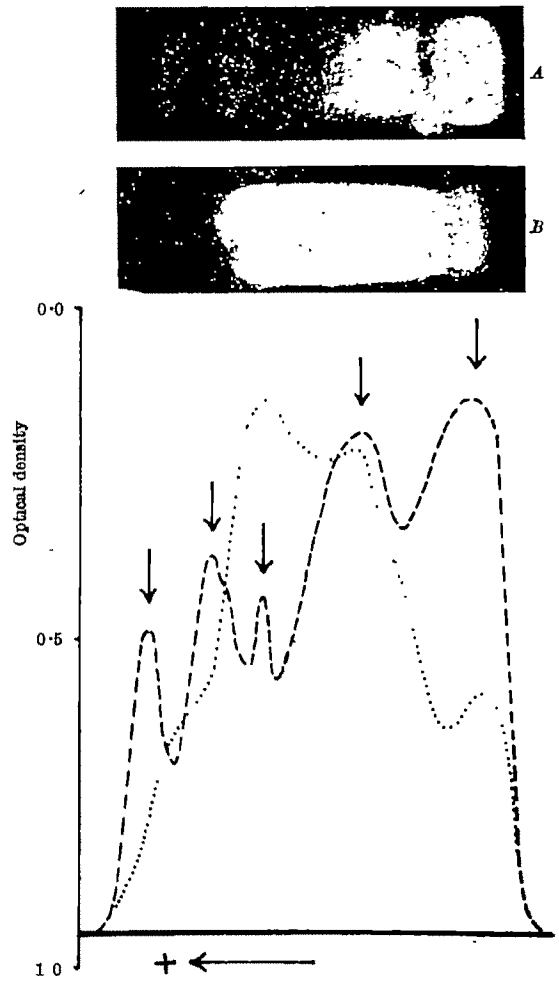

Fig. 1. Agar electrophoresis. *A*, Proteolytic activity of a purified non-crystallized trypsin preparation ('Difco'): *B*, proteolytic activity of a twice-crystallized trypsin preparation (Nutritional Biochemical Corp.); bottom, photometric scanning of upper images: ---, *A*; . . ., *B*

The following examples illustrate two of the different types of application of the method.

The proteolytic activity of preparations of trypsin have been studied in the following manner: freshly prepared trypsin solution (100 μgm. per analysis) were subjected to electrophoresis according to the technique of Grabar and Williams[3] for 60 min. at a potential difference of 6–7 V./cm. in agar gel of 1 per cent containing sodium veronal buffer (*p*H 8·2, Γ/2 0·025). After electrophoresis the plates were immersed in a 0·5 per cent solution of casein in veronal buffer (*p*H 8·2, Γ/2 0·05) and incubated with occasional stirring for 45 min. at 25° C. They were then fixed for 2 hr. in a 50 per cent ethanol solution containing 3 per cent acetic acid, dried under filter paper and coloured by amido black[2]. The results obtained with two commercial preparations of trypsin are shown in Fig. 1. The heterogeneity of these preparations is obvious.

The proteolytic activity of an aqueous extract of rabbit spleen has also been studied by carrying out the electrophoresis at *p*H 8·2 and then incubating the plate in a solution of human serum albumin at *p*H 3·5 (the technical details of the experiment will be given elsewhere[4]). A parallel electrophoresis of the spleen extract was done and stained for protein in the usual way[2]. Fig. 2 shows that despite the heterogeneity of the spleen extract its proteolytic activity is localized in one well-defined zone, thus confirming the results of Lapresle and Webb[5].

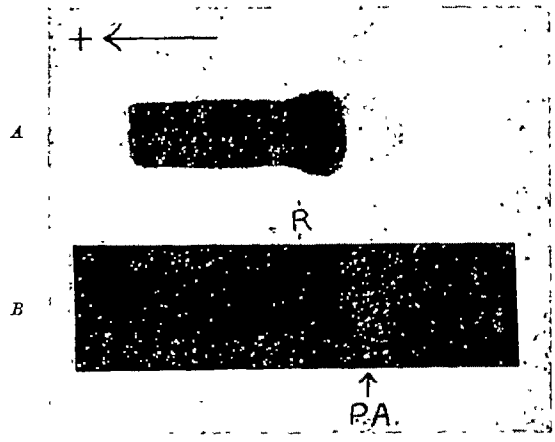

Fig. 2. Agar electrophoresis. *A*, Electrophoretic pattern of the proteins in an aqueous extract of rabbit spleen; *B*, proteolytic activity (*P.A.*) in the same extract, *R*, starting place

These two examples illustrate one advantage of this method. It permits one to determine if the heterogeneity of an enzyme preparation is due to the existence of several constituents possessing a proteolytic activity (Fig. 1) or to the presence of non-enzymatically active protein impurities (Fig. 2).

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Neurohormonal Properties of Royal Jelly

ROYAL jelly has significance in polymorphic development of bees. Bee larvæ fed on an over-abundance of royal jelly develop into queens; those given food differing quantitatively and qualitatively become worker bees[1]. Royal jelly has other interesting properties, for evidence is available of its therapeutic value in transplantable mouse leukæmia[2] and of the presence of an antibiotic[3]. These effects might be termed anti-growth properties. It is remarkable that royal jelly is stated to contain acetylcholine[4] in an amount calculated to be about six times that found in the brain of insects[5]. Nothing is known about the origin of acetylcholine in royal jelly or indeed whether this substance, obtainable from bees other than those used by Henschler[4], contains acetylcholine. The occurrence of a neurohormone in royal jelly is of considerable interest for it suggests that acetylcholine may have a function different from that associated with nervous transmission.

Partition chromatography and the frog rectus abdominis muscle were used to identify acetylcholine. Royal jelly was heated to boiling point in a small volume of distilled water, *p*H 3·9, and when the extract was cool, trichloracetic acid was added to give a final concentration of 1 per cent. The extract was centrifuged at 4,000 r.p.m. for 5 min., the supernatant decanted and shaken with an equal volume of ether for four successive extractions. The resulting clear liquid was evaporated to a small volume *in vacuo* and spotted on Whatman No. 1 filter paper. For reference, standard solutions of acetylcholine were used with trichloracetate, bromide or chloride associated anions. Chromatograms were run in wet butanol as the solvent, and choline esters were detected by the use of Dragendorff's reagent, which reacts to give a pink spot. The results show that extracts of royal jelly gave one spot with an R_F of 0·45 identical to that found with a solution of acetylcholine trichloracetate. By use of the frog rectus abdominis muscle it was determined that 1 gm. of royal jelly contained an active substance equivalent in activity to 683±64 μgm. of acetylcholine bromide. The active substance was readily hydrolysed by bovine purified erythrocyte or cockroach acetylcholinesterase and destroyed by alkali and heating; stability was found at *p*H 3·9. Atropine reduced contraction of the frog muscle. On the basis of this evidence it is suggested royal jelly contains acetylcholine, thus confirming the report of Henschler[4] for the royal jelly of European bees. It was determined that acetylcholine was not destroyed in royal jelly held in storage for about two years. The *p*H of royal jelly, 3·9–4·1, appears to be about optimal for the preservation of acetylcholine.

The hypopharyngeal glands of nurse worker bees are said to produce royal jelly[1]. These glands and the post-cerebral glands were used as sources for choline acetylase. The synthesis medium contained optimum amounts of coenzyme *A*, transacetylase, acetyl-phosphate, choline salts, and phosphate buffer (*p*H 6·9). Glands dissected from bee heads were frozen immediately in 0·9 per cent potassium chloride and homogenized just before use. No synthesis of acetylcholine was found with gland extracts although brain tissue synthesized up to 50 mgm. acetylcholine per gm. of brain in 1 hr. Furthermore it was determined by use of a standard manometric technique, with 0·01 *M* acetylcholine as substrate, that glands did not contain acetylcholinesterase. It is concluded

that, although a hydrolysing esterase was absent, no evidence has been obtained for the presence of choline acetylase in gland tissue to account for the acetylcholine of royal jelly. Extra-cellular enzymic synthesis of acetylcholine could occur in the lumen of glands, but it is doubtful whether this would happen at royal jelly *p*H, for optimal choline acetylase activity occurs at *p*H 7·0–7·5 with acetate as the acetyl donor[6].

Goldschmidt and Burkert[7] report the occurrence of acetylcholine in honey. This fact dispels evidence of an especial property of the secretion of hypopharyngeal glands, but suggests that acetylcholine may be a necessary inclusion in both honey and royal jelly, for these substances are the natural food of bees. Disregarding the possibility that acetylcholine appears in royal jelly or honey during muscular activity of the pharynx necessary for the expulsion of these substances from worker bees, it could be that acetylcholine has ecto-hormonal properties. Acetylcholine has no apparent effect when injected into insects in high amounts, but the possibility exists that it has a muscarinic action on the gut of bee larvæ, and in this way promotes rapid ingestion and movement of food. Choline as a hydrolysis product would provide a source of methyl groups for the process of transmethylation, which may be a factor in growth. In any event it would appear that acetylcholine of royal jelly and honey may have another purpose in insects different from that thought to be associated with the neurohormone in nervous tissue.

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Effect of Fluoride on the Biogenesis of Thyroid Hormones

THE biogenesis of thyroid hormones occurs in several successive stages. Accumulation of iodine in the thyroid may be considered as the first of these, while the second is represented by the binding of 'active iodine' on the tyrosine radical, 3-monoiodotyrosine being formed in the process. It would seem that a further enzymatic system[1] is responsible for the production of 3 : 5-diiodotyrosine, and a fourth phase in this biogenesis consists in the synthesis of iodinated thyronines into thyroxine, 3 : 5 : 3′-triiodothyronine, 3 : 3′ : 5′-triiodothyronine and 3 : 3′-diiodothyronine. In addition to these biosynthetic enzyme systems intervening in the thyroid, it is necessary to mention also the deiodinating enzyme, acting selectively on iodinated tyrosines and the proteolytic enzymes which liberate amino-acids from the thyroglobulin.

Table 1. PERCENTAGE OF IODINATED AMINO-ACIDS AND IODIDE IN PANCREATIC HYDROLYSATES OF THYROGLOBULIN IN THE RAT ASSESSED CHEMICALLY (IODINE-127)

	Control ($n = 4$)	Fluorized ($n = 7$)
Start	9·9	11 2
3 : 5-Diiodotyrosine	47·6	46 5
3-Monoiodotyrosine	23 2	23 5
Iodide	5 9	5 7
Thyroxine	8·7	8 9
3 . 5 : 3′-Triiodothyronine	4·3	3 6
Total iodine in the thyroid gland	6·73 μgm	6 62 μgm.

The present experiment bears on the effects of fluoride on the biogenesis of thyroid hormones in rats (females, weight 180–230 gm.). The animals received a daily dose of 2·2 μgm. of iodine in their basic diet[2] or 0·2 μgm. of iodine in a carbohydrate diet[3] in addition to 750 μgm. of fluoride given by means of a gastric tube in 1·0 ml. of water. Two months following the intraperitoneal application of 25 μc. of iodine-131 without carrier, the rats were killed at various time-intervals by bleeding under ether anæsthesia. The thyroids were homogenized and hydrolysed by means of pancreatine at 38° C. for 24 hr. 0·03 ml. of the hydrolysate was transferred directly to Whatman No. 1 chromatographic paper and developed in the *n*-butanol/dioxane/ammonia system (4 : 1 : 5) at 35° C. (ref. 4). The chromatograms were then analysed on an automatic radiopaper chromatographic recorder (Frieseke-Hoepfner). The percentage representation of iodinated amino-acids was assessed by chemical methods. This same procedure was also used for the assay of the protein-bound and total iodine-levels in serum and in urine[5].

The quantity of ingested fluoride had no effect either on body-weight, weight of thyroid, total composition of iodinated amino-acids or amount of iodide present in the thyroid (Table 1); it was also without effect on the iodine excreted in the urine and on the protein-bound and total iodine-levels in the rats receiving 2·2 μgm. of iodine daily. At the daily dose-rate of 0·2 μgm. of iodine, the protein-bound iodine-level in fluorized animals ($n = 12$) was lower than in the controls ($n = 7$), receiving the same diet ($P < 0·05$). In both groups, however, investigation with iodine-131 revealed a reduced rate of biogenesis of thyroxine and 3 : 5 : 3′-triiodothyronine within 12 hr. following administration of iodine-131. Fig. 1 shows a characteristic autoradiochromatogram of thyroglobulin hydrolysates of rats with a daily iodine intake of 2·2 μgm. The animals were killed 64 min. after the administration of iodine-131. The statistical evaluation of differences in rats receiving a daily intake of 0·2 μgm. of iodine is given in Table 2. Fluorized rats showed a significantly decreased amount of thyroxine ($P < 0·01$) and of 3 : 5 : 3′-triiodothyronine ($P < 0·05$) as against the controls. At a later date, after the application of iodine-131, the amount of thyroxine and 3 : 5 : 3′-triiodothyronine was the same in both the groups without regard to the diet.

Table 2. THYROXINE AND 3 : 5 : 3′-TRIIODOTHYRONINE RATIOS IN CONTROLS AND FLUORIZED RATS WITH DAILY INTAKE OF 0·2 μGM. OF IODINE, 8 HR. 32 MIN. FOLLOWING APPLICATION OF 25 μC. OF IODINE-131

	Control ($n = 2$)		Fluorized ($n = 6$)
Thyroxine	21·31 ± 2·75*	$t = 5·24$	8 00 ± 3·20
		$P < 0·01$	
3 5 : 3′-Triiodothyronine	9·37 ± 3 16	$t = 3·04$	4·43 ± 1 69
		$P < 0·05$	

* The values were obtained planimetrically and are given in sq. cm.

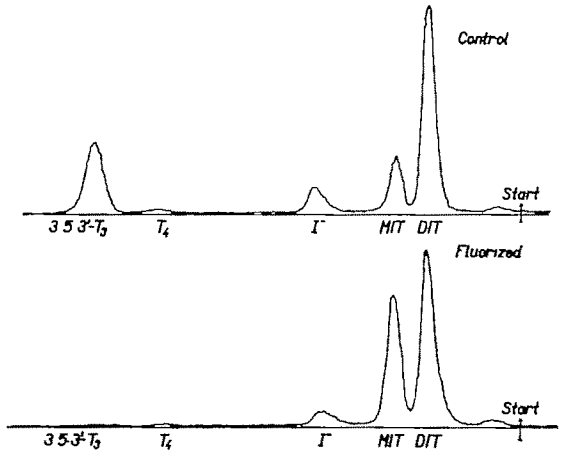

Fig. 1. Chromatograms of hydrolysed thyroglobulin in control and in fluorized rats with daily iodine intake of 2·2 μgm., 64 min. following administration of 25 μc. of iodine-131. 3 : 5 : 3'-T_3 = 3 : 5 : 3'-triiodothyronine; T_4 = thyroxine; I^- = iodide; *MIT* = 3-monoiodotyrosine; *DIT* = 3 : 5-diiodotyrosine

This finding is considered as confirmation of the fact that a special enzymatic system, which it is possible to inhibit by means of fluoride, is responsible for the synthesis of thyroxine and 3 : 5 : 3'-triiodothyronine.

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BIOPHYSICS

A Water-insoluble Trypsin Derivative and its Use as a Trypsin Column

THE conversion of enzymes into water-insoluble products possessing specific catalytic activity is of interest since such 'water-insoluble enzymes' may readily be removed from the reaction mixture, and can be used for the preparation of columns with enzymic activity. If stable, they may be employed repeatedly to induce specific chemical changes in relatively large amounts of substrate. Adsorption techniques were applied to combine enzymes with insoluble carriers[1]. These procedures led, however, to partial denaturation and resulted in preparations from which the reversibly adsorbed enzyme was removed while in contact with substrate. In order to strengthen the linkage between enzyme and carrier their attachment by chemical covalent bonds seemed preferable. Such links should obviously be carried out by functional groups non-essential for enzymic activity. Furthermore, the attachment of the enzyme to the carrier by flexible polymeric side-chains would ensure free movement of the catalyst molecules in the reaction mixture.

Various attempts to attach antigens and antibodies by chemical bonds to water-insoluble high molecular weight compounds have been reported[2]. The immunologically active columns obtained were used in the purification of the corresponding antibodies and antigens, respectively. So far as we are aware, however, only one paper deals with the chemical binding of enzymes to water-insoluble polymers[3]. Polyaminostyrene was used as carrier, and enzymes such as pepsin and carboxypeptidase were coupled with the polymer through azo bonds. The chemical properties as well as the enzymic activity of the final products were poorly characterized.

In the following we describe the preparation of a water-insoluble trypsin making use of the ideas mentioned above. A polytyrosyl trypsin containing tyrosyl peptide side-chains was prepared by initiating the polymerization of N-carboxy-L-tyrosine anhydride with trypsin. The trypsin derivative thus obtained was water-soluble and retained full enzymic activity. On coupling with a diazotized copolymer of *p*-aminophenylalanine and leucine it yielded the required water-insoluble trypsin. The latter served for the preparation of an active trypsin column.

Crystalline trypsin (75 mgm.) was dissolved in phosphate buffer, *p*H 7·2, ionic strength 0·25 (8 ml.), and the solution was mixed with N-carboxy-L-tyrosine anhydride[4] (80 mgm.) in dioxane (2 ml.). The mixture was kept at 2° C. for 24 hr. with magnetic stirring. Afterwards it was dialysed for five days against a large volume of 0·0025 *N* hydrochloric acid and was then lyophilized. The polytyrosyl trypsin obtained was free of monomeric tyrosine and of low molecular weight tyrosine peptides. A comparison of the ultra-violet absorption of polytyrosyl trypsin at 293·5 mμ in 0·1 *N* sodium hydroxide with that of trypsin revealed that the tyrosine content of the enzyme had increased from 2·8 per cent to 9·0 per cent.

The copolymer of *p*-amino-DL-phenylalanine and L-leucine was prepared by copolymerization of α,N - carboxy - *p* - amino,N - benzyloxycarbonyl - DL-phenylalanine anhydride[5] (3·5 gm.) and N-carboxy-L-leucine anhydride[5] (1·5 gm.) in dioxane (100 ml.) using triethylamine (0·1 ml.) as initiator. The product formed after standing for three days at room temperature was precipitated with water, dried and the benzyloxycarbonyl groups were removed with anhydrous hydrogen bromide in glacial acetic acid. Hydrolysis with 6 *N* hydrochloric acid for 24 hr. yielded *p*-aminophenylalanine and leucine in a molar ratio of 1 : 5. The copolymer was diazotized with nitrous acid and the diazonium salt formed precipitated at *p*H 7·5 with a concentrated sodium acetate solution. Coupling with polytyrosyl trypsin was effected in phosphate buffer, *p*H 7·2, ionic strength 0·25, at 2° C. with magnetic stirring. The reaction mixture was kept in the cold for 20 hr. and the light brown water-insoluble trypsin was separated by centrifugation and washed with 10 per cent sodium acetate solution, followed by 0·0025 *N* hydrochloric acid until no tryptic activity could be detected in the washings. The water-insoluble preparation was shown to contain 21 per cent protein as estimated from the amount of valine determined chromatographically[6] after acid hydrolysis.

The rate of hydrolysis of benzoyl-L-arginine methyl ester (4 mgm. per ml.) at *p*H 7·8 and 25° C., by

water-insoluble trypsin (1 mgm. per ml.), was equal to that by 0·045 mgm. per ml. crystalline trypsin. Since 1 mgm. water-insoluble trypsin contains 0·21 mgm. bound protein, the catalytic activity of the latter towards benzoyl-L-arginine methyl ester amounts approximately to a fifth of that of the free enzyme. The enzymic activity of water-insoluble trypsin remained practically unaltered when kept under 0·0025 *N* hydrochloric acid at 2° C. for several months. The remarkable stability of the water-insoluble trypsin is most likely due to the blocking of the ε-amino lysine groups of the enzyme on one hand, and to the fixation of the enzyme molecules to the water-insoluble copolymer on the other. The former leads to a decrease in the number of enzyme peptide bonds susceptible to tryptic digestion, while the latter inhibits interaction between trypsin molecules, thus diminishing autodigestion. Complete inactivation of water-insoluble trypsin could be effected by heating to 100° C. for 15 min. at *p*H 7·5. Addition of an excess of soybean or pancreatic trypsin inhibitor caused only partial inhibition of the enzymic activity.

A trypsin column of 0·8 cm. diameter and 5·0 cm. height was prepared by mixing water-insoluble trypsin (20 mgm.) with an inert polyvinyl resin ('Geon, 426', B.F. Goodrich Co.) (2·0 gm.) in 0·0025 *N* hydrochloric acid (20 ml.) and by pouring the mixture into a glass tube. Prior to use the column was washed with the suitable buffer. The effect of rate of flow of substrate on the degree of hydrolysis was tested in the case of L-arginine methyl ester. When a solution containing 7·0 mgm. substrate per ml. phthalate buffer of *p*H 6·0 and ionic strength 0·19 was passed through the column at 25° C. at different flow-rates (0·125 ml.–1·0 ml. per min.) the percentage of ester hydrolysed was found to be inversely proportional to the rate of flow. The column had retained full enzymic activity, even after the hydrolysis of as much as 4·0 gm. of L-arginine methyl ester during a period of two weeks.

On passing through the column a solution of poly-L-lysine hydrobromide (10 mgm. per ml. phosphate buffer, *p*H 7·4, ionic strength 0·13) at a rate of 1 ml. per hr., the effluent was found to contain dilysine, trilysine, tetralysine and traces of lysine[7]. Protamine and insulin oxidized by performic acid could be digested under similar conditions to products identical to those formed by normal tryptic digestion as detected by paper chromatography.

To test the action of the water-insoluble enzyme on a native protein, water-insoluble trypsin (1 mgm.) was mixed with a solution of 0·68 per cent rabbit myosine in 0·5 *M* potassium chloride, 0·03 *M* phosphate, *p*H 7·0 (5 ml.), and the reaction mixture was incubated at 22° C. After given time-intervals, 1-ml. aliquots were withdrawn, the water-insoluble trypsin was removed by centrifugation and the ultracentrifuge pattern of the supernatant was determined in a Spinco model-*E* ultra-centrifuge at 56,100 r.p.m. The pattern obtained after a digestion period of 200 min. showed clearly the presence of light and heavy meromyosin, and was similar to that formed by tryptic digestion of the myosin solution with 0·04 mgm. crystalline trypsin for 10 min.[8].

The trypsin column described here may be of particular use in the degradation of peptides and proteins for amino-acid sequence analysis. Since the various lysyl and arginyl peptide bonds of proteins and peptides may differ in their susceptibility towards trypsin, it is possible that preferential hydrolysis might be achieved by varying the rate of flow of the substrate through the trypsin column. Finally, it is possible that the principle used for attaching the enzyme with the aid of linear polymeric chains to a water-insoluble carrier might be used for the preparation of other water-insoluble proteins with biological activity. In such cases it will be of primary importance to determine the functional groups which are non-essential for the activity, and to find the suitable chemical reactions for forming the desired biologically active water-insoluble products.

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PHYSIOLOGY

Phosphorylation as a Factor in promoting the Crabtree Effect in the Amytal Ascites Sarcoma of White Mice

CRABTREE[1] has demonstrated an inhibition of oxygen consumption in several different malignant tissues following the addition of glucose. Many attempts have since been made, especially during recent years, to explain the mechanism of this phenomenon. Certain workers[2,3] regard adenine nucleotides, others[4,5] inorganic phosphorus, as responsible for the production of the Crabtree effect and postulate a competition between the oxidative and glycolytic systems for one of these substances. Ács *et al.*[6] have suggested that a location of enzyme systems unique for the cells involved also plays some part in producing the inhibitory effect.

The hypothesis of a direct competition for adenosine diphosphate seems to be disproved by the experimental observation that the inhibitors of glycolysis do not counteract the Crabtree effect, although they completely stop the glycolytic phosphorylation of adenosine diphosphate. The significance of the role of inorganic phosphorus, on the other hand, seems to be substantiated by the experiments of Brin and McKee[4], who succeeded in partially arresting the Crabtree effect by raising the concentration of inorganic phosphorus to 55 m.moles/l.

Data are very scanty as regards changes in the level of inorganic phosphorus during the incubation of ascites cells with glucose, and even the available reports refer to cases observed in phosphate-buffered media[7].

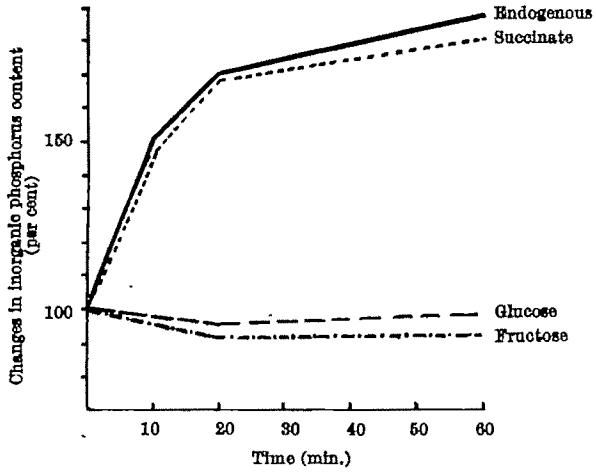

Fig. 1. Percentage changes in the inorganic phosphorus content of ascites cells in the course of incubation without substrate, with glucose (200 mgm. per cent), with fructose (200 mgm. per cent) and sodium succinate (0 02 *M*) regarding initial value as 100 per cent

We have studied changes in the inorganic phosphorus content of amytal ascites sarcoma cells occurring in the presence of different substrates without phosphate buffer. Incubation on endogenous substrate resulted in a significant increase of inorganic phosphorus; regarding the initial value as 100 per cent, it went up to 187 per cent within 1 hr., while the level of inorganic phosphorus decreased to 97 per cent in a medium containing 200 mgm. per cent of glucose. Fructose in a similar concentration is likewise capable of preventing the release of inorganic phosphorus, while both sodium succinate and sodium fumarate fail to prevent any effect (Fig. 1). This change in the level of inorganic phosphorus is not affected by the presence of either sodium fluoride or monoiodoacetic acid. Unlike glucose or fructose, fructose-1,6-diphosphate is unable to prevent the accumulation of inorganic phosphorus; this cannot be ascribed to a possible impermeability to phosphorylated sugars since similar results have been observed in homogenized systems as well. A typical change in inorganic phosphorus occurs if ascites cells are first incubated for an hour without substrate and glucose is added thereafter: inorganic phosphorus increases rapidly in the first phase, and drops to the initial level 10 min. after the addition of glucose (Fig. 2).

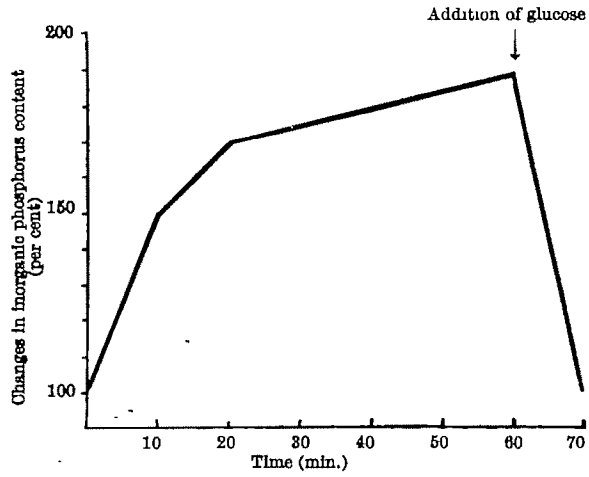

Fig. 2. Effect of glucose on changes in inorganic phosphorus contents of ascites cells. Glucose was added to cells after their incubation for an hour on endogenous substrate

All these observations substantiate the significance of phosphorylation as a factor responsible for the Crabtree effect. Phosphorylation and not complete decomposition of the sugars is necessary for the production of the effect, since—apart from glucose, fructose and mannose which undergo phosphorylation and metabolization—2-deoxy-D-glucose, too, is capable of provoking the Crabtree effect[7], although 2-deoxy-D-glucose undergoes phosphorylation without suffering complete breakdown. The role of phosphorylation is further emphasized by the fact that galactose, which gains access to the cells but undergoes no phosphorylation, fails to elicit the Crabtree effect[7]. Nor is it reduced by glucosone which, while being bound to the hexokinase of the Krebs-2 ascites cells, is phosphorylated only to a very moderate extent[5].

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New Evidence for a Cholinergic Process in Sympathetic Transmission

RECENTLY a cholinergic mechanism has been proposed in sympathetic transmission[1-3]. This suggestion was based on the following pieces of evidence. Sympathetic nerves contain cholinergic fibres[2]. Acetylcholine can exert a sympathomimetic effect acting at sites beyond the sympathetic ganglion cell, and this action depends on the presence of a store of catecholamine in the peripheral tissue[4]. Larger doses of acetylcholine can block the response to stimulation of postganglionic sympathetic fibres[3]. It was visualized that acetylcholine liberated from the endings of the cholinergic sympathetic fibres would impinge on a store of noradrenaline in the vicinity of the effector cells to bring about a final adrenergic response.

MacIntosh, Birks and Sastry[5] have shown that the drug hemicholinium inhibits the synthesis of acetylcholine in brain tissue, and that this effect of hemicholinium produces failure at sites where acetylcholine is a neurohormone. Hemicholinium injection into animals caused death by respiratory paralysis, and other effects similar to those of tetanus and botulinum toxins[6]. The addition of hemicholinium to the fluid perfusing the cat's superior cervical ganglion led to failure of transmission and simultaneously the rate at which acetylcholine was released decreased[5]. Hemicholinium produced block at the neuromuscular junction and at parasympathetic nerve endings[5,7-9]. The action of hemicholinium in inhibiting acetylcholine synthesis could be reversed

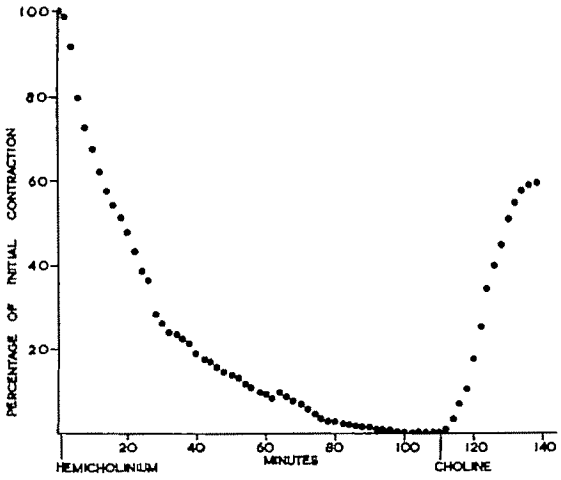

Fig. 1. Contractions of the guinea pig vas deferens in response to stimulation of the hypogastric nerve with 2-msec. pulses at 20/sec. for 10-sec. periods at 2-min. intervals. Each point is the mean of two–four experiments. After hemicholinium (20 μgm./ml.) the responses gradually decreased. The failure of transmission persisted after the bath was washed out at the 100th min. Choline (100 μgm./ml.) restored the response to nerve stimulation

by choline[4]. This finding could explain the effect of choline in restoring the response to nerve stimulation when hemicholinium had produced a failure of transmission[5–8].

We have investigated the effect of hemicholinium on the response to stimulation of a sympathetic nerve in order to test the proposal of Burn and Rand that a cholinergic process is involved in sympathetic transmission.

We chose for this investigation the isolated vas deferens of the guinea pig with the postganglion sympathetic hypogastric nerve attached. (This preparation was developed by Dr. S. Hukovič, working in the Department of Pharmacology, Oxford.) The vas deferens was suspended in an organ bath and the nerve stimulated with 2-msec. pulses at supramaximal strength for periods of 10 sec. every 2 min. The amplitude of the contraction of the vas deferens in response to nerve stimulation depended on the frequency of stimulation. With frequencies ranging from 7 to 20/sec., the response to successive periods of stimulation remained constant over long periods of time. A dose of tolazoline which specifically blocked the response to noradrenaline abolished the response to nerve stimulation. A dose of atropine which specifically blocked acetylcholine did not affect the response to nerve stimulation. Thus the hypogastric nerve to the vas deferens answers to the requirements of a sympathetic innervation.

When hemicholinium was added to the bath to make a concentration of 20 μgm./ml., the responses of the vas deferens to hypogastric stimulation gradually decreased and were finally abolished (Fig. 1). The rate at which the responses declined increased with increasing frequencies of stimulation. Previous observations that failure induced by hemicholinium depended on the frequency of stimulation have been reported for transmission in the superior cervical ganglion[5], and the neuromuscular junction[7,9].

Wilson and Long[8] have stated that hemicholinium is less active in blocking the response to nerve stimulation in sympathetically innervated structures than at parasympathetic nerve endings or at the myoneural junction. Their experiments were made on organs *in situ*, whereas our observations have been made on an isolated organ. In order to make a comparison between a sympathetically innervated structure and the myoneural junction, we have examined the isolated diaphragm innervated by the phrenic nerve taken from the guinea pig. In this preparation a higher concentration of hemicholinium (200 μgm./ml.) was required to produce a failure of transmission than was the case with the vas deferens. However, it is difficult to make comparisons because we observed again in this preparation that the rate at which failure was produced increased with increasing rates of stimulation. A further comparison of the action of hemicholinium on the response to nerve stimulation has been made in which we used a parasympathetically innervated structure. For this we used isolated rabbit atria with the vagus nerves attached[10]. Stimulation at 25 pulses/sec. applied to the vagi for periods of 1 min. duration at 4-min. intervals produced constant responses. After the addition of hemicholinium to the bath in a concentration of 40 μgm./ml., we observed a gradually developing decrease in the response to vagal stimulation, and the response was almost abolished by the fifth period of stimulation.

When the responses of the vas deferens or the diaphragm to stimulation of the appropriate nerve had been completely blocked by hemicholinium, they could be restored by the addition of choline (0·1–1·0 mgm./ml.) to the bath.

In our experiments we have shown that hemicholinium produced a failure of transmission at two sites in which it is not disputed that acetylcholine is a transmitter, namely, in the innervation of the diaphragm by the phrenic nerve, and in the innervation of the atria by the vagus. The effect of hemicholinium in producing a failure of transmission in the sympathetic innervation of the vas deferens has two features in common with its actions at cholinergic sites; the failure depends on the frequency of stimulation, and it is reversed by choline. Thus there is additional evidence for the hypothesis of Burn and Rand that there is a cholinergic process operating at sympathetic nerve endings.

We are indebted to Dr. J. P. Long of the Department of Pharmacology, State University of Iowa, Iowa City, U.S.A., for a generous gift of hemicholinium. This work was done while one of us (M. J. R.) held a fellowship of the Life Insurance Medical Research Fund of Australia and New Zealand.

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Histochemical Demonstration of the Mode of Action of the Alkaloid in Mussel Poisoning

It is generally accepted that the heat-resistant alkaloid which may be extracted from the digestive gland or liver of shellfish in coastal areas where poisoning of humans has occurred is responsible for the clinical picture in these cases. The same poison has been found in the dinoflagellate *Gonyaulax catenella*[1] on which the bivalves feed at certain times of the year, and the plankton has, therefore, been held responsible for the production of the toxin.

The exact mode of action and the nature of the poison are as yet unknown[2]. It is described as an alkaloid with muscarine-like actions[3], and is a potent neurotoxin, but, apart from the central and peripheral neurotoxic actions, Sapeika[2] has also described a direct depressant action of the toxin on the myocardium and its conducting tissues.

In the present investigation the small amount of mussel extract (2 c.c.) which was used was kindly supplied to us by Dr. N. Sapeika. The extract was prepared from uncooked black mussels according to Dack's[4] method.

On testing the extract, it was found that 0·6 mgm. injected intraperitoneally caused the death of rats weighing 70 gm. in a few minutes.

The extract contained 225 mgm. of the alkaloid per ml. Various dilutions of this extract were tested on 20-μ thick sections of cold, formalin-fixed rat brain and intercostal muscle. The acetylcholinesterase was demonstrated according to Gomori's[5] modification of the Koelle method. The sections were pre-incubated in toxin plus buffer for 1 hr. before being transferred to the same concentration of the toxin in the substrate mixture. Control sections were pre-incubated in buffer alone. The degree of inhibition obtained and the concentrations used are listed in Table 1. The caudate nucleus was used to assess acetylcholinesterase inhibition.

Table 1. Inhibitory Effect of Mussel Extract on Rat Brain and Intercostal Muscle

Concentration	mgm./ml.	Percentage inhibition
Rat brain		
0·1 ml. toxin/ml. substrate	22 5	100
0 07 ,, ,,	15 75	100
0 05 ,, ,,	11 25	100
0 04 ,, ,,	9	100
Motor endplates		
0 04 ml. toxin/ml. substrate	9	±10
0·027 ,, ,,	5·075	0
0 02 ,, ,,	4 5	0
0 016 ,, ,,	3 6	0

In the concentrations used only slight inhibition was observed in the very strong motor end-plate acetylcholinesterase activity; but, due to the small amount available, this could unfortunately not be tested in a higher concentration-range. However, total inhibition of acetylcholinesterase was produced in the caudate nucleus in the entire concentration-range of the toxin studied. At the same time, marked inhibition was also observed in the supra-optic neurones.

No inhibition of pseudocholinesterase could be seen in the capillary walls or myelinated areas[6].

From the above observations, it appears that the alkaloid has a very marked specific acetylcholinesterase inhibitory effect similar to some of the organo-phosphorus compounds. In view of this, it is suggested that future cases of poisoning be treated with one of the oximes such as pyridinealdoxime methiodide[7].

We are indebted to Dr. N. Sapeika for supplying us with the toxin and to Dr. R. Smit for advice.

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Nature of the Leucocytosis-inducing Factor in Plasma

It is now well known that fever[1] and leucocytosis[2], brought about by typhoid vaccine, are the result of the formation of at least two separate factors and not due to the direct action of vaccine (endotoxin) on the fever centre or on the bone marrow. Fukuda and Matsumoto[3] have recently demonstrated that the two factors act quite independently of each other and that in adrenalectomized animals, in particular, in spite of the normal occurrence of fever response due to the formation of the endogenous fever factor, leucocytosis fails to occur, and the leucocytosis-inducing factor cannot be detected by the use of passive transfer technique. The formation of the leucocytosis-inducing factor was found to depend solely on the presence of glycocorticoids. Moreover, the formation of this factor after the injection of vaccine could be inhibited by insulin administration, and conversely enhanced in an alloxan-diabetic state[4]. It was the object of the present work to examine whether or not this leucocytosis-inducing factor which is detectable in the circulating blood is identical with the 'leucocytosis-promoting factor' of Menkin[5] which was isolated from sterile exudates.

Typhoid–paratyphoid vaccine for clinical use (0·1 ml./kgm.) was first administered intravenously to a rabbit weighing about 2 kgm. At the time when a pronounced leucocytosis occurred (usually 8 hr. after), the animal was bled from the well-arterized ear vein (25 ml. in 10 min.) and serum was obtained. This serum was found to be capable of inducing a prompt rise in leucocyte counts (pseudo-eosinophilia) when given intravenously to a test rabbit (5 ml./kgm.). The promptness of the occurrence of leucocytosis without appreciable fever and preceding leucopænia is very characteristic and strongly suggests that this reaction differs greatly from the leucocytic response brought about by the vaccine itself or eventual pyrogenic contamination. The effectiveness of the leucocytosis-inducing factor did not diminish during dialysis through 'Cellophane' tubing against running tap water. Its activity was not reduced by heating at 57° C. for 30 min., but was completely lost at 100° C. within 30 min. The leucocytosis-inducing factor, like Menkin's leucocytosis-

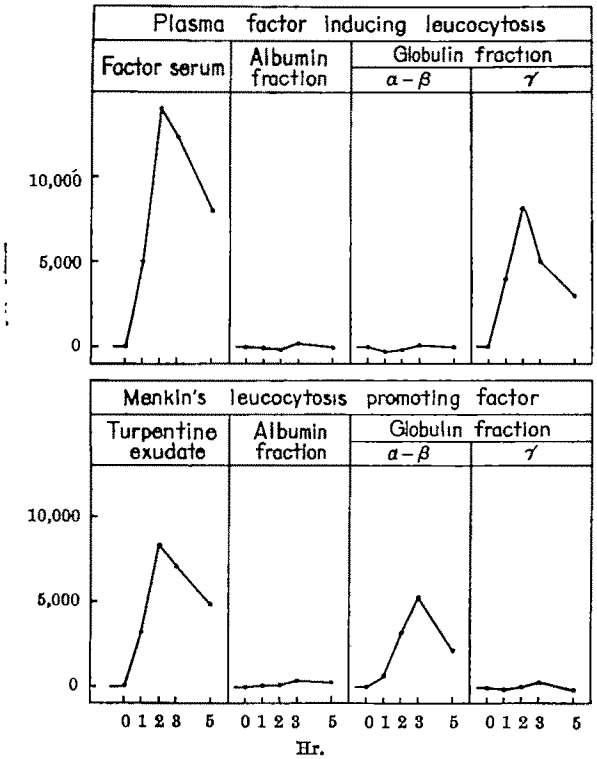

Fig. 1. Effective protein fraction of factor serum and turpentine exudate

promoting factor, is thus non-dialysable and thermolabile.

Next, protein fractions were prepared from the effective serum by the ordinary fractionation with ammonium sulphate and examined for their activity in inducing leucocytosis.

Each fraction, which had been dialysed and equilibrated with a physiological saline solution, was injected intravenously into test animals in an amount equivalent to 10 ml. of serum. As illustrated in Fig. 1, only a γ-globulin fraction precipitable by 35 per cent saturation of ammonium sulphate was found to be effective in producing the characteristic leucocytosis. This finding seemed to us very striking, for it has been reported that Menkin's leucocytosis-promoting factor is found in a pseudoglobulin fraction of the exudates[6], being distributed between α_1- and α_2-globulin[7].

For the sake of comparison, turpentine pleuritic exudate from rabbits which would contain Menkin's leucocytosis-promoting factor was also fractionated by the same method. The results of intravenous administration of each of the fractions corresponding to 5 ml. of the exudate (*p*H 7·4) are also given in Fig. 1. It will be seen that the activity is associated with the α- and β-globulin fractions, which are precipitable by 50 per cent saturation of ammonium sulphate. The pleuritic exudate from adrenalectomized animals was found to be also effective. The formation of Menkin's leucocytosis-promoting factor, therefore, does not appear to depend on the presence of glycocorticoids, forming a sharp contrast with the case of the leucocytosis-inducing factor.

It may therefore be concluded that there exist two distinct factors both responsible for the production of leucocytosis. One will be formed in the circulating blood in response to typhoid vaccine or other pyrogenic large molecular substances, whereas the other is formed in inflammatory exudates by the injured cells, even in the absence of the adrenal. Although Menkin has expressed the opinion that the latter factor (leucocytosis-promoting factor) may enter the circulating blood stream and then comes to be responsible for the leucocytosis frequently associated with inflammatory processes, there is no likelihood that the leucocytosis-promoting factor enters the circulation in large quantities, except under conditions of stress such as epinephrine administration.

Details of the experiments concerning these problems will be published elsewhere.

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Importance of Insulin and of the Adrenal Cortex in determining the Toxicity in Baboons (*Papio ursinus*) of Human Anterior Pituitary

GROWTH hormone administered to normal, diabetic or hypophysectomized dogs produces severe toxic reactions which may terminate fatally[1]. Human anterior pituitary preparations may also precipitate severe toxic reactions in spontaneous human diabetes and mild reactions even in non-diabetics[2,3]. Similarly, saline suspensions of acetone-dried, human anterior pituitary lead to fatal reactions in insulin-deprived, depancreatized baboons[4]. Cortisone prevents the adverse reactions of growth hormone in hypophysectomized dogs[5], but not in diabetic baboons[4].

During the course of our investigations into the endocrine control of the metabolic disorder induced by complete pancreatectomy in the baboon, we had occasion to administer human anterior pituitary to 2 normal and 3 adrenalectomized baboons, and to 15 baboons either with the hypophysis or the adrenal removed in addition to the pancreas. Unlike the normal dog, the normal baboon fails to develop any gross clinical reactions if treated with ten times the amount of human anterior pituitary necessary to produce death in the insulin-deprived, depancreatized baboon. In the presence of an intact pancreas, human anterior pituitary is well tolerated by adrenalectomized baboons maintained with doca and/or hydrocortisone and by hypophysectomized baboons. Indeed, unlike the dog, human anterior pituitary greatly improves the physical state of the hypophysectomized baboon. Furthermore, although human anterior pituitary induces an intensely fatty liver in the diabetic baboon, provided sufficient insulin is administered, the animal remains well. Doubly operated, adrenalectomized-depancreatized baboons receiving doca but no insulin are unaffected by

human anterior pituitary. However, if the latter baboons, in addition to doca, also receive hydrocortisone, then severe toxic reactions manifest themselves within 10–12 hr. and these may prove fatal if human anterior pituitary is continued. Hypophysectomized-depancreatized baboons deprived of insulin may die rapidly after the injection of human anterior pituitary.

From these several experiments, it would appear that the toxic effects of human anterior pituitary depend primarily on an insufficiency of insulin and on the presence of at least some 11-oxycorticosteroids akin to cortisone or hydrocortisone. The fact that toxic reactions develop in hypophysectomized-depancreatized baboons deprived of insulin but receiving human anterior pituitary would indicate that the adrenal cortex of the hypophysectomized-depancreatized baboon continues to secrete 11-oxycorticosteroids, albeit in reduced amounts, for several months at least after hypophysectomy.

We wish to express our appreciation to Dr. J. Friedman, Department of Forensic Medicine, University of the Witwatersrand, and to Dr. M. Prates, director of Pathological Services of Mozambique, for making available the human pituitaries.

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Phosphate and Salt Uptake by Bakers' Yeast

UPTAKE of phosphate by *Saccharomyces cervisiae* has three components as indicated by first-order kinetic analysis of uptake under steady-state conditions as a function of phosphate concentration. Two of these components, having Michaelis–Menten constants $K_m = 10^{-5}$ and 10^{-3}, respectively, are evident on a plot of rate of uptake m against m/phosphate concentration[1] (Fig. 1). Action of glycolytic and respiration inhibitors, including anaerobiosis —illustrated by the action of iodoacetate (Fig. 1)— indicates that both these components are coupled to oxidative phosphorylation associated with the action of glyceraldehyde-3-phosphate dehydrogenase. The component reaction with $K_m = 10^{-5}$ is found to be rate-limited by formation of adenosine triphosphate, which acts as a competitive inhibitor in the oxidative phosphorylation, and the component with $K_m = 10^{-3}$ by the action of hexokinase, which becomes rate-limiting for utilization of adenosine triphosphate. The coupling of phosphate uptake with glycolysis, but not its components, was recognized by Strickland[2] and Goodman and Rothstein[3]. Rothstein[4], in particular, has related the uptake to glycolytic activity at a membrane surface.

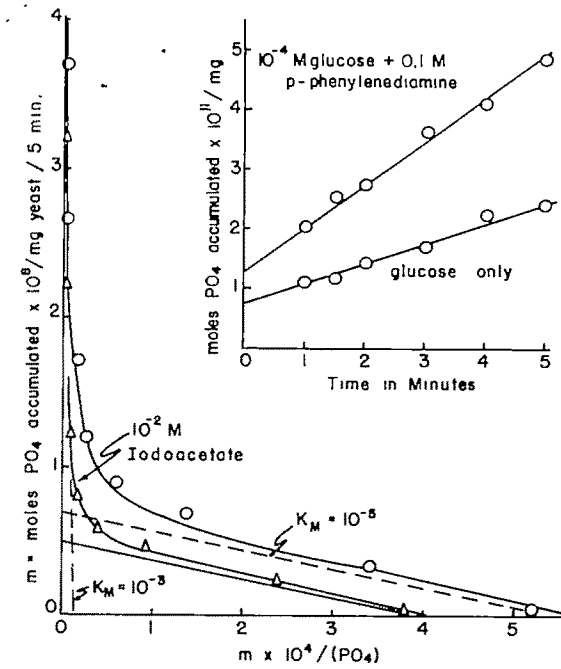

Fig. 1. Hofstee graph for aerobic accumulation of phosphate at concentration of 10^{-2} to 10^{-6} M by bakers' yeast in the presence of 0·3 M glucose at pH 4·0

Fig. 2. Effect of 0·1 M p-phenylenediamine on aerobic phosphate accumulation by bakers' yeast from a 2×10^{-2} M solution in the presence of 10^{-4} M glucose

A third component of phosphate uptake having $K_m = 10^{-6}$ is observed with great consumption of oxygen when phosphate and glucose concentrations are low. It is responsive to respiration inhibitors (Fig. 2), increasing, for example, in the presence of p-phenylenediamine by increase of site with constant rate of turnover, and is found to be coupled to oxidative phosphorylation associated with oxidation of cytochrome b. The contribution of this component to uptake with phosphate concentrations greater than 10^{-5} M in the presence of glucose ($>0·01$ M) is negligible. The conclusion is that in bakers' yeast the activity of the respiratory chain is coupled to only a minor extent to phosphate uptake at an external membrane surface.

That these observations are general for salt accumulation is indicated by rubidium uptake by bakers' yeast under aerobic and anaerobic conditions (Fig. 3). Anaerobiosis increases the concentration of sites without affecting rate of turnover.

Barley roots, in contrast to bakers' yeast, take up phosphate only under aerobic conditions. The sites of uptake in barley roots are associated with oxidative phosphorylation in the respiratory chain[5]. The mitochondria seem to be effective at a limiting membrane and simply might be embedded in that membrane. In bakers' yeast the respiratory chain, whatever its particulate nature, appears to be functioning inside the limiting membrane and acts in phosphate uptake chiefly as an oxidant for reduced diphosphopyridine nucleotide. Under anaerobic conditions the oxidation is chiefly accomplished by the action of alcohol dehydrogenase. Barley roots also form ethanol[6], but the triose phosphate dehydrogenase action utilizing oxidized diphosphopyridine nucleotide is internal to the cells and thus not anaerobically functional.

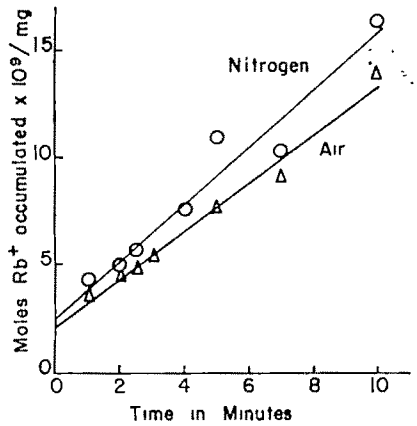

Fig. 3. Accumulation of rubidium ions by bakers' yeast from 10^{-3} *M* solution at *p*H 4·0 under aerobic and anaerobic conditions

The yeast cells used in this work were grown in pure culture, to eliminate a common and very troublesome bacterial contaminant, on beef extract peptone medium containing 0·15 *M* sodium chloride and with 0·3 *M* glucose as a substrate. The oxygen consumption was $2 \cdot 3 \times 10^{-8}$ mole oxygen/mgm. dry weight. Cells were washed once with 0·15 *M* sodium chloride and introduced at zero time into a salt solution containing phosphorus-32 or rubidium-85. Uptake was terminated by centrifuging (10 sec.) and washing.

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HÆMATOLOGY

An Albumin Gradient Method for separating the Different White Cells of Blood, applied to the Concentration of Circulating Tumour Cells

THE albumin sedimentation method of Vallee *et al.*[1] has been applied to the problem of isolating tumour cells from the circulating blood[2]. This method and its modifications involve the collection of the cells at an interface. When a variety of cells together with platelets are packed at an interface they are apt to sink or float as a unit. Such artefacts may seriously interfere with separation in a centrifugal field[3]. Moreover, we have found the cells to show morphological changes after prolonged centrifugation in contact with a foreign solution. It is therefore desirable to use a gradient method[4].

The present method avoids interfaces, dispenses with the necessity for making up solutions of accurately known specific gravity, and exposes the cells for the shortest possible time to the minimum possible concentration of foreign substances. The cells are suspended throughout in their own plasma.

16 ml. of venous blood is taken with a siliconed syringe into a siliconed vessel containing 4 ml. of 6 per cent dextran in saline ('Dextraven') with 40 mgm. of ethylenediamine tetraacetic acid dipotassium salt. A silicone rubber bung is inserted, and the contents mixed. The tube is stood for about ½ hr. until the red cells have sedimented. The supernatant plasma containing the white cells is removed and centrifuged at 1,000 r.p.m. for 10 min. The procedure so far is that of Alexander and Spriggs[5] except for the use of ethylenediamine tetraacetate instead of heparin in order to prevent platelet clumping. The deposit is resuspended in 0·5 ml. of its own plasma, and is referred to as the 'leucocyte suspension'. The supernatant plasma, which was poured off, is centrifuged again at 3,000 r.p.m. for 5 min. before being used in subsequent stages of the separation.

Bovine albumin solution is prepared as described by Roberts *et al.*[2]. We have used Armour's bovine plasma albumin (fraction V). The final concentration is immaterial provided that the solution has a higher density than the red cells; it should have a specific gravity 1·100 or above.

About 0·5 ml. of the albumin solution is placed in the bottom of a siliconed tube of 6 mm. bore, and an equal volume of the plasma is layered on top. Using a sealed-off Pasteur pipette (with an angle at the end) as a stirrer, the interface is broken, and the fluids are mixed by passing the stirrer up and down with gradually increasing amplitude, but avoiding the top and bottom of the column. A visible gradation in the colour of the column is used as a guide to the correct degree of mixing; the operation takes not more than 30 sec.

The white cell suspension is layered on to the column, and the tube is centrifuged for 15 min. at 3,000 r.p.m. By this time several layers have formed, as shown in Fig. 1.

The topmost layer consists of platelets with monocytes and some lymphocytes. This layer is often double, the upper part consisting almost entirely of platelets and the lower containing the mononuclear cells. Turk cells and any megakaryocytes which have retained their cytoplasm are also present in this layer.

Fig. 1

The plasma between layers *A* and *B* is often clear, but it may contain cells, particularly lymphocytes and myelocytes if present.

Layer *B* consists of the polymorphonuclear leucocytes. The basophils are commonest near the top and the eosinophils near the bottom, but they do not segregate from the neutrophils. Bare megakaryocyte nuclei are usually found in layer *B*.

Layer *C* consists of red cells. This layer may be translucent, owing to the high refractive index of the medium; the red cells are not in fact hæmolysed.

To find tumour cells, the whole of layer *A* together with all the fluid above it is pipetted off, diluted with plasma, and centrifuged until the cells are deposited. The deposit is then spread on slides, air-dried and stained with May–Grünwald and Giemsa. We have found that if a drop of the deposit from an

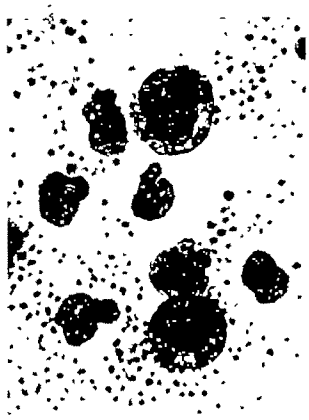

Fig. 2

effusion containing tumour cells is added to a 16-ml. sample of blood and processed by the above method, the tumour cells can be recovered from above the platelet layer, sometimes practically pure. They are also present in numbers in the platelet-monocyte layer (layer *A*), but very few sink below this.

Fig. 2 shows a film of layer *A* from a patient with reticulosarcoma whose direct blood film was normal. Besides monocytes and platelets, two reticulosarcoma cells are shown. The photograph demonstrates the good cell preservation and the absence of platelet agglutinates.

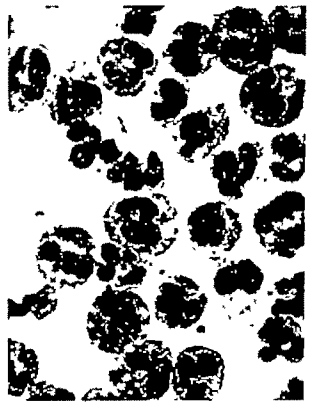

Fig. 3

Fig. 3 shows a film of the polymorphonuclear leucocyte layer (layer *B*); red cells are practically eliminated. This layer is not used in the examination for tumour cells; but the photograph shows that the same method would be useful for the preparation of polymorphonuclear leucocyte suspensions for other purposes.

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Properties of a Further Variant of Hæmoglobin M

Hæmoglobin M, discovered in 1948 by Horlein and Weber[1], is an abnormal hæmoglobin of rare occurrence, three variants of which have since been identified[2,3]. In two members of a family of Leipzig, Germany—a child and his father, the former having been clinically studied, on account of congenital methæmoglobinæmia, by one of us[4]—we were able to demonstrate a new type of hæmoglobin M.

Absorption spectra of destromatized hæmolysates made from washed erythrocytes of the patient and a normal adult control are shown in Fig. 1. After conversion of the oxyhæmoglobin to methæmoglobin by means of potassium ferricyanide, an absorption band at about 600 mμ (contrary to methæmoglobin A) and an inflexion at 540 mμ (similar to methæmoglobin A) appeared in the spectrum of the patient's hæmolysate. No difference was observed in cyanmethæmoglobin spectra of both hæmolysates. Isolation of methæmoglobin M in a pure state from the patient's hæmolysate (= hæmoglobin A + M), using starch block electrophoresis at *p*H 7·0 according to Gerald and George[5], was not entirely satisfactory. A brown front and a slower portion of grey-green colour appeared in the otherwise unseparated spot. On elution, the grey-green portion spectrophotometrically showed an intensified absorption band near 600 mμ and a more distinct inflexion at 540 mμ. However, an inflexion in the region 640–620 mμ indicated that separation from methæmoglobin A had not been complete. On the evidence that 20–25 per cent of the patient's hæmoglobin is of type M (see below), the spectrum of 'pure' methæmoglobin M was calculated from the data of the patient's and a normal adult's methæmoglobin spectra (Fig. 1): there is a rather prominent peak at 602 mμ and a second absorption band at 540 mμ, the inflexion around 630 mμ being practically straightened.

Reaction of potassium cyanide ($1 \cdot 45 \times 10^{-3}$ *M*) and methæmoglobin A + M ($1 \cdot 35 \times 10^{-5}$ *M*) proceeded in two phases when followed at 630 mμ, *p*H 6·8: a very rapid one, identical with the reaction of methæmoglobin A, and a slow one (Fig. 2). At

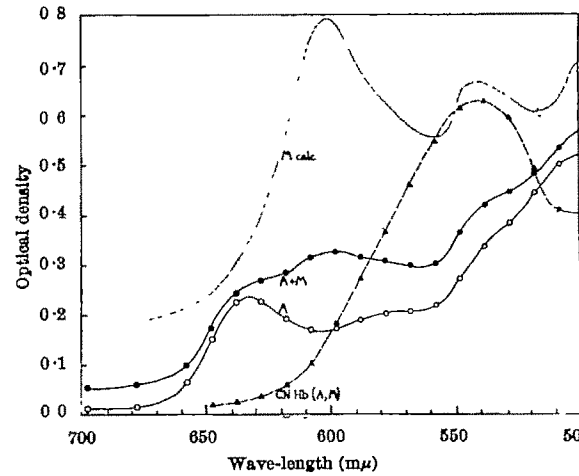

Fig. 1. Methæmoglobin absorption spectra of destromatized hæmolysates of the patient (A + M, ●) and a normal adult (A, ○). ▲, Cyanmethæmoglobin (identical for A and A + M); . . . , 'pure' methæmoglobin M calculated from A + M and A, assuming that 25 per cent of hæmoglobin M are present in A + M. Hæmoglobin concentration: 92 mgm./100 ml. = $1 \cdot 38 \times 10^{-5}$ *M*, *p*H 6·8 (phosphate)

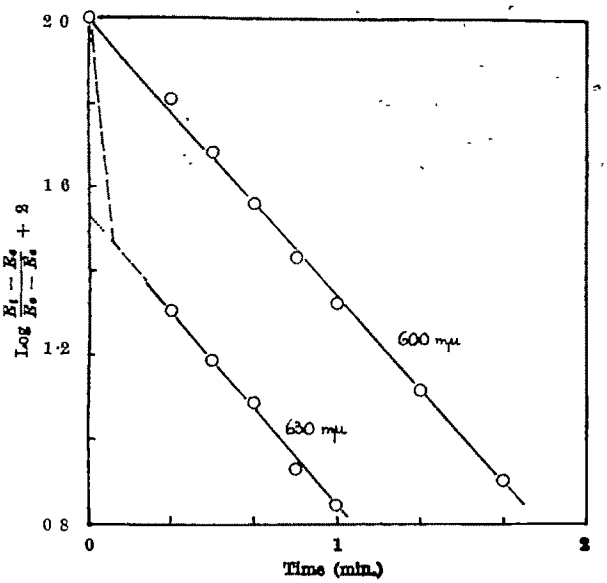

Fig. 2. Reaction of methæmoglobin A + M and potassium cyanide followed at 600 mμ and at 630 mμ

600 mμ only a slow reaction was demonstrable, its half-time being 27·5 sec. under the above conditions. From the data of Fig. 1 it is evident that at 630 mμ the combined reactions of both methæmoglobins and cyanide will be measured, whereas at 600 mμ—near the isosbestic point of methæmoglobin A and cyanmethæmoglobin—the reaction of methæmoglobin A is optically eliminated, leaving cyanide combination of methæmoglobin M open to analysis. By calculating the amount of methæmoglobin A which corresponds to the reduction in optical density at 630 mμ in the rapid first phase of cyanide combination, it was estimated that 79·5 per cent of methæmoglobin A and 20·5 per cent of methæmoglobin M should be present in the patient's erythrocytes. Reaction velocity of cyanide combination of methæmoglobin M at *p*H 6·8 was found to be less than 1/100, as compared with normal adult methæmoglobin under appropriate conditions (cyanide $4 \cdot 33 \times 10^{-4}$ *M*; methæmoglobin $1 \cdot 41 \times 10^{-6}$ *M*).

Oxidation of hæmoglobin M-containing oxyhæmoglobin solutions with potassium ferricyanide at *p*H 6·8 also proceeded in two phases, a rather rapid one and a slow one, the reaction velocity of the latter corresponding to the oxidation velocity of oxyhæmoglobin A. Similarly, comparative spontaneous oxidation of oxyhæmoglobin in patient's and normal adult's hæmolysates at room temperature, *p*H 6·8, showed distinctly more rapid oxidation (reaction velocities 1 : 23) of oxyhæmoglobin M. Evaluation of the experimental data confirmed that hæmoglobin M-content of the patient's hæmolysate was about 23 per cent, which is in good agreement with the finding reported above.

The spectral characteristics of the methæmoglobin M described here are distinct from those of hæmoglobin M_B of Gerald and George[2] and hæmoglobin M_M of Pisciotta *et al.*[3]. Absorption bands near 600 mμ and 540 mμ are comparable to the findings of Gerald and George[2] in hæmoglobin M_S. In contrast, hæmoglobin M_S reacts rapidly with cyanide whereas this hæmoglobin M reacts slowly.

In view of the spectrophotometric and reaction characteristics, it seems justified to assume that the type of hæmoglobin M described here is essentially different from hæmoglobin M_S, hæmoglobin M_B, and hæmoglobin M_M. Following the general practice, we propose to designate it 'HbM_L' after the place of its origin. Spectral properties suggest that this type of hæmoglobin M might be the same as the one previously studied by Hörlein and Weber[1], and Heck and Wolf[5]. It is to be noted that in the latter a rapid spontaneous oxidation has been demonstrated by Kiese *et al.*[6].

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Difference between γ-Globulins fixed on the Platelets of Patients with Idiopathic Thrombocytopenic Purpura and of those suffering from Disseminated Lupus Erythematosus or a Panhæmatocytopenia

The direct antiglobulin consumption test using leucocytes or platelets[1] is based on the indirect antiglobulin consumption test[2,3]. It has been found to give positive results with both leucocytes and platelets from about 90 per cent of patients with disseminated lupus erythematosus and 30 per cent of cases of idiopathic panhæmatocytopenia, but with platelets only from approximately 65 per cent of cases of idiopathic thrombocytopenia[4].

It will be seen from Table 1 that when two different batches of anti-human-globulin serum (or Coombs's serum) were used, different results were obtained. Consumption of the anti-human-globulin serum was measured by testing against red cells sensitized with incomplete anti-D serum. It was found that whereas anti-human-globulin serum No. 1 was absorbed by the platelets of all three groups of patients, anti-human-globulin serum No. 2 was absorbed by the platelets of those suffering from disseminated lupus erythematosus or panhæmatocytopenia, but not of those with idiopathic thrombocytopenic purpura.

Table 1

No. of cases		Anti-human-globulin No. 1 incubated with Leucocytes	Anti-human-globulin No. 1 incubated with Platelets	Anti-human-globulin No. 2 incubated with Leucocytes	Anti-human-globulin No. 2 incubated with Platelets
4	Normal, negative controls	−	−	−	−
2	D.L.E.	+	+	+	+
5	Panhæmatocytopenia	+	+	+	+
6	Idiopathic thrombocytopenic purpura	−	+	−	−

+, Anti-human-globulin consumption; −, no anti-human-globulin consumption. D.L.E., disseminated lupus erythematosus.

The results obtained using anti-human-globulin serum No. 1 showed that γ-globulin had been fixed on the platelets of all three groups of patients. Using anti-human-globulin serum No. 2 it was shown that the antigenic structure of the γ-globulin fixed on the platelets of patients with idiopathic thrombocytopenic purpura was different from that on the platelets of patients in the other two groups. If we assume that the γ-globulin attached to the platelets is an auto-antibody, then these results would seem to show that there are two varieties of anti-platelet auto-antibodies.

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PATHOLOGY

An Oncolytic Virus recovered from Swiss Mice during Passage of an Ascites Tumour

The recovery of a tumour-destroying virus from mouse ascites was recently reported by Bennette[1]. It was serially transmissible and seemingly non-pathogenic in the absence of neoplastic cells. Filtrates of ascitic fluids and extracts of cells which harboured the contaminant were highly destructive for the Ehrlich carcinoma and also five other tumours.

An agent with strikingly similar properties has been under observation in our laboratories for the past two years. The effects of this agent were first observed by one of us (G. S. T.) in Swiss *W* mice following long-continued passage of the mouse ascites tumour described by Nelson[2] in 1956. A number of sub-lines, maintained by intraperitoneal injection, were lost after the sudden appearance of abnormal ascitic fluid and aggregates of the tumour cells. Bacteriological findings were negative and a virus was indicated by passage of the active agent through Coors filters (No. 3). Most of the following observations were based, however, on the use of abnormal fluids sedimented at low speed to remove the tumour cells.

In practice, 12–15 gm. weanlings from the random-bred specific pathogen-free colony of Swiss mice maintained at the Rockefeller Institute were used. They were injected intraperitoneally in groups of 5 with 0·1 ml. of normal tumour fluid diluted 1 : 5 and the same volume of cell-free fluid containing the contaminant. The mice were usually killed on the seventh day after injection. Those which received the virus in high concentration were either normal at autopsy or showed a slight reaction. Suppression of the neoplastic cells in the peritoneal cavity was essentially complete. In some cases a solid tumour arose at the site of injection in mice held for a longer time. Injection of the virus in low concentration, declining activity being retained up to a dilution of 10^{-8}, usually resulted in an irregular tumour growth. It was characterized by watery ascitic fluid with a reduced cell content and the appearance of a white membrane composed of aggregated cells, fibrin and debris. The membrane was generally attached to the liver but less regularly extended downwards into the folds of the intestinal tract, with resultant binding and distension. During life, this reaction was accompanied by abdominal swelling and either rectal soilage or plugging. Most of the mice were otherwise normal, but an occasional animal showed external or internal signs of jaundice, yellow ascitic fluid, and yellow or white foci of necrosis in the liver.

Our observations were limited to the one tumour. In the presence of uncontaminated ascitic fluid, the virus was passaged intraperitoneally more than fifty times with similar findings. It was active in mature mice as well as in weanlings, but had little or no suppressing effect on solid tumours produced by intramuscular injection. The virus was tested in three additional mouse strains and showed no evidence of host specificity. It was recoverable from the livers of injected mice and readily maintained by intraperitoneal passage of liver suspensions. In the absence of tumour cells, it produced no detectable reaction in weanlings but continued to multiply in the liver. Phase microscopy revealed dense circular inclusions in the cytoplasm of some tumour cells from abnormal fluids. Electron micrographs, made with the co-operation of Dr. Man-Chiang Niu, showed single or multiple cytoplasmic nests of circular or elliptical particles with maximum diameters of 50–70 millimicrons.

Bennette[1] stated that his virus was not pathogenic in the absence of tumour cells, but his observations were limited to weaned mice. Our virus was similarly inactive in weanlings, but was highly pathogenic for nurslings 1–2 days old. Intraperitoneal injection of contaminated cell-free fluid was attended by high mortality (78 per cent of 42 mice) between the fifth and the thirteenth day. Mice that survived through the ninth day were under-developed and stunted. Some of them showed oily coats, with or without rectal soilage, and yellow or white necrotic foci in the liver. External and internal signs of jaundice were occasionally noted. Oral administration of the virus resulted in similar findings. Liver suspensions from the infected nurslings suppressed growth of the ascites tumour on combined injection in weaned mice.

The oncolytic virus was also recovered from a few mice during a minor outbreak of intestinal disease which occurred during the early development of the specific pathogen-free colony. The rigid quarantine observed in the maintenance of this colony precluded introduction of the virus by accidental contamination with experimental wastes. Outward signs of the naturally acquired disease were limited to nurslings and were similar to those induced by injection. Oily coats and yellow foci in the liver were again observed. Several female breeders which were nursing infected young but were normal in appearance also showed focal involvement of the liver at autopsy. The virus was demonstrable on combined injection in weanlings.

When first observed, it was thought that the oncolytic agent might be a member of the hepato-encephalitis group of murine viruses. The recovery of murine hepatitis virus from the same ascites tumour after prolonged passage in Princeton mice was reported by one of us (J. B. N.)[3] in 1959. This relation was soon ruled out, however, by distinct behavioural differences. The intestinal and hepatic manifestations in nurslings were strongly suggestive of those produced by the hepato-encephalomyelitis

virus described in 1953 by Stanley, Dorman and Ponsford[4,5] in Australia. Oily coats and yellow foci in the liver were characteristic features. The neurotropic properties of their virus were brought out by serial passage. The cerebral behaviour of our virus has not been fully studied. It seems probable that the Australian, British and American viruses are interrelated and are widely distributed in mouse colonies as latent invaders. Direct comparison of the three agents is clearly indicated.

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Griseofulvin and Colchicine: Lack of Carcinogenic Action

DURING the investigation of the toxicology of griseofulvin, it was shown[1] that the antibiotic when given parenterally is a mitotic poison, in some respects similar to colchicine. Clinical investigation[2,3] showed that this did not represent an acute toxic hazard in clinical use. Nevertheless, interference with mitosis seems to us to imply a greater possibility of carcinogenic action on long-term administration than is the case with compounds devoid of this property. Colchicine has not yet been studied adequately from this point of view, and it was decided to include a group treated with this drug in a study of the long-term effects of griseofulvin.

Four groups of albino, Wistar rats were used. All were newly weaned at the commencement of the experiment. Group I received colchicine, 0·5 mgm./kgm., twice weekly for 42 weeks. The colchicine was initially given subcutaneously in saline, but because of local necrosis the vehicle was changed to arachis oil after four weeks. Group II received saline and arachis oil as controls to Group I. Group III received a finely ball-milled suspension of griseofulvin as a 10 per cent w/v dispersion in 0·5 per cent aqueous mixture of 'Dispersol *LN*' and 'Dispersol *OG*', at a level of 200 mgm./kgm., twice weekly by intraperitoneal injection for 93 weeks. Group IV received the suspending agents alone as a control to Group III. Each group comprised 10 male and 10 female animals.

Colchicine proved toxic in the initial stages, but griseofulvin was well tolerated until the seventy-fifth week of the experiment when mortality began to mount. At the end of 52 weeks dosing, eight animals treated with colchicine, but only two treated with griseofulvin, had died. At the end of 78 weeks experiment, nine animals of each group treated with the drugs had died. Five animals given colchicine and seven given griseofulvin survived until the experiment was terminated at the end of the ninety-third week.

All animals were examined after death for the presence of tumours and, unless postmortem autolysis was advanced, blocks of all the major organs were fixed for histological examination. The following tumours were encountered: Group I: colchicine treatment; one fibroadenoma of mammary gland; Group II: control to colchicine, four adenomata of thyroid; one leiomyosarcoma of the vagina and one sarcoma at injection site; Group III: griseofulvin treatment, one adenocarcinoma of cervix uteri; Group IV: control to griseofulvin, one interstitial cell tumour of the testis.

In the animals treated with either griseofulvin or colchicine, the nuclei of the liver and stomach mucosa of some appeared rather more variable in size than is normally the case. Other pathological changes were found equally in control and treated groups.

Although the numbers in these experiments are relatively small, it is clear that neither griseofulvin nor colchicine is a potent carcinogen, and indeed these experiments give no evidence of carcinogenic action of any sort of either compound.

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The Hedgehog as a Source of Human Ringworm

THE dermatophyte *Trichophyton mentagrophytes* has been isolated from a variety of animals, but although Georg[1] lists 18 wild and domestic mammals living in different geographical areas which are known to be spontaneous carriers of this pathogen, the hedgehog does not appear to have been included in any survey.

During March 1960 an adult female patient attended the mycological diagnostic clinic attached to this Department, complaining of ringworm, which she stated to have been contracted from a pet hedgehog. On examination, several raised itchy lesions were found, from which a pathogenic fungus was isolated. This was readily assigned to the genus *Trichophyton*, but less readily placed in a definite species. During the same month a similar isolate was obtained from a lesion on the wrist of an adult male, who had recently returned from a country holiday.

A series of 26 living and dead hedgehogs, collected in this area, were examined for the presence of a pathogenic fungus. Isolates of *Trichophyton*, similar in macroscopic and microscopic characters, were recovered from 7 (27 per cent) of the animals. Positive cultures were obtained from the quills of 4 and from the hair on the ventral body wall, the head or the ears of a further three. A hedgehog isolate (*H*1) was sent to Dr. Lucille Georg, Communicable Diseases Centre, Georgia, United States, who kindly identified it as *Trichophyton mentagrophytes*.

Mycelial fragments taken from the *H*1 strain were applied to an area of scarified skin on a guinea pig

and on a human volunteer. Rapidly spreading itching lesions were produced in both from which were recovered isolates identical with the *H*1 strain.

Hedgehogs were first introduced into the Dunedin district in 1885[2]. Several further liberations were made in both islands of New Zealand, and these mammals have become very numerous in several areas. Their contact with man and his domestic animals may be greater than is generally realized, and there seems to be good evidence that the dermatophyte strains which they carry are transmissible to man. They appear to constitute a hitherto unrecognized source of human infections.

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BIOLOGY

A Pacific Salmon (*Oncorhynchus gorbuscha*) in Scottish Waters

ON July 16, 1960, in a salmon bagnet at Altens fishing station on the sea-coast near Aberdeen, a fish was caught which was recognized as unusual. It was sent to the Freshwater Fisheries Laboratory at Pitlochry and then to the British Museum (Natural History), where it was identified as *Oncorhynchus gorbuscha* (Walbaum)[1,2], the pink or humpback salmon, a species the natural distribution of which is along the Pacific coasts of North America and Asia from the Bering Straits to Peter the Great Bay and the Sacramento River.

This fish was 20½ in. in overall length with a standard length of about 450 mm., a depth of 135 mm., a width of 67·5 mm., and a weight of 4 lb. 2 oz. It is at once recognizable as distinct from either *Salmo salar* or *S. trutta* by the deeper body, more pointed snout and the presence of coarse oval black spots on the caudal fin; it differs from these and *S. gairdneri* (the rainbow trout) in the higher number of rays in the anal fin (*A* 17 as against 9–12, rarely 13 in *Salmo*) and of gill-rakers (26 on the whole of the first arch as against 24 or fewer in *Salmo*).

The scales, which are more numerous than in other species of *Oncorhynchus*—we counted approximately 170–174 in the lateral line—agree very well in structure with those of *O. gorbuscha* figured by Gilbert[3] and Davidson[4], showing one winter band only and the inner circuli not crowded as in the typical freshwater parr-life of *Salmo*. The humpback's life-history is well known[1,3–5]. It spawns in autumn (August–September in the River Amur). The eggs hatch in December, and the fry make their way to the sea as soon as they can swim, from April until June, at a length of 3·2–3·6 cm. They feed at first in water still brackish from the influence of the rivers (a phase consonant with the appearance of the first summer's growth of the scale) and then, at a length of 4–12 cm., move off to the open sea. Sexual maturity occurs at the end of the second year of life and no older fish have been caught in the spawning runs. Neither has any yearling fish been caught in fresh waters. Marking experiments indicate a high percentage of returns to the natal stream, but some straying may occur if suitable rivers enter the sea in the neighbourhood of the natal stream[4].

The Aberdeen fish, a male with enlarged testes, had the typical form and colouring of a 'clean' fish, with spots on the caudal fin only and none on the back, and without the kype and hump that develop at the spawning period. It is in the British Museum (Natural History).

We understand that, since 1956, the Russians have transferred very large numbers of Pacific salmon eggs, chiefly pink salmon, from Sakhalin Island north of Japan to the rivers of the Kola Peninsula. Up to the middle of September, they have had records of the return of some 75,000 fish to the rivers of the Kola Peninsula. There have also been reports of recaptures on the Norwegian coast, chiefly in the north, but extending as far south as Bergen, and in Iceland. Several thousand Pacific salmon have been caught on the Norwegian coast, though in Iceland the catches have been much smaller; probably less than fifty having been caught. It is, therefore, reasonable to assume that the pink salmon caught at Altens originated from one of the rivers of the Kola Peninsula.

We are grateful to Mr. G. G. J. Smart, of Messrs. Jos. Johnston and Sons, Ltd., of Montrose, for sending this fish caught in his firm's nets, to Mr. F. T. K. Pentelow (Ministry of Agriculture, Fisheries and Food) for helping to interpret the scales, and to Prof. G. V. Nikolsky and Dr. L. Rosseland for the information about catches in the U.S.S.R. and Norway respectively.

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Interspecific Hybrids of *Tilapia*

WHITEHEAD's claim[1] to describe hybrids between *Tilapia nigra* and *T. zillii* in two waters in which both species had been introduced could be accepted only if supported by unequivocal evidence. His only evidence that *T. zillii* was one of the parents of the problematical fishes is that this was the only species other than *T. nigra* known to be introduced. We know enough of stocking accidents to place no reliance on this, especially when, as in this case, all the evidence points in another direction.

We have had the opportunity of studying Whitehead's fuller report, which he sent to one of us for criticism. From this we see that his statement[1] that "in most anatomical characters the hybrids resembled *T. nigra*" is true, but it would be better to say that these were characters of the section of the genus including *T. nigra* but not *T. zillii*. The divergences

from *T. nigra* are not in the direction of *T. zillii*. The body- and fin-colours[1] are in fact reminiscent of *T. leucosticta*, a mouth-brooding species which is an inhabitant of Lake Albert, the source of the East African stocks of *T. zillii*, and is known[2] to have been distributed with the latter in many East African waters from ponds at Kisumu. The toothed lower pharyngeal bone of the 'hybrid' is figured in Whitehead's full report, and he notes its resemblance to that figured for *T. leucosticta*[3]. The gill-rakers on the lower part of the anterior arch are 8–12 in *T. zillii*, 15–20 in *T. nigra*, 18–22 in the 'hybrids', 19–24 in *T. leucosticta*. The dorsal spines are 14–16 in *T. zillii*, 17–19 in *T. nigra*, 15–18 in the 'hybrids' and in *T. leucosticta*[3].

Whitehead's claim to have effected the cross *T. zillii* × *T. nigra* in a pond rests on the presence there after six weeks of a female carrying eggs in the mouth, and this is not adequate evidence.

We suggest that many of the supposed hybrids were *T. leucosticta*—individuals inadvertently introduced with *T. zillii* or their progeny. It would be less surprising if some hybridization should occur between these and *T. nigra*, and some of the problematical fishes need re-examination with this possibility in mind, as Mr. Whitehead now agrees in correspondence with us.

Since we wrote the above, we have examined one of the 'hybrids' from Tebere ponds and find it indistinguishable from *T. leucosticta*.

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Aquarium Behaviour and Breeding of *Hymenochirus*

Hymenochirus[1] is a genus of West African clawed aquatic toads which are considered to be closely related to *Xenopus*. In fact its members were originally described as belonging to the genus *Xenopus*[2].

Two years ago we were by chance able to obtain 15 young specimens of *Hymenochirus boettgeri* (Torn.) from a German importer of pet fishes, who had offered "afrikanische Kleinfrösche". As it turned out that nothing is known about the biology of this toad and that, so far as we can find, neither the breeding habits nor even the larvæ have hitherto been described, we decided to study the aquarium behaviour of the toads instead of using them for tissue preparations.

Hymenochirus is a true aquatic toad, and in spite of the fact that it moves, with jumps, much more easily on dry land than does *Xenopus* it has never been possible to find a toad on the terrestrial part of the aquarium. There are no external sex differences in the genital region but the females are usually identified through their broad body form. The toads are apparently exclusively carnivorous and feed willingly on *Tubifex* worms, *Daphnia* and various kinds of gnat larvæ, but also on different kinds of 'dead' food such as raw fish meat. The prey is

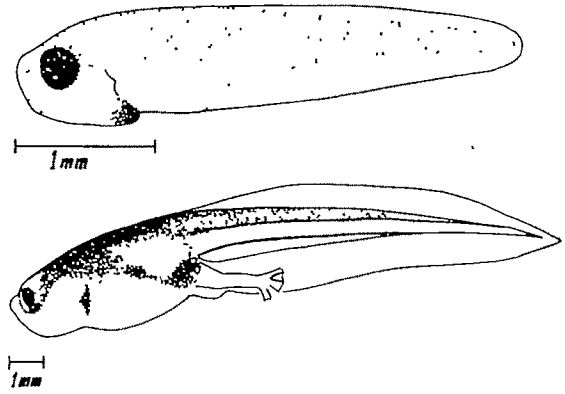

Fig. 1. Tadpoles of *Hymenochirus boettgeri*. The upper specimen is newly hatched, the lower one is 14 days old

obviously discovered and caught mainly with the aid of sight.

A vibration sound, which recalls that of *Xenopus*, is produced by the *Hymenochirus* males. In this case, however, short croaking periods alternate with silent periods. Each croaking interval terminates with a sudden rise in the pitch of the voice.

The males are often seen clasping females as well as other males in the typical *Xenopus* manner. Two attempts were made to induce spermiation and ovulation with luteinizing gonadotrophin, but without success. However, a sunny position of the aquarium has recently been sufficient to induce the spawning act, which has taken place during the night hours in a slightly alkaline water at 23–24° C.

Copulation is performed in a very peculiar manner. It occurs at the surface, usually in connexion with an inhalation of air, and starts with the female turning upside down with the male still clinging to her back. Her genital tract is now kept slightly protruding above the surface of the water and 2–10 eggs are deposited. After this process the couple return to the bottom. The surfacing is repeated about every second minute until the ovaries are apparently exhausted after about fifty times.

The eggs float on the surface but they do not stick together. They are about 0·9 mm. in diameter, with jelly about 1·5 mm. The larvæ hatch after 2 days at a length of 3·2–3·5 mm. and are already pronouncedly pigmented at this stage. On the fourth day they start feeding on small aquatic animals, and much to our astonishment they took exclusively to a carnivorous diet during the whole larval period. Consequently the tadpoles of *Hymenochirus* are quite unlike those of *Xenopus* in this respect; they are unlike them in several other respects also. The filtering apparatus and the tentacles are omitted, they do not rest in the water in the typical oblique position, and the whole appearance is very fish-like.

It is clear that a study of the larval and adult biology of *Hymenochirus boettgeri* discloses a number of interesting differences between this species and *Xenopus laevis*. The adaptational and taxonomical significances of these diversities between the two genera of African pipide toads are under consideration.

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Akinetoplastic Strain of *Trypanosoma evansi* produced by 'Prothidium'

SINCE Werbitzki's[1] observations that organic dyes having Ehrlich's orthoquinoid constitution caused disappearance of the kinetoplast in trypanosomes, several workers have, from time to time, reported the occurrence of both spontaneous and chemically induced strains of akinetoplastic *T. evansi*. Hoare[2] has fully discussed the early literature on the subject. Recently, Muhlpfordt[3] has published his observations on the effect of trypaflavin on the kinetoplast of various trypanosomes, and has shown that repeated administration of trypaflavin caused the complete disappearance of kinetoplast in *T. evansi* in 81 days. With other trypanosomes such as *T. equiperdum*, *T. brucei* and *T. gambiense* it took 54, 121 and 122 days, respectively, for the complete disappearance of this organelle.

Hoare and Bennett[4] in 1938 showed that both spontaneous and induced akinetoplastic strains of *T. evansi* behaved like the normal ones, and that the absence of kinetoplast did not in any way alter the vital functions of the trypanosomes.

We have observed: (1) the quick disappearance of the kinetoplast from the otherwise normal strain of *T. evansi* as a result of treatment with a phenanthridinium compound 'Prothidium'; and (2) some apparent change in the functional activity of the akinetoplastic 'Prothidium'-treated strain.

The chemical composition of 'Prothidium' (Boots) is 2-amino-7-(2-amino-6-methyl-4 pyrimidylamino)-9-amino-phenyl-phenanthridine : 10 : 1-dimetho-bromide. 0·5 ml. of a freshly made 0·015 per cent solution of this drug was given subcutaneously to white rats weighing 100–125 gm. and showing a fair number of trypanosomes in the peripheral circulation. Three sets of experiments were carried out with two rats in each set. The ratio of kinetoplastic to akinetoplastic trypanosomes was estimated by counting a hundred trypanosomes in a stained smear made from one of the rats in each series. The akinetoplastic 'Prothidium'-treated strain is now being maintained in this laboratory and its functional behaviour so far observed (up to its 8th passage in rats) is reported as follows.

From Table 1 it will be seen that there was complete disappearance of the kinetoplast 44–60 hr. after treatment with the drug.

Table 1. PERCENTAGE OF KINETOPLASTIC (*K*) AND AKINETOPLASTIC (*AK*) TRYPANOSOMES AT DIFFERENT HOURS

	18 hr.	44 hr.	60 hr.
Series I	*K*.28 : *AK* 72	All akinetoplastic	All akinetoplastic trypanosomes disappeared*
Series II	*K*.42 . *Ak* 58	*K*.17 : *Ak* 83	
Series III	*K*.34 . *AK* 66	*K*.20 : *AK* 80	

* There was a relapse after 30 days when only *AK* forms were seen.

The akinetoplastic strain thus obtained was found to breed true when passaged through rats. Table 2 shows an alteration in the functional activity of the akinetoplastic 'Prothidium'-treated strain as compared to the normal.

From Table 2 it is apparent that the akinetoplastic trypanosomes multiply less rapidly than the normal strain, and this leads to longer survival after infection. Ultimately, however, the host succumbs to infection with the same clinical and pathological picture as seen in rats infected with a normal strain of *T. evansi*. This akinetoplastic strain is now in its 8th passage, and the results are awaited with regard to its course of infection in larger animals (dog and horse).

Table 2. PREPATENT AND SURVIVAL PERIODS OF RATS INFECTED WITH NORMAL AND 'PROTHIDIUM'-TREATED STRAIN OF *T. evansi*

	Normal strain	'Prothidium'-treated strain
Incubation period in days in six rats	2, 2, 2, 2, 3, 3	5, 5, 6, 9, 12, 12
Survival time in days after first appearance of trypanosomes	3, 3, 3, 4, 3, 4	3, 5, 8, 9, 12, 12

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Studies on Phycobilin Formation with Mutants of *Cyanidium caldarium*

VARIOUSLY pigmented mutants of *Cyanidium caldarium*, an organism classified in succession as a blue-green, green, and red alga by Hirose[1] and which Allen[2] regards as an anomalously pigmented chlorophyte, appear to be excellent experimental materials for study of the synthesis of phycocyanin.

Pigment analysis of light-grown wild-type *C. caldarium* confirmed Allen's[2] report of the presence of chlorophyll *a*, carotenoid, and phycocyanin in this organism. In addition, allophycocyanin was found to be present. Absorption spectra of the extracted pigments are shown in Fig. 1. Dark-grown wild-type cells, unlike those reported by Allen[2], have been found to yield measurable amounts of chlorophyll *a* as well as carotenoid. As in the work reported by Allen[2] no phycobilins have been found in dark-grown wild-type cells. Mutant forms were obtained by exposure of wild-type or mutant cells to ultraviolet light. Absorption spectra of whole-cell suspensions of the wild and mutant types are shown in Fig. 2. Solutions of individual pigments were obtained as follows: (*a*) Cells were broken by grinding with polishing alumina or by means of a 10 kc./s. Raytheon sonic oscillator. (*b*) The chlorophyll and carotenoid pigments were then extracted in methanol and petroleum ether and separated on a sugar column developed with petroleum ether and *n*-propanol after the method described by Strain[3]. (*c*) The water-soluble phycobilins were separated on a calcium phosphate column[4] developed with 0·06 *M* sodium phosphate. Absorption spectra of extracted pigments and whole-cell suspensions were determined with a Cary recording spectrophotometer, model No. 11. The opal glass procedure of Shibata *et al.*[5] was used for the determination of absorption spectra of suspensions of intact cells. The organisms were grown at room temperature or at 43° C. on a medium similar to that used by Allen[2], to which 1 per cent glucose was added.

Four general types of variant forms have been found.

(1) *Dark-greening mutants*. Cultures of wild-type cells grown in darkness are yellow; carotenoid and traces of chlorophyll are detectable spectrophoto-

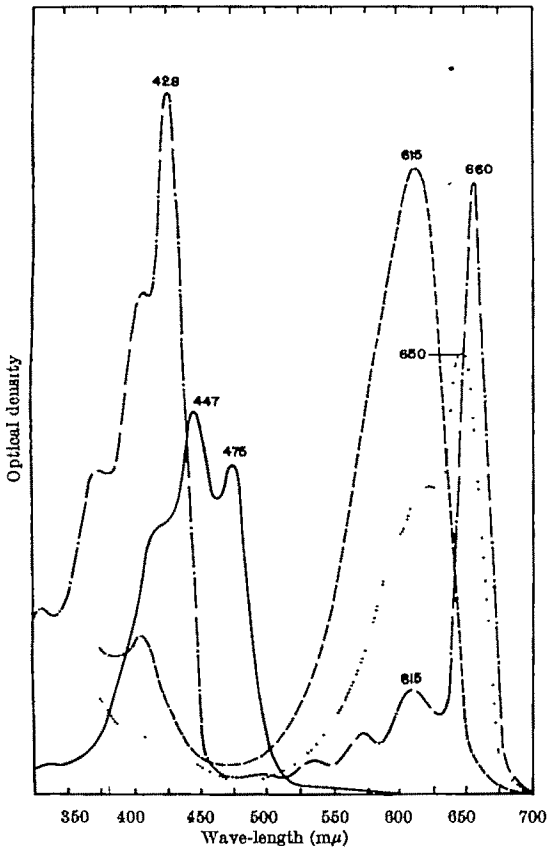

Fig. 1. Absorption spectra of pigments of wild-type *Cyanidium caldarium*. (Chlorophyll *a* and carotenoid in petroleum ether; phycobilins in water.) —.—, Chlorophyll *a*; – – –, phycocyanin; . . , allophycocyanin; ——, carotenoid

metrically. The 'dark-greening mutants', as represented by mutant III–*D*–2 (Fig. 2), are, however, visually green when grown in the dark. Cells of this mutant contain both chlorophyll *a* and carotenoid pigments, and like the dark-greening *S*–1 and *S*–5 *C. caldarium* mutants described by Allen[2], phycocyanin is also formed. The level of all pigments in the dark-grown, dark-greening mutant is lower than in light-grown wild-type cultures; however, light-grown cultures of the dark-greening mutants consistently accumulate more of each pigment than similarly grown wild-type cells.

(2) *Phycobilin-less mutants.* Light-grown cultures of this variant form, represented by mutant III-*C* (Fig. 2), accumulate chlorophyll *a* and carotenoid pigments but no measurable phycobilins. The absorption band seen at 615 mμ in spectra of whole-cell suspensions of this mutant appears to be that of a minor band of chlorophyll *a*. Absorption spectra of fractions obtained by calcium phosphate chromatography of aqueous extracts of ground III-*C* mutant cells appear to confirm the absence of phycobilins in this mutant.

(3) *A chlorophyll-less mutant.* The obligately heterotrophic mutant, *GGB* (Fig. 2), produces phycobilins and carotenoid pigments when grown in light, but no chlorophyll has been found. Ultra-violet irradiation of this mutant has yielded the following variant cell type.

(4) *A chlorophyll-less, phycobilin-less mutant.* Light-grown cultures of mutant *GGB-Y* (Fig. 2) accumulate no chlorophyll or phycobilin pigments. Carotenoids are found to be present in these cells.

Studies of the action spectrum for the formation of phycocyanin in the chlorophyll-less mutant (*GGB*) have shown that cultures exposed to 30,000 foot-candle min. of either 450 or 600 mμ light form this pigment; whereas a similar exposure to light of 550, 660 or 700 mμ results in no measurable formation of phycocyanin. The effects of light of other wave-lengths have not yet been investigated. The effectiveness of 600 mμ light in formation of phycocyanin in *C. caldarium* is in agreement with the recent work of Hattori and Fujita[6], in which it was noted that the effective part of the spectrum relative to phycocyanin and allophycocyanin formation in *Tolypothrix tenuis* lies somewhere between 550 and 700 mμ. It was, however, further noted by Hattori and Fujita[6] that blue light, ranging in wave-length from 400 to 550 mμ, was ineffective in inducing the formation of phycocyanin and allophycocyanin in *T. tenuis*. The screening effect of the chlorophyll in cells of *T. tenuis* might account for the difference in the

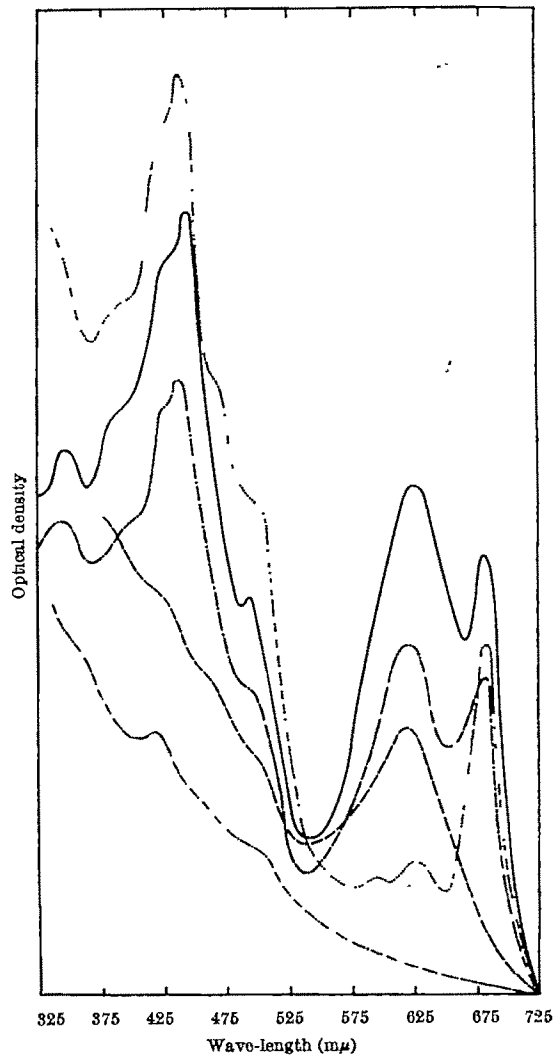

Fig. 2. Absorption spectra of cell suspensions of *Cyanidium caldarium* using the opal glass technique of Shibata (ref. 5). Cell types: —·—, wild; ——, III-*D*-2; . . . . , III-*C*; – – –, *GGB*; –·–·–, *GGB-Y*. Wild and III-*D*-2 spectra are at half-strength

observations that phycocyanin is formed in light of 450 mμ by the chlorophyll-less *C. caldarium* mutant *GGB*, but not by *T. tenuis*.

Hattori and Fujita[6] suggested, on the basis of the ineffectiveness of blue light for phycobilin formation, that the substance acting in the formation of phycocyanin and allophycocyanin could be neither chlorophyll nor carotenoids in *T. tenuis*. The existence of the phycobilin-producing chlorophyll-less *C. caldarium* mutant described here as well as the data on the action spectra provide evidence that phycocyanin and allophycocyanin are not derived from chlorophyll.

Further work on the action spectra for phycobilin formation in wild-type and mutant *C. caldarium* cells is in progress. The limited data from the present work are not inconsistent with the possibility that one or more hæm proteins might serve as photoreceptors (and perhaps as precursors) in the biosynthesis of phycobilins.

We wish to extend our thanks to Dr. Mary Belle Allen, who supplied the original culture of *Cyanidium caldarium* used in this work, and for the support provided in part by grants from the National Science Foundation and the United States Public Health Service, Institute of Arthritis and Metabolic Diseases (*A*–1010), and in part by the Dr. Wallace C. and Clara A. Abbott Memorial Fund of the University of Chicago.

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Biochemical Classification of Yeasts

IN a discussion of yeast taxonomy from a biochemical point of view, Barnett[1] made some valuable suggestions for its improvement. These emphasized: (1) the possibility that each group of yeasts may require its own particular set of biochemical tests; (2) that many of the biochemical tests now used in yeast taxonomy are of dubious value; (3) that our present understanding of the diverse biochemical processes carried out by these organisms is often very inadequate. The author accepted the view that taxonomy should embody a synthesis of results from various fields of inquiry, and that the progressive growth of knowledge necessarily renders any system of classification impermanent.

However, in a recent criticism of the methods employed by the Dutch school of yeast taxonomy[2,3], Barnett[4] now suggests that an improved and stable classification of the yeast fungi could eventually be achieved by employing exclusively biochemical criteria. The diagnostic value of these criteria in the comparative study of yeasts is regarded as being self-sufficient, since "imprecise and subjective morphological observations are avoided and there is no need to search for spores". It is not made clear whether this statement refers exclusively to the species-level, where, in the Dutch system, morphological distinctions are admittedly of less significance than physiological; but in any event it accords with the author's previous contention[1] that "the important thing about yeasts is their biochemical behaviour". This point of view, which appears to be common in contemporary biology, is not shared by us.

The proposal to classify yeasts by means of biochemical distinctions is evidently based on the belief that other biological criteria are, if not trivial, merely expressions of the physicochemical nature of the cell, in particular its constituent enzymes, proteins and nucleic acids, and are therefore redundant.

Barnett proposes tests which are designed to determine the enzyme content of any particular yeast in the hope that each test will reveal the presence or absence of a single enzyme. The diagnostic value of this type of investigation is indisputable since possible groupings could be envisaged from data which showed, let us say, that enzyme *X* occurs in only 25 per cent of the yeasts, or that of the 20 enzymes known to be regularly present in yeast *A*, 17 are common to yeast *B*, while only 8 are found in yeast *C* and 6 in yeast *D*. But here two questions can reasonably be asked: (1) Are such classifications supposed to reveal phylogenetic relationships, or are they primarily intended as artificial practical groupings? (2) Is a yeast cell to be regarded as nothing more than an assemblage of enzymes?

With respect to the first question, it is not clear what Barnett expects his new system of classification to reveal, apart from the presence or absence of specific enzymes and an improved understanding of the biochemical processes in which they participate. These *per se* constitute an admirable objective, though, with reference to classification, one to which the epithet 'stable' scarcely applies. The primary concern of any new microbial classification deserving of the name should be an attempt to demonstrate the natural relationships of the organisms involved. Otherwise it is mere cataloguing and devoid of intrinsic biological interest. In the absence of a fossil record of the yeast fungi, can one expect their natural relationships to be disclosed solely by a knowledge of the enzymes contained in their cells, even if this were extended to include studies of enzymatic organization and metabolic pathways? We think not. While biochemical processes are the basis of life, they are not synonymous with it, and to ignore life's outward manifestations, however subjective they may be, can only lead to an imperfect conception of the taxonomic whole: no one, in attempting to distinguish between a lion and a tiger, would ignore morphological criteria in favour of enzymatic. Although all schemes of microbial classification naturally embody a strong subjective element, certainly the truest and most satisfying picture will be derived from a synthesis and integration of all available knowledge. In the words of Pirie[5], "many different types of information can be, and should be, woven into the classificatory scheme, and there is no obvious advantage in attaching overriding importance to any one type".

As for the yeasts—that motley assemblage of micro-organisms defying definition—are we really asked to consider them as nothing more than bags of enzymes? For those who have devoted consider-

able time to observing through the microscope the multitudinous and variegated forms which these organisms assume and the beauty and elegance of their structures, it is almost an affront to be told that such observations are to be avoided because of their imprecision and subjectivity. It is not irrelevant to stress that hitherto one of the basic driving forces of the natural scientist has been his æsthetic appreciation of and affection for his subject-matter; the extinction of this attitude is likely to do no good to science in particular or to culture in general. It is understandable that the spirit of disinterested inquiry should lead man behind the outward forms of life in his search for its physical and chemical basis, but to ignore wilfully, in this unremitting itch for abstraction, that which can be perceived directly and appreciated æsthetically can never be biologically sound. It is quite true, as Barnett points out, that the factors influencing sporulation in yeasts are ill-understood, and that when a yeast will not sporulate under laboratory conditions this is no proof that it is incapable of doing so. But from this it does not logically follow that one need not search for spores. Sporulation in the ascosporogenous yeasts is indicative of sexuality, reproduction, recombination and maintenance of the species, and is a manifestation of life and evolution. For our part, we shall continue to search for it.

Through years of patient observation under the leadership of Kluyver, the Dutch school of yeast taxonomy created order out of chaos, and in spite of methodological shortcomings and imperfect knowledge, it was a magnificent attempt. As it stands to-day, it is primarily a practical system which most probably permits only faint and vague glimpses of the true phylogenetic relationships of the yeasts; but because it is based on a sound biological approach including morphology, sporulation, alternation of generations, and physiology, we believe that in the course of time it is destined to be revised rather than superseded. It is likely that such a revision will eventually encompass some of the alternative views of yeast classification[6-8], which, however, are themselves neither permanent nor stable, particularly since the evolutionary speculations which they contain are probably premature. But it is certain that besides dealing with the large number of new yeasts recently described, any taxonomic revision must include a more thoroughgoing genetic approach. Herein lie many fundamental problems: the possible elucidation of the species concept[9], the possible pooling of hereditary characters by means other than sexual reproduction[10], the determination of linkage groups and chromosome number, and the study of mutation and adaptation in their bearing on experimental evolution[8]. In addition to genetic data, more detailed knowledge is needed of the sexual process, of life-cycles, of comparative cytology, of morphological response to changing environmental conditions, of natural habitats and distribution[7], and certainly of the biochemical activities of these organisms. Here, in particular, the recent findings of instability in certain fermentative characters[11,12] may have significant taxonomic implications.

It may be expected that patient research in these various fields will gradually elucidate some of the natural relationships existing among the yeast fungi, although a complete picture of their evolutionary history is scarcely attainable. But even partial taxonomic enlightenment will not be in vain, if it can induce a sense of wonder and humility at the vast diversity of life manifest even in this small group of micro-organisms.

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BACTERIOLOGY

Knall-gas Reaction-linked Fixation of Labelled Carbon Dioxide in an Autotrophic *Streptomyces*

THE occurrence of a *Streptomyces* capable of growing autotrophically in the presence of a Knall-gas (oxyhydrogen) mixture has previously been reported (*St. autotrophicus*, Takamiya and Tubaki[1]). The present work was planned to investigate the autotrophic assimilation of labelled carbon dioxide in this organism.

An autotrophic growth of *Streptomyces autotrophicus* was obtained by inoculating an inorganic medium of the following composition with spores or small flakes of fresh growth taken from a culture of the organism grown on an inorganic agar slant. (Composition of the inorganic nutrient medium: 1·22 gm. potassium dihydrogen phosphate, 2·46 gm. crystalline magnesium sulphate, 1·32 gm. ammonium sulphate, 2·8 mgm. crystalline ferrous sulphate, 1 ml. Arnon's micronutrient solution A_5, and 0·84 gm. sodium bicarbonate in 1,000 ml. distilled water (pH 7·0).) The culturing was carried out at 27° C. in an air/hydrogen gas mixture (1 : 1). After 3–4 weeks, the surface of the culture medium was found to be covered with a snow-white growth of the organism, amounting to 5 mgm. dry weight per 100 cm.^{2} liquid surface. For the purpose of comparison, heterotrophic culturing was also performed, using an organic medium containing peptone (1 per cent; pH 7·0) as the source of carbon and nitrogen. The culture was poured into a separation funnel to float the colonies to the surface of the liquid. The floating colonies were washed with distilled water and with 0·03 M phosphate buffer (pH 7·2), and desired amounts of the organism were collected by loopfuls into a reaction vessel.

The measurement of gas-uptake was performed with a Warburg manometer (27° C.) with hydrogen

Table 1. CARBON DIOXIDE FIXATION COUPLED WITH OXYHYDROGEN REACTION IN *Streptomyces autotrophicus*

Gas atmosphere	Time of reaction (min.)	Radioactivity incorporated (c.p.m./mgm. cell dry weight)			Carbon dioxide fixed (calculated) (μmol./mgm. cell dry weight)	Hydrogen consumed (μl./mgm. cell dry weight)
		Insoluble	Soluble	Total		
80 per cent hydrogen + 20 per cent oxygen	10	89	1,168	1,257	0.048	7
80 per cent hydrogen + 20 per cent oxygen	30	272	2,058	2,330	0.089	21
80 per cent hydrogen + 20 per cent oxygen	90	980	4,919	5,899	0.225	56
Air	90	8	138	146		

and nitrogen introduced in the reaction vessel after evacuation of the air. A preliminary investigation revealed a marked consumption of oxyhydrogen gas in the autotrophically grown cells, which was in accord with the equation of a Knall-gas reaction. In a typical experiment, 110 μl. hydrogen and 66 μl. oxygen, as determined by the manometric method of Schatz and Bovell[2], were consumed in 50 min by 5-mgm. dry weight cells taken from a 90 day-old autotrophic culture (endogenous respiration: 8 μl. oxygen-uptake). No Knall-gas reaction was detected with heterotrophically grown cells of the same organism.

An isotope experiment was performed to detect the capacity of the organism to fix inorganic carbon. Autotrophically grown cells (80 day-old) were floated on the surface of a 0·03 *M* phosphate buffer (*p*H 7.2) placed in the main chamber of a Warburg vessel. The gas atmosphere was a hydrogen/oxygen mixture (4 : 1) freed from contamination of carbon dioxide. In the course of manometric measurement of oxyhydrogen reaction at 27° C., the solution of labelled carbon ($NaH^{14}CO_3$, 4·5 μmols; 1·18 × 10^5 c.p.m.) contained in the side-arm of the vessel was introduced into the main chamber. The reaction was stopped by adding 0.5 ml. of an acetic/hydrochloric acid mixture (4 : 1) after 10, 30 and 90 min. of reaction. Each sample of test organism was extracted and repeatedly washed with ethanol (final concentration, 80 per cent). The soluble fraction was separated from the insoluble cell material by centrifugation; the extract and the insoluble residue were dried in air on metal disks under an infra-red lamp. The results of the radioactivity measurements are presented in Table 1. It will be seen that bicarbonate carbon is readily incorporated by the organism when an oxyhydrogen mixture is present in the gas atmosphere. It must also be noted that the greater portion of the assimilated radiocarbon is discovered in the alcohol-soluble fraction. (Essentially the same results were obtained on stopping the reaction with boiling ethanol (final concentration, 80 per cent), instead of the acid mixture.) The efficiency of carbon assimilation as expressed by the ratio of incorporated carbon to consumed hydrogen and oxygen was as follows:

$$H_2 : O_2 : CO_2 = 10 : 5 : 1$$

In another set of experiments, autotrophically grown cells (120 day-old) were pre-incubated for 70 min. at 27° C. in an oxyhydrogen gas atmosphere (or air in control experiments) freed from carbon dioxide. The gas was then removed by evacuation and flushing with air or pure nitrogen: this procedure was repeated twice. After varied periods of such *blank* incubation, the organism was supplied with $NaH^{14}CO_3$ injected through a rubber stop-cock (fitted in this case instead of the side-arm of Warburg vessel), and further incubated for 10 min. to be tested for the amount of fixed carbo dioxide. All the experimental procedures after tl introduction of acid mixture were the same as thos described above. From the results presented i Table 2, it will be seen that the capacity for carbo dioxide fixation under the conditions of these exper ments remains unabolished for some time. Unde aerobic conditions in the blank period, however, significant decrease in fixation capacity occurs, s that after 3 min. in air, the fixation capacity of tl test organism was as low as about 30 per cent that c the anaerobic control.

Table 2. CARBON DIOXIDE FIXATION IN *Streptomyces autotrophicus* PRE-INCUBATED WITH OXYHYDROGEN GAS MIXTURE

Pre-incubation (for 70 min.)	Condition of blank incubation after removal of hydrogen gas (min.)	Reaction with $^{14}CO_2$ (min.)	Total radioactivity incorporated (c.p.m./mgm. cell dry weight)
80 per cent hydrogen + 20 per cent oxygen	in air 0.5	10	513
	in air 3.0	10	319
	in air 10.0	10	219
	in N_2 3.0	10	935
	in H_2+O_2 (that is, no gas exchange)	10	1,290
Air	in air (that is, no gas exchange)	10	143

It can be concluded from these results: (1) Tha the autotrophically grown cells of *Streptomyce autotrophicus* are capable of fixing carbon dioxid (2) The utilization by this organism of the energ derived from the oxyhydrogen reaction is als evident, the endogenous fixation of carbon dioxide i the absence of hydrogen gas being negligibly smal It is also to be noticed (3) that the inducing effect c the oxyhydrogen reaction on carbon dioxide assim lation is retained, for some time, in cells pre-treate with the gas mixture. The occurrence of a Knall-ga reaction-linked fixation of carbon dioxide ha repeatedly been observed in the group of hydroge bacteria[2-6]. However, this type of autotroph carbon assimilation has not yet been reported in th class of actinomycetes. The sluggishness of th process in our test organism, which may also be th

Table 3. KNALL-GAS REACTION-LINKED FIXATION OF CARBON DIOXI IN HYDROGENOTROPHIC AUTOTROPHS

Organism	Q_{H_2} (μl./hr., mgm., cell dry weight)	Q_{CO_2} (μl./hr., mgm. cell dry weight)	Efficiency $CO_2 : H_2$
*Hydrogenomonas facilis**	446	72	1 : 6·2
Hydrogenomonas ruhlandii†	264	34	1 : 7·8
Streptomyces autotrophicus‡	37	3·4	1 : 10·9

* Manometric data by Schatz (ref. 3).
† Manometric data by Packer and Vishniac (ref. 4).
‡ Isotopic experiments (present work, see Table 1).

cause of the slowness in its growth, is conspicuous, although the efficiency of the assimilatory process, as expressed by the carbon dioxide/hydrogen ratio, is not inferior. For the purpose of comparison, typical data in this connexion are summarized in Table 3 together with our own results. The slow rate found in the present case may partly originate from the circumstance that we had to use cells taken from old cultures, often several weeks old, in order to secure sufficient amounts of the organism for the test.

We wish to acknowledge here the continuous interest of Prof. H. Tamiya, University of Tokyo, during this work, which was supported in part by a research grant from the Ministry of Education.

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Action of 6-Aminopenicillanic Acid on Gram-negative Bacteria

THERE is abundant evidence to support the theory that at least one way in which penicillin exerts its antibacterial effect is to prevent the synthesis, during cell division, of a rigid component of the cell wall. If this action takes place in normal culture medium, the result is lysis; if in a hypertonic environment, the cell changes into a spherical body or spheroplast[1]. We have found that the parent amine, 6-aminopenicillanic acid[2], from which the natural penicillins may be considered to be derived by acylation, induces morphological changes similar to those produced by benzylpenicillin, 6-(α-phenoxypropionamido)penicillanic acid ('Broxil'), and phenoxymethylpenicillin (penicillin V).

In our experiments, 0·15 ml. of a 17-hr. culture of the organism, grown on a rotator at 37° C., was added to 10 ml. of the following medium, containing per litre: sodium chloride 5 gm., 'Lab. Lemco' (Oxoid) 5 gm., peptone 10 gm., sucrose 114 gm., crystalline magnesium sulphate 2·5 gm. The sodium salt of 6-aminopenicillanic acid was added to give the desired final concentration. Examination by interference microscopy after incubation for 4–5 hr. at 37° C. gave the results shown in Table 1.

Table 1. CONCENTRATIONS OF SODIUM BENZYLPENICILLIN AND SODIUM 6-AMINOPENICILLANATE TO INDUCE SPHEROPLAST FORMATION IN CERTAIN GRAM-NEGATIVE BACTERIA

	Sodium benzyl-penicillin (μmole/ml.)	Sodium 6-amino-penicillanate (μmole/ml.)
E. coli (formerly N.C.T.C. 5934)	0·167	0·68–1·7
Cloaca cloacae (N.C.T.C. 8155)	0·167	0·34
E. coli (K12)	1·67	3·4
Ps. pyocyanea (N.C.T.C. 7244)	0·42	0·84
Serratia marcescens	1·67	1·7–3·4
Proteus vulgaris (N.C.T.C. 7052)	1·67	1·7–3·4

It can be seen that sodium 6-aminopenicillanate in concentrations approximately twice those of sodium benzylpenicillin induced spheroplast formation. In lower concentrations, bizarre morphological variants were obtained. The spheroplasts underwent lysis on dilution of the medium with water.

Batchelor *et al.*[3] report that 6-aminopenicillanic acid possesses definite antibacterial properties, but of a much lower order than benzylpenicillin. It would appear that the presence of the acyl side-chain on the primary amine is not essential for spheroplast formation. Quantitative differences may be due to factors involving access to the site of action.

We thank Drs. J. Farquharson and E. T. Knudsen, of Beecham Research Laboratories, for a generous gift of 6-aminopenicillanic acid and 6-(α-phenoxypropionamido)penicillanic acid.

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VIROLOGY

Serological Detection of a Virus in Cherry Trees with a Leaf Roll Disease

LEAF roll virus disease of sweet cherry (*Prunus avium*)[1,2] has been identified (by graft-transmission to indicator plants) in eight orchards in Kent and one in Worcestershire. Six of these outbreaks have been investigated further, and in each of them the same virus was isolated from infected trees. When buds or young leaves were macerated in 0·05 *M* phosphate buffer (*p*H 7·8) or 0·01 *M* sodium diethyl-dithiocarbamate solutions and rubbed on to the leaves of young herbaceous plants, chlorotic and necrotic spots, rings and lines developed on the leaves of tobacco (var. White Burley), while *Chenopodium amaranticolor* plants were stunted, with mottled and distorted leaves. The virus was also transmitted by sap inoculation from tobacco to *Prunus avium* and *P. pennsylvanica* seedlings, and from *Prunus avium* to *P. pennsylvanica*.

An antiserum was prepared by intravenous injections into a rabbit of virus preparations precipitated from the infective tobacco sap by ammonium sulphate.

Precipitation tests were made in a gel containing 0·7 per cent 'Ionagar' No. 2, 0·9 per cent sodium chloride and 0·02 per cent sodium azide. This medium was run into Petri dishes to a thickness of 3 mm., and holes cut in the gel with a small cork borer to receive diluted antiserum or antigen. Single precipitation lines formed between holes filled with antiserum and those with undiluted sap from *Chenopodium* plants infected with this virus. No precipitation lines formed with sap from healthy *Chenopodium* plants or from plants infected with *Arabis* mosaic and tomato black ring viruses.

Specific precipitation lines were formed when sap from buds or young leaves from infected cherry trees was used as the antigen; the sap was antigenic

when diluted 1 : 2 with water, phosphate buffer or sodium diethyl-dithiocarbamate and also when undiluted. No precipitation lines formed with similar preparations from trees infected with *Arabis* mosaic, raspberry ringspot, necrotic ringspot, little cherry, ring mottle and rusty mottle viruses.

There is no previous record of the transmission of a virus within or between species of *Prunus* by sap inoculation, and none has proved antigenic in cherry sap except necrotic ring spot and sour cherry yellows, which need to be purified and concentrated before they can be detected serologically[3].

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A Lipid Component of Murray Valley Encephalitis Virus

FOLLOWING the early work of Taylor *et al.*[1], it is generally believed that the arthropod-borne viruses contain ribonucleic acid, protein and lipid. Recent work has shown that the ribonucleic acid fraction extracted by phenol from several viruses of this group is infective[2]. In the intact virus the protein fraction probably protects this ribonucleic acid and may have other functions. The present report considers a lipid component of the virus of Murray Valley encephalitis virus, and shows that this virus is inactivated by phospholipase *A*.

Crude virus was prepared as a 20 per cent baby mouse brain extract and purified virus was prepared from such a suspension[3]. Standard infective ribonucleic acid was prepared by treating crude virus with phenol[4]. Virus and ribonucleic acid were titrated on the chorioallantoic membrane of chick embryos[4]. Phospholipase *A*, supplied to us by Miss H. Doery of the Commonwealth Serum Laboratories, had been purified from the venom of the black snake (*Pseudechis porphyriacus*) (Doery, H. M., and Pearson, S. E., to be published). To ensure that so far as possible the only functional enzyme in the preparation was phospholipase *A*, each sample was boiled for 10 min. in physiological saline (*p*H 6·0) before being used.

Equal volumes of undiluted virus and phospholipase diluted in physiological saline were mixed and held at 37° C. for 30 min. The remaining infective virus was titrated. Both crude and purified viruses were rapidly inactivated by 100 μgm./ml. of phospholipase *A* (Table 1). The inactivated virus preparations were then treated with phenol to liberate infective ribonucleic acid. The yield of ribonucleic acid was always higher than the titre of virus, a result which indicated that phospholipase *A* acted on some component of the virus other than the ribonucleic acid.

Titration of the enzyme was attempted by using serial dilutions of enzyme in the above system, and defining the end-point as that concentration of enzyme which reduced the infectivity of undiluted virus by 2 logs. The end-point against crude virus was consistently at 0·05 μgm./ml. of enzyme. The end-point against purified virus varied from 2·0 to 0·1 μgm./ml. in 10 experiments: this wide variation was thought to be related to the varying lability of purified virus at 37° C., even in the absence of phospholipase *A*.

Standard infective ribonucleic acid prepared from crude virus was much less susceptible to phospholipase *A* than was virus, the end-point of the enzymic action against ribonucleic acid being at 100 μgm./ml. The high concentration suggested that the action was due to a contaminant and not to the phospholipase *A*. For example, the presence in the phospholipase preparation of 7 parts per million of a nuclease similar to pancreatic ribonuclease could explain the result[4].

From the above results, it was concluded that Murray Valley encephalitis virus was inactivated by the cleavage of fatty acid(s) from phospholipid(s) contained in its structure. It was unlikely that infective ribonucleic acid contained lipid as a vital component.

Purified influenza virus is known to contain large amounts of phospholipid. Influenza virus strain *WSE* was purified from infected allantoic fluid[5], and treated with phospholipase *A* (1,000 μgm./ml., 37° C., 30 min.) both with and without added normal baby mouse brain extract. Virus infectivity, as titrated in the allantoic cavity of chick embryos, was not reduced by this treatment. The failure of phospholipase *A* to inactivate influenza virus might mean either that intact phospholipid was not necessary for infectivity, or that the phospholipid was not accessible to the action of the enzyme.

Two interpretations of the results with Murray Valley encephalitis virus seem to be possible. The most direct hypothesis is that viral phospholipid has a specific function during infection of the chorioallantoic membrane. For example, it might assist in the absorption of virus to host cell, or might allow the virus particle to react with some intracellular system. A second possibility is that the phospholipid is not functional in this sense. It might be largely host cell lipid incorporated during intracellular growth or emergence of virus from the host cell; or it might be synthesized under the influence of the viral genome. In any event it will contribute to viral structure. On this view the alteration of phospholipid in a mature Murray Valley encephalitis virus particle might so distort the viral architecture as to render the particle non-infective.

Table 1. INFECTIVE TITRE OF VIRUS, AND POTENTIAL YIELD OF RIBONUCLEIC ACID AFTER TREATMENT OF MURRAY VALLEY ENCEPHALITIS VIRUS WITH PHOSPHOLIPASE *A* (37° C., 30 MIN.)

	Control	Treated
Crude virus		
Titre of virus	7·0*	0·4
Yield of ribonucleic acid	4·5	2·5
Pure virus		
Titre of virus	8·0	0·6
Yield of ribonucleic acid	5·0	1·6

* Log_{10} titres of infectivity.

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FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, December 5

INSTITUTE OF METAL FINISHING (at the Café Royal, Regent Street, London, W.1), at 2.30 p.m.—Annual General Meeting, followed by Prof. J. W. Cuthbertson: "A Metallurgist's Thoughts on Electrodeposition" (Hothersall Memorial Lecture).

BRITISH SOCIETY FOR THE PHILOSOPHY OF SCIENCE (in the Joint Staff Common Room, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Mr. G. Buchdahl: "Model, Symbol and Fact".

UNIVERSITY COLLEGE (in the Physiology Theatre, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. W. Feldberg, F.R.S.: "Mediators of Allergic Reactions".*

UNIVERSITY OF LONDON (in the Anatomy Lecture Theatre, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. John O. Corliss (University of Illinois): "Phylogeny and Evolution of the Ciliated Protozoa—Application to Systematics".* (Last of three lectures on "The Evolution of the Protozoa".)

Tuesday, December 6

INSTITUTION OF CHEMICAL ENGINEERS (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Mr. D. O. Heinrich: "Study on Electro-Precipitator Performance in Relation to Particle Size Distribution, Level of Collection Efficiency, and Power Input".

INSTITUTION OF ELECTRICAL ENGINEERS, MEASUREMENT AND CONTROL SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Prof. D. Gabor, F.R.S., Dr. W. P. L. Wilby and Dr. R. Woodcock: "A Universal Non-Linear Filter, Predictor and Simulator, which Optimizes Itself by a Learning Process".

RESEARCH DEFENCE SOCIETY (in the Physiology Lecture Theatre, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. J. H. Burn, F.R.S.: "Testing Drugs on Man" (Twenty-ninth Stephen Paget Memorial Lecture).

UNIVERSITY OF LONDON (at the Imperial College of Science and Technology, London, S.W.7), at 5.30 p.m.—Prof. H. Elliot "Cosmic Rays and the Exploration of Space" (Inaugural Lecture).

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. D. G Catcheside: "Functional Structure of Genes".* (Fourteenth of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

ROYAL AERONAUTICAL SOCIETY, ASTRONAUTICS AND GUIDED FLIGHT SECTION (at 4 Hamilton Place, London, W.1), at 6 p.m.—Dr. G. H. S. Young: "Solid Propellant Rocket Motors".

OIL AND COLOUR CHEMISTS' ASSOCIATION (at Manson House, 26 Portland Place, London, W.1), at 7 p.m.—Mr. G. Phillips and Mr. P. Walker "Newer Methods of Testing Paint Film".

BRITAIN CHINA FRIENDSHIP ASSOCIATION, HAMPSTEAD BRANCH (at Hampstead Town Hall, Haverstock Hill, London, N.W.3), at 7.45 p.m.—Dr. Joseph Needham, F.R.S.: "China and the Development of World Science".

Wednesday, December 7

UNIVERSITY OF LONDON (at the Postgraduate Medical School of London, Ducane Road, London, W.12), at 2 p.m.—Dr. A. E. Kellie: "Steroid Assays".*

ROYAL STATISTICAL SOCIETY (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5 p.m.—Mr. A. J. Miller; "A Queueing Model for Road Traffic Flow"; Mr. J. C. Tanner: "Delays on a Two-Lane Road".

INSTITUTE OF FUEL (at the Instituton of Civil Engineers, Great George Street, London, S.W.1), at 5.30 p.m.—Mr. P. A. Alexander, Mr. R. S. Fielder, Mr. P. J. Jackson, Mr. R. Raask and Mr. T. B. Williams: "Acid Deposition in Oil-fired Boilers, Comparative Trials of Additives and Testing Techniques".*

INSTITUTE OF PETROLEUM (at 61 New Cavendish Street, London, W.1), at 5.30 p.m.—Mr. M. E. Hubbard: "The Changing Energy Pattern in Europe and Its Possible Effect on Product-Mix".

SIR THOMAS MIDDLETON MEMORIAL TRUST (in the Physiology Theatre, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. J. D. Findlay "Cattle and Climate" (Eighth Memorial Lecture).

BRITISH INSTITUTION OF RADIO ENGINEERS, RADAR GROUP (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6.30 p.m.—Mr. H. G. Hinckley: "Flight Evaluation of Airborne Electronic Equipment".

SOCIETY FOR ANALYTICAL CHEMISTRY (in the Main Chemistry Lecture Theatre, Imperial College, Imperial Institute Road, London, S.W.7), at 6.30 p.m.—Discussion Meeting on "The Flask Combustion Technique".

BRITISH PSYCHOLOGICAL SOCIETY, SOCIAL PSYCHOLOGY SECTION (in Room 411, Birkbeck College, Malet Street, London, W.C.1), at 8 p.m.—Prof. Fritz Heider: "On Person Perception".

Wednesday, December 7—Friday, December 9

SCIENTIFIC AND TECHNICAL GROUP of the ROYAL PHOTOGRAPHIC SOCIETY OF GREAT BRITAIN (in the Lecture Theatre of the Royal Society of Arts, John Adam Street, Adelphi, London, W.C.2)—Conference on "The Ultimate Sensitivity in Photography—To-day and To-morrow".

Thursday, December 8

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Sir Bryan Matthews, F.R.S., and Mr. T. C. D. Whiteside: "Tendon Reflexes in Free Fall"; Mr. Q. Bone: "The Organization of the Atrial Nervous System of *Amphioxus* (*Branchiostoma*)".

INSTITUTION OF ELECTRICAL ENGINEERS, UTILIZATION SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. J. Ravenscroft: "The Determination of the Electrical Characteristics of an Arc Furnace".

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. E. J. L. Lowbury: "Drug Resistance and the Response to Chemotherapy". (Last of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W. C.1), at 5.30 p.m.—Sir Solly Zuckerman, F.R.S.: "The Social Function of Science—1960" (Rickman Godlee Lecture).*

ROYAL INSTITUTE OF CHEMISTRY, LONDON SECTION (at the Northampton College of Advanced Technology, St. John Street, London, E.C.1), at 7 p.m.—Prof. M. Stacey, F.R.S.: "Aromatic Fluorine Compounds".

CHEMICAL SOCIETY (in the Lecture Theatre, The Royal Institution, Albemarle Street, London, W.1), at 7.30 p.m.—Prof. R. Huisgen: "1,3-Dipolar Cycloadditions" (Centenary Lecture).

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE (at Manson House, 26 Portland Place, London, W.1), at 7.30 p.m.—Symposium on "Hookworm Diseases". Contributors: Dr. S. Stott, Dr. E. van Oye and Dr. Henry Foy.

Friday, December 9

ASSOCIATION OF APPLIED BIOLOGISTS (at the Royal Entomological Society, 41 Queen's Gate, London, S.W.7), at 10.15 a.m.—Paper Reading Meeting.

BRITISH PSYCHOLOGICAL SOCIETY, OCCUPATIONAL PSYCHOLOGY SECTION (in the Department of Psychology, Birkbeck College, Malet Street, London, W.C.1), at 1 p.m.—Mr. John Spencer: "Thoughts about Automation".

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 9 p.m.—Dr. R. L. F. Boyd: "Rocket Astronomy".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

POSTGRADUATE STUDENT (recent graduate with a good degree in physics or physical chemistry) IN THE DEPARTMENT OF PHYSICS, to research under the supervision of Dr. J. G. Powles on some aspects of magnetic resonance—The Registrar, Queen Mary College (University of London), Mile End Road, London, E.1 (December 9).

RESEARCH ASSISTANT (graduate biochemist or biologist with training in chemistry) IN THE ZOOLOGY DEPARTMENT, to assist in research in tank culture or bivalve shellfish—The Registrar, The University, Southampton (December 10).

TUTORIAL STUDENT IN THE DEPARTMENT OF BIOCHEMISTRY—The Registrar, King's College (University of London), Strand, London, W.C.2 (December 12).

SCIENTIFIC OFFICER, Grade 1 (with an honours degree in physics, mathematics or electrical engineering, and preferably some postgraduate experience in ionospheric research) AT THE WEAPONS RESEARCH ESTABLISHMENT, Salisbury, near Adelaide, Australia, to engage in research and development work in the field of ionospheric physics—The Senior Representative (AV.91/6), Department of Supply, Australia House, Strand, London, W.C.2 (December 15).

SCIENTIFIC OFFICER, Grade 1 (with an honours degree in physics, and preferably some research experience) AT THE WEAPONS RESEARCH ESTABLISHMENT, Salisbury, near Adelaide, Australia, for research and development in physics, mainly in the field of solid state and infra-red physics—The Senior Representative (AV.89/6), Department of Supply, Australia House, Strand, London, W.C.2 (December 15).

FELLOW or SENIOR FELLOW IN PHILOSOPHY within the Department of Social Philosophy, Institute of Advanced Studies, Australian National University—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, December 30).

SENIOR LECTURER/LECTURER IN SCIENTIFIC THOUGHT in the School of Philosophy, University of New South Wales, Kensington, N.S.W., Australia—The Agent-General for New South Wales, 56 Strand, London, W.C.2 (Australia and London, December 30).

POST-DOCTORAL RESEARCH FELLOW IN PHYSICAL CHEMISTRY, to study properties of solids by mass spectrometry—The Registrar, The University, Edgbaston, Birmingham 15 (December 31).

READER-IN-CHARGE (with a special knowledge of the physical and dynamic aspects of the subject) OF METEOROLOGY at the University of Melbourne, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, December 31).

CHAIR OF THEORETICAL PHYSICS at Birkbeck College—The Academic Registrar, University of London, Senate House, London, W.C.1 (January 5).

LECTURERS (2) IN CHEMISTRY at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, January 6).

CHAIR OF CIVIL ENGINEERING—The Registrar, University College, Singleton Park, Swansea (January 14).

JAMES WATT CHAIR OF ELECTRICAL ENGINEERING—The Secretary of University Court, The University, Glasgow (January 14).

POSTGRADUATE RESEARCH FELLOW IN THE DEPARTMENT OF BOTANY, for the study of micro-organisms involved in cellulose decomposition—Prof. C. J. Hickman, Department of Botany, University of Western Ontario, London, Ontario, Canada (February 28).

IMPERIAL CHEMICAL INDUSTRIES RESEARCH FELLOWS IN CHEMISTRY, PHYSICS, METALLURGY, ENGINEERING, GEOLOGY, AGRICULTURAL SCIENCE and related subjects—The Registrar of the University of Wales, University Registry, Cathays Park, Cardiff (March 6).

ASSOCIATE PROFESSOR OF CLINICAL PSYCHOLOGY—Prof. F. Hilton Page, Head of the Department of Psychology, Dalhousie University, Halifax, Nova Scotia, Canada.

DEMONSTRATOR/LECTURER (with a degree in physics or general science) IN THE DEPARTMENT OF PHYSICS, Middle East Technical University, Ankara—Room 139, Foreign Office, London, S.W.1.

PHYSICIST, CHEMICAL or MECHANICAL ENGINEER, Scientific/Senior Scientific Officer grade (with a first- or second-class honours degree in physics, chemical or mechanical engineering), at the Fire Research Station (D.S.I.R.), Elstree, Herts, to join a group studying the growth and spread of fire—Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting A.484/0A.

POSTDOCTORATE FELLOW (suitably qualified candidate interested in theoretical calculations of the hydrogen bond energy between water molecules and the energy of ice as a function of hydrogen orientation)—Dr. E. S. Campbell, Department of Chemistry, New York University, New York 53, N.Y., U.S.A.

SENIOR LECTURER (with an honours degree and suitable teaching and research experience, and preferably a higher degree and specialization in modern and atomic physics) IN PHYSICS—The Clerk to the Governors, South-West Essex Technical College and School of Art, Forest Road, Walthamstow, London, E.17.

SENIOR LECTURER (with qualifications and experience to teach mathematics for the Diploma of Technology courses and for degree courses in engineering and science) IN MATHEMATICS—The Registrar, Bradford Institute of Technology, Bradford 7.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Current Bibliography for Aquatic Sciences and Fisheries, Vol. 3, Part 1. Compiled by F. A. O. Fisheries Biology Branch. Pp. iv+184. 17*s*. 6*d*.; 2.60 dollars. Subscription price per volume of 12 parts £9 0*s*. 0*d*.; 27 dollars. (London: Taylor and Francis, Ltd., 1960. Published by permission of the Food and Agriculture Organization of the United Nations.) [188

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Report of the Astronomer Royal for Scotland for the year ending 31st March 1960. Pp. 8. (Edinburgh: The Royal Observatory, 1960.) [198

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INTERNATIONAL CO-OPERATION IN RESEARCH

IN an address at the opening of the new Physics Building of the Imperial College of Science and Technology on October 20, Sir John Cockcroft referred to the growing complexity of equipment required for physical and chemical research, and consequent mounting of costs during the past three decades. The scale of expenditure on physics has doubled and redoubled, partly from the feed-back from technology, which is providing ever more powerful and discerning tools, and partly from the frequent combination of several different disciplines to attack new problems. Sir John instanced the combined British Universities liquid hydrogen bubble chamber project, and Prof. McGee's work on an electronic device to convert beams or radiation from stellar and other sources into electrical currents, from which was expected to come a 120-in. telescope as powerful in most respects as the 200-in. giant of Mount Palomar. With the use of modern tools, chemistry departments already have operating costs comparable in scale with those of the Cavendish Laboratory.

Sir John said Britain is inevitably left far behind by the Americans and Russians in the immensely expensive projects of space science and space travel, although Sir Harrie Massey is playing a leading part in the almost uncharted field of space research. Britain is still holding her own in most basic fields of science. Britain started with the advantage of a good flow of first-class young scientists from the universities. An increasing amount of support also came through the Research Grants Committee of the Department of Scientific and Industrial Research and the other Research Councils. During Prof. Blackett's tenure of the chair of the Research Grants Committee, funds for the support of basic science in the universities had increased five-fold, and are now more than double those for major items of equipment coming through the University Grants Committee.

Nevertheless, at a College of Science and Technology of which Sir John is vice-president, only some £500 per research worker is available from the University Grants Committee and College funds for all departmental supplies, though this is increased by about 80 per cent by contributions from outside bodies, including the United States Army; 20 per cent of this external support comes from the Department of Scientific and Industrial Research. Sir John thought that this pattern is characteristic of many university institutions, and while he suggested that diverse channels of support for science would always be a safeguard and assist its growth, he believes that in strengthening Britain's science and technology it is more important to strengthen them in the universities than anywhere else at the present time.

As regards the growing scale of science in the next five years or so, he emphasized that to take full advantage of the present great opportunities the universities in Britain need several computers one hundred times faster than those now available to them. These would cost one or two million pounds apiece, but, thanks to the so far unrequited initiative of British industry, could be available from home sources if there was no long delay. Radio astronomers also need increased support to maintain their outstanding position in this new field of science and, apart from the increasing demands of theoretical astronomy, there are the claims of space research. Sir John did not attempt to discuss how far we would be justified in entering this field for the sake of developments in future technologies, but pointed out that present technologies are still far from adequately supported. The great potentialities for scientific and technological development in the universities of Britain could be exploited much more fully and with great benefit to the country if we increased the funds available to them for research equipment, technicians and urgently needed laboratories by only 1 per cent of the total sum now spent on research and development.

In this address on the strengthening of science in Britain, Sir John Cockcroft thus far largely followed the argument of the latest report from the Advisory Council for Scientific Policy. Like the Advisory Council, he recognizes, too, that the general growth in the scale of equipment and the costliness of science is leading to some evolution of the organization of science. While, however, he noted that we have already found it necessary to build the largest accelerators in the National Institute for Nuclear Science, where ten universities are already experimenting with the first of the accelerators to be built, the future relation of such national institutes to the central Government has still to be worked out. The first National Institute has made a good start and can, Sir John believes, be taken as a pattern for other collaborative university activities, such as space research and astronomy, though, to facilitate collaboration, the difficulties of working away from a university base require easing, and universities must recognize research work carried out at the National Institute for higher degrees.

Sir John also referred to the desirability of powerful research tools in Government establishments, such as the 20-MV. research reactors at Harwell and the powerful computers of the Atomic Energy Authority, being available so far as possible to university research workers. Comparatively modest expenditure on travel and equipment for university workers could do much to make this possible, but he also thought that co-operation should include a greater

participation in university teaching by the staffs of Government establishments than is at present the practice. Moreover, if and when other Government technological establishments are being founded, there is much to be said for building them on the campus of a university (as is the case in Australia), provided that by then the embarrassing differences of salary-level have disappeared.

Sir John did not pursue that issue; nor did he follow up the implications of his comment that in many fields the cost of technological research is of the order of £7,000 per annum per research worker, and that the universities are making nothing like the contribution to the advancement of technology that they do to the advancement of science. He was content to point to the great opportunities and to stress the need for more inter-disciplinary projects. There are, indeed, in some Government establishments and in some Medical Research Council units, such as the Molecular Biology Research Unit at Cambridge, teams of mathematicians, engineers, physicists, physiologists and others, but more of this is needed in the universities in the future.

Perhaps the most important of Sir John's suggestions for the strengthening of science lie in the field of international co-operation. Referring to the building of the high-energy proton synchrotron at Geneva, in which Britain has joined forces with eleven other European nations, he said that a far better team had been collected than could have been obtained in Britain, and the combined technical resources of the member countries greatly exceeds those of any single country. As in the similar co-operative project to build the *Dragon* reactor at Winfrith Heath, British leadership has played a decisive part, and he believes that similar international co-operation is desirable for other large-scale projects such as a future radio telescope, which might cost ten times as much as that at Jodrell Bank, or for the large optical telescope for the southern hemisphere now being discussed.

Such international co-operation is the major theme of a report, to which Sir John Cockcroft referred, on increasing the effectiveness of Western science, prepared by a study group of the Science Committee of the North Atlantic Treaty Organization, and also sponsored by the Ford Foundation*. This report begins by stressing the importance of increasing the effectiveness of Western science, both from the point of view of security and from that of raising the standard of living in the Western countries, quite apart from the dominant part which science holds in our twentieth-century civilization and its challenge and inspiration to the spirit of men. Indeed, the report urges not simply a conscious effort to devote adequate resources to science, but also pleads for a greater unity, for much more interpenetration among the nations until national labels are no longer attached to fields of science. Incidentally, the report appears to accept 2 per cent as about the right proportion of the gross national product to be devoted to research and development, and some 10 per cent of this, as in the United Kingdom and the United States, to fundamental research.

What the report notes of obstacles to the advance of science is largely common knowledge. Shortage of funds, of buildings, of qualified science teachers, of trained technicians and craftsmen, administrative difficulties, and the traditional structure of universities, are common experience in varying degrees in the Western world, but there are also artificial international obstacles to be removed such as restrictions on visas, inadequate budgets for international travel, customs or currency barriers to the acquisition or replacement of essential equipment, and sometimes restrictions on the tenure of permanent university posts to nationals of that country. Some of these barriers can obviously be removed by national action, as the report does not hesitate to indicate; and the temper favourable to the removal of barriers by national action may well be a pre-requisite to the international action on which the report lays its main stress.

Some of the suggestions are familiar, and the report merely adds its authority to proposals already advanced. Among these are the encouragement by international agencies, in close co-operation with national agencies, of the exchange and employment of scientists between nations. Again, it is suggested that the International Council of Scientific Unions, in collaboration with the International Federation for Documentation and the United Nations Educational, Scientific and Cultural Organization, should be asked to do everything possible to improve documentation. To this end certain specific suggestions are made, such as organization of collaboration between editors of the chief scientific periodicals to ensure uniformity in publication practices; affiliation of the principal documentation centres; evolution of a single international system of indexing; arrangements for providing authors' abstracts; encouragement of additional reviews of broad scientific fields but discouragement of the proliferation of scientific periodicals; and reduction of airmail tariffs for transmitting single copies of scientific publications to libraries and scientific associations. It is also suggested that international funds should be available to assist the technically less-developed nations, especially in the North Atlantic Treaty Organization, to promote science and engineering on the national level, on condition that such funds are used to mobilize national funds for this purpose.

More novel is the proposal to create an international clearing house to expedite the transfer of research equipment, the value of which has already been demonstrated by the Training Centre for Experimental Aerodynamics in Belgium. But the most significant proposal is probably that noted by Sir John Cockcroft—the founding of an International Institute of Science and Technology. Research and educational centres serving the needs of two or more countries are regarded as of particular importance at

* Increasing the Effectiveness of Western Science. (Fondation Universitaire, 11 rue d'Egmont, Bruxelles, 5.)

the present time, and the report instances oceanography, meteorology, the ecological effects of pesticides and pollution, and the science of materials and space science as fields in which such centres could well be distributed among different nations and preferably attached to universities. The recent report of the Advisory Council for Scientific Policy shows that, to some extent at any rate, the Advisory Council already recognizes the importance of international collaboration in such fields; but Sir John Cockcroft goes further, and puts the weight of his authority behind the alternative proposal that one or more such centres could form part of an International Centre of Science and Technology or an Atlantic or European University. He maintains that the only chance of such a project coming to fruition is for Britain to take the lead and build such an Atlantic Institute here, as part of the university expansion programme of Britain, but with powerful help from Western Europe.

The Advisory Council for Scientific Policy's last report is calculated to stimulate some fresh thinking about university co-operation, and apart from all considerations of international co-operation, collaboration between universities must clearly play an increasing part if we are to make the most effective use of our own natural resources for research. These possibilities must obviously be considered by the University Grants Committee, which should also note the suggestions advanced in the NATO report, and even examine them further in their British context without waiting for the consideration of the proposal by an appropriate study group which is recommended. Meanwhile, Sir John Cockcroft's address should help to focus attention at a high level on an aspect of scientific and technological development—no less than of university expansion—which has urgent claims for consideration by the Minister for Science, as well as by the Advisory Council for Scientific Policy and the University Grants Committee.

ROSSBY POSTHUMOUSLY HONOURED

The Atmosphere and the Sea in Motion

Scientific Contributions to the Rossby Memorial Volume. Edited by Bert Bolin. Pp. 509. (New York: The Rockefeller Institute Press; London: Oxford University Press, 1959.) 105*s*. net.

PROF. C.-G. ROSSBY, a 'life force' in meteorology and oceanography from the late 'thirties until his sudden and untimely death in 1957 at the age of fifty-eight, was to have been honoured by his colleagues and former students with a special volume of papers to commemorate his sixtieth birthday. Those papers, with some notable additions, have now been published, but as a memorial to him.

Rossby's last complete paper was a retrospect and prospect entitled "Aktuella Meteorologiska Problem", given to the National Science Research Council of Sweden in 1956. This paper, translated, happily appears first in the present volume under the title "Current Problems in Meteorology". In its fifty pages, Rossby covers in masterly fashion all the major meteorological interests of his career, showing us the way his mind moved, and what he and some others sought to achieve in their approach to a science which has so resisted but now and again partially capitulated to the attack of great minds. No other paper of Rossby so exposes, to my mind, the man and the scientist—so much greater he seemed than the sum of his parts.

The other "additions" to the volume are two biographical sketches, one by Prof. Bergeron on the young Rossby, the other by Prof. Byers on Rossby the organizer; followed by a complete Rossby bibliography. Bergeron's study is particularly interesting, revealing to us the Rossby that very few knew except, as it were, by extrapolation—restless, receptive yet highly speculative, anxious to break new trails and become his own master. One sees in part why Rossby took longer than most of his stature to express himself as scientist.

The major part of the volume, the original papers, is arranged in five sections, under headings "The Sea in Motion", "Distribution of Matter in the Sea and Atmosphere", "Characteristic Features of Atmospheric Motion", and "Weather Forecasting". One cannot pass all the papers in review but a few are appropriately mentioned for their relation to some of Rossby's work.

In the early 'forties Rossby realized, by that physical intuition which was so strong in him, that the evolution of the large-scale flow-field of the atmosphere is not much affected, in the immediate sense, by its thermal field. (Ultimately, of course, practically all air motion derives from the thermal field.) As one contributor puts it, "Rossby . . . recognized at a very early date that this must be true and he felt no need for a mathematical proof of this principle". It was his great gift to meteorology that the evolution takes place very nearly under conservation of the absolute vertical vorticity of the air, and by this simplification he greatly encouraged the early introduction of numerical forecasting to practical meteorology. But intuition has to be followed by consolidation and there are two lengthy papers here in which the necessity of Rossby's principle is more or less demonstrated. It is shown that evolutions arising from the large-scale thermal field are generally self-immolating—a result related to recent experience that numerical forecasting, in which the thermal field is included at all stages, gives disappointingly little more success than the simpler Rossby model.

Rossby was always much concerned with the almost discontinuous properties of the atmosphere and oceans—fronts, jet streams and sharp shear lines are just three examples—so that it is very appropriate and highly welcome to find a notable contribution to the theory of fronts in this volume. A. Eliassen argues that the front "is not the asymptotic result of a gradual process (the large-scale horizontal deformation field operating on the field of isotherms) but a catastrophic development" in which wind shear and temperature contrast are formed simultaneously by means of a frictionally induced overturning of air transverse to the isotherms and the release of latent heat in the rising arm. The process is self-maintaining and reversible, and is a development of ideas put

forward earlier by Eliassen himself, and by J. S. Sawyer in the United Kingdom. The same mechanism seems likely to account for the eye of the tropical cyclone.

Finally, one should mention a stimulating essay by Bergeron on the history of ideas in weather analysis and forecasting, with hints on their further development. The author is admittedly depressed by much of the story, of promising lines forsaken and sterile paths pursued, and he finds a major ill in the want of meteorological knowledge of theoreticians (Helmholtz is his first example) and a too-poor mathematical training of 'weather men'. The subject, he says, needs a Maxwell–Hertz in one person and the nearest approximation to have appeared so far was V. and J. Bjerknes, father and son. He pleads for a Lagrangian rather than an Eulerian approach to weather analysis, instancing the success of the Bergen frontal school and of Rossby's Chicago school in this respect, but he recognizes that Lagrangian techniques have not yet been well developed. Perhaps the study of the evolution of the atmosphere will never become an exact science, though the limits of climatic variation suggest that, appropriately formulated, the problem should be soluble. Even in its present formulation there is ample scope for development and Bergeron helps to point the way.

This is a volume of which, one can be sure, Rossby would be proud, a fine example of the growth and stature of the sciences with which it deals and which Rossby spent himself in building. P. A. Sheppard

PLANT GEOGRAPHY

Introduction to Plant Geography and Some Related Sciences

By Prof. Nicholas Polunin. Pp. xix+640. (London: Longmans, Green and Co., Ltd., 1960.) 60*s*. net.

THIS volume is intended to provide "an introduction not only to Plant Geography in the wide sense, but also to much of Plant Ecology and Sociology, to the Plant Kingdom as a whole, and to Economic Botany". Such a task has obvious difficulties, and the subjects make a strange mixture for what is presumably meant to be essentially an introductory text-book on plant geography.

After a preliminary chapter, there follow several dealing with plant classification, physiological reactions, 'adaptations', life-forms, dispersal and migration, and fossil plants. Two chapters deal with foundations of modern distribution and with types and areas of natural distributions. There are then interpolated matters under the headings "Modification and Distribution of Crops (and Weeds)" and "Vital Importance to Mankind". There follow a summary account of environmental factors and an outline of main habitats, successions, and climaxes. Not until more than half-way through the book are the 'vegetational types' dealt with. These are subdivided into those of temperate and adjacent lands, of polar lands and high altitudes, of tropical and adjacent lands, of fresh and inland saline waters, and of seas. The book ends with two chapters entitled "Landscapes and Vegetation" and "Plant Adjustments and Applications", respectively. A great deal of space is occupied by material not immediately relevant to plant geography. As one consequence of this, many of the important phytogeographical subdivisions of the world are very inadequately considered. Another criticism concerns the sequence of the chapters. Thus, polar lands are dealt with between those with temperate and those with tropical climates.

On the other hand, it must be fairly stated that on the whole the descriptive statements are accurate so far as they go. Controversial matters, such as transoceanic dispersal, continental drift, and nunataks are outlined with the various points of view given without bias. The account of the vegetation of polar lands is a good résumé; but other areas, such as the Mediterranean region, are inadequately treated. The inclusion of a chapter on marine vegetation is commendable.

The fount and format are excellent, and there is a good index. A coloured map has the caption "Generalized Land Vegetation Map of the World" and was prepared by A. W. Küchler (1958) with northern forest and arctic limits by N. Polunin. This map is in parts difficult to interpret and appears to have little connexion with the text. There are 184 figures, the majority from photographs, and many of these are clear and relevant to the text. Bibliographical references are given at the ends of chapters, but these are mostly to books and not to original papers. W. B. Turrill

A TRILOGY OF VIROLOGY

The Viruses

Biochemical, Biological, and Biophysical Properties. Edited by F. M. Burnet and W. M. Stanley. Vol. 1: General Virology. Pp. xvii+609. 16.50 dollars; 118*s*. Vol. 2: Plant and Bacterial Viruses. Pp. xvi+408. 13 dollars. Vol. 3: Animal Viruses. Pp. xvii+428. 12 dollars. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1959.)

VIRUS research originated in pathology, and for more than half the nearly 70 years during which the existence of viruses has been recognized their study was an activity almost confined to pathologists, but the 34 articles that make up these three volumes carry few signs of this. The sub-title, "Biochemical, Biological and Biophysical Properties", makes it obvious that this would be no place to seek such mundane things as clinical descriptions or methods of controlling virus diseases, but it is unexpected that pathogenicity should be so neglected; no article is devoted specifically to it and fewer than 1 per cent of the nearly 1,500 pages even mention it. Yet pathogenicity is not only what makes viruses economically important, but is also the feature that usually first brings their existence to notice and that provides the means for their detection and assay in most kinds of work. If their biochemical and biological properties do not determine the many and varied ways in which viruses interfere with the normal functioning of host cells, what does? It is true that the ability to infect and multiply, rather than to cause disease, is the prime feature of a virus and the one with the greatest significance to biology in general; the emphasis given to this feature is therefore understandable, but it does not justify excluding other abilities rich in scientific interest and unsolved problems. Indeed, the replication of nucleic acid and its relation to protein synthesis already looms so large in virus research that such exclusions can only lead to the subject becoming increasingly unbalanced by attracting a still greater

proportion of workers to this currently fashionable line.

The major adverse criticisms to be brought against this trilogy stem from sins of omission, perhaps because the title and sub-title seem to promise too much. "The Viruses" suggests a completeness that is far from fulfilled, for most of the known viruses are not even mentioned. Markham's admirable survey of the properties of plant viruses is exceptional in dealing in some detail with as many as 10 viruses, but most articles are concerned only with tobacco mosaic virus, with $T2$-coliphage, or with one or other of three animal viruses. Wildman's article, for example, though called "The Process of Infection and Virus Synthesis with Tobacco Mosaic and Other Plant Viruses", in fact mentions only one other virus, and this in only two sentences, one in a footnote. Similarly, although Fraenkel-Conrat's article entitled "The Chemical Basis of the Infectivity of Tobacco Mosaic Virus and Other Plant Viruses" does contain a table showing the sizes and shapes of ten plant viruses, the text mentions only one other than tobacco mosaic virus, and this one gets less space than the two brief paragraphs devoted to animal viruses and bacteriophages.

"Chemical, Physical and Genetical Properties of a Few Viruses" would more accurately reflect the contents of the three volumes, but does not, any more than the existing title, show that nearly 300 pages of Volume 1 are not specifically concerned with viruses. These pages are no less valuable because of this. Indeed, Cohen's scholarly article of 189 pages, plus about 1,000 references, on "Structural and Chemical Architecture of Host Cells with Special Reference to the Synthesis of Polymers" will not only tell most virus workers much more than they previously knew about what goes on in cells, but will also do so for workers in many other subjects. Similarly, the excellent critical discussion of methods used to measure particle sizes that fills 80 of the 100-page article by Schachman and Williams, called "The Physical Properties of Infective Particles", applies to macro-molecules in general.

There is no space here to give the titles of all the articles, let alone comment on them. All that can be done is to list the contributors not already named to show that all are well qualified to write with authority. They are, in order of first appearance, F. M. Burnet, W. M. Stanley, C. E. Schwerdt, S. Gard, O. Maaløe, E. A. Evans, W. Schafer, G. H. Bergold, S. E. Luria, C. A. Knight, L. M. Black, A. Lwoff, A. Garen, L. M. Kozloff, G. S. Stent, C. Levinthal, F. Jacob, E. L. Wollman, F. W. Stahl, S. G. Anderson, A. Gottschalk, F. B. Bang, A. Isaacs, W. Schlesinger, F. L. Horsfall, F. Fenner, J. Cairns, T. Francis, H. B. Andervont, K. M. Smith. With such a galaxy of talent, although the articles are not all of the same quality, it need scarcely be said that in total they contain a wealth of information and that the volumes will be required equipment of laboratories where viruses are being studied. This is probably more than enough to justify the exercise, but it is impossible not to regret that, valuable as these collected articles are, they do not constitute the definitive work on viruses these authors might have produced.

Each volume has a subject and author index, and each article its own bibliography, some running to hundreds of titles. There are many illustrations and the whole production is excellent, as it ought to be at a total cost of 41.50 dollars.

F. C. BAWDEN

TRENDS IN METROLOGY

Acta Imeko 1958

Proceedings of the International Measurements Conference, Budapest, 24–30 November 1958. Vol. 1: Pp. 443. Vol. 2: Pp. 444. Vol. 3: Pp. 372. Vol. 4: Pp. 460. Vol. 5: Pp. 419. (Budapest: Hungarian Scientific Society for Measurement and Automation, 1959.) n.p.

THE published proceedings of the 1958 International Measurements Conference, the first to be organized by scientific societies in Hungary, Poland and the U.S.S.R., provide Western readers in particular with a convenient means of reviewing the present state and development of metrology and instrument technology in these and other countries of Eastern Europe. Seventy of the 127 papers originate from the organizing countries, and there are 37 from the German Democratic Republic with six from Czechoslovakia. In addition, there are two each from Austria, the German Federal Republic, Italy, the United Kingdom and Rumania, and one each from Belgium, Bulgaria, Denmark and the Netherlands. The official languages of the conference were Hungarian, Russian, German and English (or French). As summaries in English are provided with 121 of the papers printed in languages other than English or French, it is possible for readers of English to gain a reasonable first impression of the contents of practically all the papers without recourse to translation. At the end of each volume is reproduced, in each of the four official languages, a list of the titles and authors of the papers appearing therein. No discussions of papers are recorded.

The conference was organized into three main sections dealing with the following topics: (1) Contributions of general interest (10 papers); (2) (comprising 9 sub-sections) geometric quantities; mechanical quantities; optical measurements; temperature, flow and humidity; electric quantities; magnetic quantities; electric and electronic measuring techniques; chemistry, physical chemistry and structure analysis; measurement and application of the ionizing radiations (102 papers in all); (3) organization, economy, technology and education (15 papers). Among the contributions of general interest appearing in Volume 1, mention is made of those on the international organization of both scientific and legal metrology, on international standardization and on the progress towards adopting natural reference standards, for example, an atomic wave-length, an atomic frequency and a constant, such as the gyromagnetic ratio of the proton, as the means of practical definition of basic units of measurement. Other papers discuss the applications of electronics, radio and microwave methods, semiconductors and digital computers to the techniques of measurement and control.

Papers in the various sub-divisions of Section 2 appear in the latter part of Volume 1, and in Volumes 2, 3, 4 and part of Volume 5. The two contributions from the United Kingdom fall in this Section; one deals with problems of determination of particle size by scanning microscopy (W. T. Welford), and the other describes an X-ray diffractometer operating automatically through a punched-tape programme (W. A. Wooster). Among methods and apparatus for measuring geometric and mechanical quantities, attention may be directed to the highly developed applications of optical interferometric methods in the U.S.S.R. and to the novel Czechoslovakian system,

applicable to gear and angle measurements, which depends on the use of sinusoidal magnetic impressions recorded on tapes or bands as highly sensitive and accurate angle-measuring devices. A paper in Volume 3 on the calibration and examination of electronic and visual pyrometers in the U.S.S.R. refers to pyrometers which are available for measuring temperatures up to 10,000° C. to an accuracy of 0·1 per cent (0·05 per cent at the gold point, 1,063° C.). Another paper discusses the measurement of radiation energy with a platinum bolometer sensitive to 10^{-10} W. Indeed, a very large proportion of the papers in Volumes 3 and 4 describe special instruments and techniques developed for use in the various fields of measurement covered. The U.S.S.R. paper on reference measurements for the ionizing radiations (Volume 5) shows that standards and measurements in this important field are well controlled by the work of the national standards laboratory in Leningrad. Contributions to Section 3 in Volume 5 reveal the intense interest, especially in the U.S.S.R. and the associated countries, in the applications of automation to methods of production and the control of inspection.

It is difficult for a single reviewer to give in brief an adequate indication of the wide scope and interest of the papers appearing in these five volumes. There is no doubt that, on the whole, they will amply repay notice by all those interested in the present-day trends of metrology and instrument technology. Preparations are in hand to hold another conference of the same kind during 1961 (June 25–July 9).

H. Barrell

FLUCTUATION NOISE IN RADIO CIRCUITS

Electrical Noise

Fundamentals and Physical Mechanism. By Dr. D. A. Bell. Pp. x+342. (London: D. Van Nostrand Company, Ltd.; Princeton, N.J.: D. Van Nostrand Company, Inc., 1960.) 50*s*.

To the electrical engineer, the title "Electrical Noise" might convey the impression that this book deals with unwanted radiation causing interference with telecommunications. The author is not, however, concerned with this field; and his book deals comprehensively with the fluctuation-type noise which arises within the apparatus and components used in the generation and reception of radio signals, It summarizes the results of more than twenty years experimental and theoretical research on the random fluctuations of current which arise from various causes in electrical circuits over a very wide range of frequencies.

Following introductory sections on mathematical techniques and general noise theorems, there are chapters on noise in diodes, grid-controlled amplifying valves, and the more recently developed beam, maser and parametric amplifiers. Current noise, which is generated when a direct current passes through a semiconducting material, is then discussed in considerable detail; and it is shown that the satisfactory explanation of the origin of such noise is an important outstanding theoretical problem. Further chapters deal with the types of noise which arise in thin metal films, in rectifiers and transistors, and in ferromagnetic materials. A chapter on "Radiation Detectors" shows that the measurement of noise can be applied to useful ends in, for example, radio astronomy, temperature measurement, and photoelectric detectors.

The book is to be welcomed as a specialist monograph presenting a detailed review of the current state of knowledge of a subject in which there has been a certain amount of confused thought and much controversy in the past. Although the author has on occasions appeared to be in conflict with his contemporary workers in parts of this controversy, this has not materially affected the scope or presentation in the book under review. A good selection of references is given at the end of each chapter; these will enable the serious student to explore any part of the field and examine the points of view of other advanced research workers. The book has a few short-comings in that the chapter sub-headings are inadequate in some cases, and some of the diagrams are by no means self-explanatory. Apart from such limitations, however, the book is welcomed as a very useful survey of knowledge in this rather complex field.

R. L. Smith-Rose

PLANT PATHOLOGY

Plant Pathology

An Advanced Treatise. Edited by J. G. Horsfall and A. E. Dimond. Vol. 3: The Diseased Population, Epidemics and Control. Pp. xiii+675. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1960.) 27 dollars.

As the editors make clear in their prologue, this third and final volume of their comprehensive theoretical treatment of plant pathology covers the newer or younger aspects of the subject, and to that extent it is truly theoretical in places. After a stimulating discourse by S. D. Garrett on the various forms of inoculum and on inoculum potential, there are chapters dealing with the natural spread of inoculum in soil, seeds and planting material, by animal and insect (mainly virus), and by air and water, including take-off, flight and landing. Other chapters deal with the analysis of factors and processes involved in primary and secondary disease epidemics, the possibility and value of predicting epidemics, and the biological factors that affect or interfere with them. The rest of the volume is concerned with the basic principles of disease control by cultural practices, soil treatment, the use of fungicides, the breeding of resistant varieties and plant legislation. Plant legislation, concealed under the misnomer "Quarantines", includes a useful account of recent international efforts to ensure that essential regulations are uniform, justifiable and soundly based biologically. The intricacies of this subject are, however, largely a closed book to all but a few officials, and many readers would no doubt have welcomed a reasoned exposition of the basic principles and problems involved, especially by one so well qualified to prepare it.

The international nature of the treatise is well maintained, with six contributions from the United States, four from the United Kingdom and single ones from Germany, Denmark, France and South Africa. The treatise is intended for the creative worker and advanced student of plant pathology, but even he will not get wholly by without more than a nodding acquaintance with mathematics and chemistry. But those who can spare £25 for the three volumes will find that the fifty distinguished contributors have given them plenty to think about.

W. C. Moore

Advances in Space Science

Vol. 1. Pp. xii+412. (1959.) 12 dollars. Vol. 2. Pp. xiii+450. (1960.) 13 dollars. Edited by Frederick I. Ordway. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd.)

THE title of this series is misleading. It would be much more indicative of the contents if it were "Advances in Space Technology". The editor's view on 'space science' is revealed in the foreword where he states that "The principal objective of space science is to make it possible for man, and not merely instruments, one day to travel into space and to explore the planetary and satellite bodies of the solar system (and perhaps, in some undiscernible future, even the stars)".

The headings of the articles and the authors (most of whom are affiliated to American military or industrial laboratories) are as follows: Volume 1, "Interplanetary Rocket Trajectories" (D. F. Lawden), "Inter-planetary Communications" (J. R. Pierce and C. C. Cutler), "Power Supplies for Orbital and Space Vehicles" (J. H. Huth), "Manned Space Cabin Systems" (E. B. Konecci), "Radiation and Man in Space" (H. J. Schaefer), "Nutrition in Space Flight" (R. G. Tischer), "A Decimal Classification System for Astronautics" (H. H. Koelle); Volume 2, "Experimental Physics Using Space Vehicles" (C. P. Sonett), "Tracking Artificial Satellites and Space Vehicles" (K. G. Henize), "Materials in Space" (F. L. Bagby), "Plasma Propulsion Devices" (M. Camac), "Electrostatic Propulsion Systems for Space Vehicles" (E. Stuhlinger and R. N. Seitz), "Altitude Control of Satellites and Space Vehicles" (R. E. Roberson).

The articles, which are in general highly technical, are likely to be of interest mainly to professional engineers. They are not intended for, and would not be understood by, the general reader.

Author and subject indexes are supplied to each volume. The printing and production are of the customary high standard of the Academic Press.

D. R. BATES

Modern Aspects of Electrochemistry

No. 2. Edited by Dr. J. O'M. Bockris. (Modern Aspects Series of Chemistry.) Pp. ix+416. (London: Butterworths Scientific Publications; New York: Academic Press, Inc., 1959.) 75*s*.

THIS book continues the survey of selected topics in electrochemistry begun in the first volume, published in 1954. There are five chapters, dealing with the present state of the theory of electrolytic solutions (by H. Falkenhagen and G. Kelbig), physical chemistry of ion exchange resins (by J. A. Kitchener), molten electrolytes (by H. Bloom and J. O'M. Bockris), the anodic behaviour of metals (by T. P. Hoar), and the semiconductor–electrolyte interface (by M. Green). Each chapter has a full bibliography; the literature references seem mostly to end about 1955.

The first chapter is a very informative and detailed review of a subject which continues to attract interest. It is really a small monograph, the theory being developed from the beginning with the Debye–Hückel treatment. The mathematics is often rather advanced. Activity coefficients, conduction, and (rather briefly) viscosity are dealt with, and there are many tables. The chapter on ion-exchange resins is on the lines of a small book on the subject published fairly recently. The discussion of molten electrolytes deals with a subject of increasing importance; Russian work, as well as that of the authors, find places in it. There are several tables of results, and the treatment is well balanced between theory and experiment.

The chapter on anodic behaviour of metals includes topics of technical importance, such as anodic polishing, and also deals with subjects of theoretical interest. The phenomena are still far from completely understood. The final chapter, on the semiconductor–electrolyte interface, is almost entirely theoretical, with only a brief discussion of the germanium electrode; the subject was scarcely at such a stage as to warrant a review. The book as a whole is very well written, with a good balance in each individual chapter, and good editing has brought together a most interesting selection of material.

J. R. PARTINGTON

Proceedings of the International Symposium on Microchemistry

Held at Birmingham University, August 20th to 27th, 1958. (Organized by the Midlands Section and the Microchemistry Group of the Society for Analytical Chemistry.) Pp. xxvi+583. (London and New York: Pergamon Press, 1960.) 100*s*. net.

THIS volume consists of a collection of lectures delivered at the International Symposium of Microchemistry held at the University of Birmingham in 1958. Many of the contributors are world-renowned in their respective fields, and the individual papers present a wealth of authoritative practical and theoretical information. Some papers also deal with the unique problems associated with the teaching of micro-analytical methods.

I almost feel it invidious to single out individual authors or topics for consideration, but the wide field covered by this remarkable book can only be illustrated in this way. F. Feigl's lecture to the whole meeting is devoted to the pyrolytic treatment of materials prior to spot-test analyses; F. J. Welcher reviews theoretically the employment of selective organic reagents; H. Weisz describes the more recent 'ring oven' technique; G. F. Hodsman and M. Corner present informative papers on 'weighing accurately'; H. Lieb reviews forty years of quantitative organic micro-analysis, and many other experts give supporting papers of great practical value. The practical fields of ion exchange, chromatography, polarography, radiochemistry, spectrochemistry and complexonistry are dealt with by chemists of standing, and one welcomes the papers by A. A. Benedetti-Pichler, C. J. Van Nieuwenberg and R. Belcher on the history and teaching of microchemical methods.

This is a book which will find a place not only with the individual researcher but also in the libraries of every up-to-date industrial or academic research institution. It offers, in small compass, a comprehensive survey of recent advances in widely separated fields of microchemical application and contains the valued opinions and laboratory experiences of many eminent research workers.

D. T. LEWIS

ORIGIN AND NATURE OF LUNAR SURFACE FEATURES

By J. J. GILVARRY

Research Laboratories, Allis-Chalmers Manufacturing Company, Milwaukee, Wisconsin

THE dark and smooth appearance of the lunar maria has generally been viewed as sufficient evidence to identify their surfaces as lava flows. Interpretations on this basis, but differing in detail, have been given by Baldwin[1], Urey[2], and Kuiper[3]. Gold[4] has argued strongly against the presence of lava, in view of the consequent difficulty in correlating temporal sequences of crater origin and the paucity of definite volcanic features. I[5] have pointed out that the known presence of a dust layer over the entire surface of the Moon vitiates the reasoning for the presence of lava. The arguments for lava presuppose the absence of a lunar atmosphere or hydrosphere lasting any significant length of time. During the past few decades, however, it has become increasingly clear that the terrestrial atmosphere and hydrosphere were formed by exudation from the Earth's interior. The purpose of this article is to consider the possibility of an analogous process in the case of the Moon. It will be shown that the origin and nature of major surface features on the Moon can be explained in terms of effects of the former presence of a lunar hydrosphere.

Life-time of the Lunar Hydrosphere

By considering the cosmic and terrestrial abundances of the inert rare gases, Brown[6] and Suess[7] have demonstrated that any element which existed primarily as a gas at the time of the Earth's formation could not have been retained to a significant extent in its atmosphere. It follows that the present atmosphere and hydrosphere of the Earth are not residual from primordial antecedents, but are almost entirely of secondary origin. Rubey[8] has adduced purely geological arguments leading to precisely the same conclusion; he presents compelling evidence that the terrestrial atmosphere and hydrosphere were formed by leakage from the underlying earth through its surface.

In view of the Moon's smaller mass, the conclusion follows *a fortiori* that it could have retained no residue of any primordial atmosphere or hydrosphere, since it necessarily was formed at essentially the same distance from the Sun, at approximately the same time, and under roughly the same conditions as the Earth. Accordingly, the question of the life-time of a lunar atmosphere or hydrosphere cannot be discussed without deciding the type of secondary atmosphere or hydrosphere formed by leakage of fluid through its surface, by a degassing process exactly analogous to that postulated for the Earth. To answer this question, a scaling law must be assumed. It will be hypothesized that the total masses of a constituent in the secondary atmosphere and hydrosphere for the Moon and Earth should be proportional to the corresponding masses of these bodies. Let Q_i represent the number of molecules above unit area on the Moon's surface for the ith constituent in its atmosphere and hydrosphere, and let Q_i^* be the corresponding quantity for the Earth. If the difference in mean density between the Moon and Earth is ignored, this assumption yields:

$$Q_i/Q_i^* = R/R^* \qquad (1)$$

where R is the radius of the Moon and R^* that of the Earth. As will appear, the order of magnitude of resultant life-times is not sensitive to the precise choice of scaling law.

In determining the value of Q_i for fluids on the Moon from equation 1, it clearly is necessary to consider in Q_i^* the total amounts on the Earth of any compound of atmospheric or hydrospheric provenance. In the case of hydrospheric water, for example, one must include the contribution from continental ice, and in the case of carbon dioxide, the fossil quantity locked in sediments. Values of Q_i have been determined for water, carbon dioxide, oxygen and nitrogen by equation 1 from data of Wildt[9]. The resulting Q_i for water corresponds to a surface density of 79 kgm./cm.^{2} and exceeds by a large factor those for the other fluids, as a consequence of the large mass of water in the terrestrial oceans.

For simplicity, it will be assumed that the secondary lunar atmosphere and hydrosphere were formed by exudation from the interior in a time short compared with the corresponding life-time. The life-time L_i of the ith constituent of the lunar atmosphere and hydrosphere is then fixed by:

$$L_i = Q_i/j_i \qquad (2)$$

where j_i is the thermal escape-rate of Jeans[10] and Spitzer[11]. Equation 2 applies to the atmosphere and hydrosphere combined, since it presupposes that loss of a constituent (water vapour, for example) from the atmosphere can be replenished by gain from the hydrosphere. Thus, the model presumes that the entire hydrosphere is gaseous; the fact that it is liquid lengthens the actual life-time over that computed. It is unnecessary to consider the correction factor B of Spitzer[11] or my A_i (ref. 12) in connexion with equation 2, since use of these parameters is obviated when a direct estimate of Q_i is available. I have determined the height of the escape layer above the Earth's surface from data obtained by observation of satellite orbits[13]. Theoretical relations[12] have been used to scale the result for night conditions to yield an approximate height of 2,300 km. for the escape layer above the lunar surface. The mean temperature of the critical level for the Earth varies between 1,000 and 2,000 °K diurnally[12]. An upper limit of 3,000 °K. will be assumed for the escape layer of the Moon, which is about the value apparently required to explain the loss of atmospheric helium-4 from the Earth[12,13].

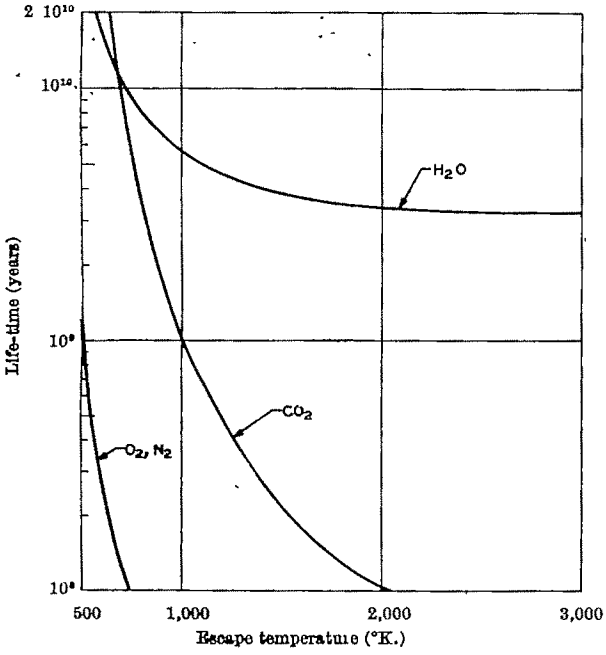

Fig. 1. Life-time L_i of various constituents of the primitive lunar atmosphere and hydrosphere, as a function of assumed temperature in the escape layer. The curves for oxygen and nitrogen are indistinguishable on the scale used

The life-time L_i on the assumptions made is shown in Fig. 1 as a function of assumed temperature of the escape layer, for water, carbon dioxide, oxygen and nitrogen. One sees that the life-time of water is the longest by a large margin for any temperature above 1,000 °K. Moreover, this life-time is measured in milliards of years, and thus is comparable with the duration (of order $4 \cdot 5 \times 10^9$ years) of the Moon's life-time. Corresponding to uncertainties in assumed initial conditions, the estimates shown can reasonably be increased or decreased by a factor $10^{1/2}$, giving an overall spread of a factor of 10 in the results. The conclusion remains unaffected, that the lunar hydrosphere lasted a period at least of the order of 10^9 years. Computations of the life-time of water on the Moon have been made previously[1,10]; they yielded values insignificant on an astronomical scale because the possible existence of a lunar hydrosphere capable of continuously replenishing the atmosphere was ignored.

The maximum depth of the lunar hydrosphere can be estimated on the assumption that the time of its exudation from the interior was short compared with its life-time. If the surface of the Moon below the hydrosphere were smooth, the value of Q_i for water would indicate a maximum water depth of about 1 km. However, about half the visible surface of the Moon consists of highlands about 2 km. higher on the average than the lowlands, which, if true for the other face, would yield a mean water depth of roughly 2 km. Height estimates for the averted face are not possible, since only a few crude photographs are available[14]. In spite of this uncertainty, it is clear that sufficient water existed in the lunar hydrosphere to drown all the lowlands and to encroach significantly on the highlands, at one time.

On these considerations, a large part of the erosion evident for the lowland regions of the Moon must have taken place subaqueously; a significant amount may have been done by turbidity currents[15]. Because of the relatively low surface gravity, small area available for watersheds, and thinness of the atmosphere (composed in later stages primarily of water vapour), erosion by flowing rivers and their tributaries should not have been very significant. Thus, dendritic drainage patterns should appear in the highlands but should not be prominent; Pickering[16] has shown observationally that such actually seems to be the case.

Craters on Land

If it is indeed true that the Moon possessed an appreciable hydrosphere throughout a large fraction of its history, it follows that the level floors of the maria were formed by sediments deposited from the water in the course of its dissipation. Compaction of these sediments should yield a softer rock than that forming the highlands, and this circumstance should be reflected systematically in the mensuration of the corresponding craters, to some degree. Evidence of a systematic difference between craters formed in the highlands and the maria will be sought in an extension of Baldwin's correlation of diameter and depth to include the effect of crater formation in hard or soft rock. Baldwin's curve of diameter versus depth for the lunar craters of Class I (presumably the youngest) exhibits a continuous variation through the analogous curve for terrestrial meteoritic craters into the corresponding curve for explosion craters on the Earth. This correlation is one of the strongest arguments that the lunar craters were formed by explosion of meteorites on impact. It can be shown that such explosions necessarily occur close to the surface[17].

It will be assumed that the relation between the diameter D and depth d of a crater can be written as the quadratic form:

$$D = a_1 d \, [1 + (d/a_2)] \qquad (3)$$

with the set of coefficients a_1 and a_2 different in the cases of hard and soft rock. The coefficients a_1 for hard and soft rock were determined from the results of measurements of the dimensions of craters formed by explosion of chemical charges in basalt and sedimentary rock, respectively[18]. These experiments were carried out under closely controlled conditions, with the centre of mass of the charge at ground-level. The resulting least-square linear relations $D = a_1 d$ for the two cases are shown (dashed in part) in Fig. 2. As a check, data points for the craters formed by the nuclear explosions Jangle (S) and Jangle (U) in compacted desert alluvium are shown also[18]; the latter was an underground explosion but the scaled depth of burst was sufficiently small for it to approximate a surface explosion. One sees that agreement of the two points with the line for soft rock is excellent.

Of the craters in Baldwin's Class I, 80 have been classified in Class IH, occurring in the highlands, 84 in Class IS, occurring in the floors of the maria, and 30 as ambiguous on this score. With the value of a_1 fixed as above for hard and soft rock, the corresponding values of a_2 were determined by a least-squares fit to the data of Baldwin for the dimensions of the craters of Class IH and IS, respectively. The resulting curves are shown in Fig. 2. They become nearly identical for large diameter and depth, as is clearly necessary, since the larger craters

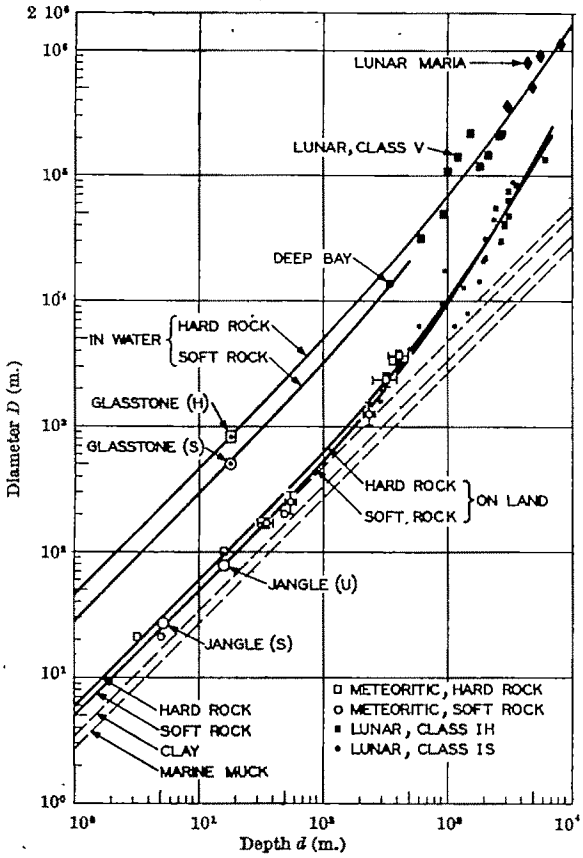

Fig. 2. Correlation of diameter versus depth for various classes of craters and the lunar maria. The solid curves correspond to fitted functions for craters on land and in water, for hard and soft rock. In general, points for only every tenth lunar crater in Classes I*H* and I*S* appear

on the floor of a mare must extend into the harder rock below the sediments. The association of the lunar craters of Classes I*H* and I*S* with hard and soft rock, respectively, is inferential; one sees that the difference between the two curves computed on this assumption is too small in the region of large dimensions to be of diagnostic value.

However, a significant difference does appear for the two curves in question for the intermediate range of depth and diameter. To show that the difference is real, recourse will be made to the data for terrestrial meteoritic craters. Ten such craters for which dimensions are known with relative accuracy were classified in Class I*H*, formed in hard rock, and Class I*S* formed in soft rock. The basis of distinction between hard and soft rock is the shear strength, primarily; granite and dolomite are regarded as hard, and limestone and sandstone as soft. Schist and gneiss are considered soft, in view of their low shear strength along planes of foliation and banding, respectively. The craters of Class I*H* are Brent[20], Chubb[21], Holleford[22], Sall[23], and Dalgaranga[24]; those of Class I*S* are Barringer (Arizona)[1], Le Clot[25], Merewether[26], Odessa[1] 1, and Odessa[1] 2. The dimensions of these craters are plotted in Fig. 2, as differentiated into the two classes.

The close correlation between the data points for terrestrial meteoritic craters of Classes I*H* and I*S*, and the corresponding curves constructed on the assumption that the lunar craters of Classes I*H* and I*S* were formed in hard and soft rock, respectively, is obvious from the figure. Furthermore, one notes that no data on the dimensions of terrestrial meteoritic craters were used in the construction of the curves in question, as is not the case for Baldwin's curve. In spite of this fact, the curves yield a separation of the terrestrial meteorite craters into two classes, for hard and soft rock, correctly. When corresponding coefficients of correlation are obtained for each type of crater, one finds that the values from this work exceed, or at least are equal to, those obtained using Baldwin's equation, in all instances.

The considerations of this article suggest strongly (but are insufficient to prove) that the rocks of the mare floors are sedimentary in origin. On this basis, they should be softer than the rocks of the highlands, and not basalt from lava flows. This view is diametrically opposed to those generally current. That the maria are vast pits filled with dust, as asserted by Gold[4], is rendered highly unlikely by observed dimensions of craters formed in clay and marine muck[18]. Least-square lines for craters in these materials, analogous to those for hard rock and soft rock, appear in Fig. 2; the order of decreasing shear strength corresponding to the curves is to the right. Since dust has negligible shear strength, the points for the lunar craters of Class I*S* with smallest dimensions should be displaced far to the right in Fig. 2 if Gold's hypothesis were correct. Hence, the dust on the Moon, the presence of which is revealed by analysis of eclipse and radio observations[5], is superficial in distribution.

Craters in Water

Baldwin's correlation curve applies only to lunar craters of Class I, as do the curves discussed in the preceding section. The remaining craters have been classified by Baldwin in Classes II, III and IV, in order of increasing age on the basis of apparent degree of erosion. When the dimensions of these craters are plotted in a diagram of the type of Fig. 2 the points lie in a broad band above the curves for Class I, at distances correlated roughly with the ordinal numbers of the classes. The nine craters of Class IV for which the representative points are displaced farthest from the curves for Class I have been placed in a separate Class V in this work. These craters are Hörbiger, Grimaldi, Schickard, Hipparchus, Ptolemæus, Neper, Letronne, Hansteen and Encke. The locus of the corresponding representative points in Fig. 2 represents the upper bound of the band in which all the lunar craters lie.

Baldwin explained the upward progression of the representative points with ordinal class of the craters in a plot similar to Fig. 2 as purely an effect of some unknown erosive process, filling the bottom at the expense of the rim after crater formation. A similar explanation is inherent in Gold's arguments[4], but suggested erosive agents[27] seem insufficient. It will be asserted that the basic cause is a progressive change of the circumstances in which the craters were formed initially, corresponding to the gradual loss of the Moon's hydrosphere. Specifically, the relative dimensions of a crater were fixed by the depth of the water in which the meteorite exploded to produce the crater. The craters of Class V are the oldest and were formed when the hydrosphere was at its maximum depth. The physical arguments of Gilvarry and Hill[17] can be used to show that the

impinging meteorite must explode close to the surface of the water. It is not denied that erosion is of some consequence in modifying the relative dimensions of lunar craters, but the process is assigned a secondary role in this connexion; however, the correlation of age and eroded appearance of a crater is assumed valid.

Glasstone[28] gives curves for the dimensions of craters formed by nuclear bombs in strata lying under water, with the seat of the explosion close to the water surface. The curves apply specifically to a water depth of 18 m. for a bottom of soft rock, but conversion factors for a bottom of hard rock are given. It has already been established that the maximum depth of the lunar hydrosphere was at least 1 km. and possibly 2 km. Inspection of Fig. 2 reveals that these figures represent the order of the depths for craters of Class V. Accordingly, the dimensionless parameter μ defined by:

$$\mu = \delta/d \qquad (4)$$

in terms of the water depth δ must have had closely the value unity for these craters, on the assumption that they are among the oldest. Therefore, to relate the lunar craters of Class V with terrestrial explosion craters, it is reasonable to make the correlation with explosion craters for which $\mu = 1$. The dimensions of two craters satisfying this prescription, Glasstone (H) and Glasstone (S) for a bottom of hard and soft rock, respectively, have been obtained from Glasstone's data and plotted in Fig. 2.

Since the points in Fig. 2 for the lunar craters of Class V lie at an extreme displacement from the curves for Class I, it will be assumed that they were formed in hard rock, in agreement with the relative positions of the points for Glasstone (H) and Glasstone (S). Their dimensions were fitted by a relation of the form:

$$D = a_1 d\,[1 + (d/a_2)^n] \qquad (5)$$

where a_1 was fixed by means of Glasstone (H), and the coefficient a_2 and exponent n were determined by a least-squares fit to the data. The corresponding curve is shown in Fig. 2 (labelled hard rock). One sees that the points for Glasstone (H) and Class V lie on one smooth curve, roughly parallel to those obtained for the craters of Class I. The curve is not changed appreciably by an alternative choice of the dimensions of Glasstone (H), if the parameter of equation 4 lies in the range $1/10 < \mu < 2$.

The lunar maria can be divided into two broad classes. One class shows irregular borders. The other, of which Mare Imbrium is the archetype, is characterized by a nearly circular outline and the presence of an encircling ring of mountains, with an escarpment on the inner wall and a gradual slope on the outer face. It will be hypothesized that the maria of Imbrian type were formed by explosions of large meteorites, occurring at a time when the lunar hydrosphere exhibited roughly its maximum depth. If such were the case, the dimensions of these maria should show a correlation with those of the craters of Class V and Glasstone (H).

Values for the diameters of the maria have been given by Baldwin; the diameter was considered to extend fully to the encircling mountains (the Altai in the case of Mare Nectaris). The maximum height of these mountains can be taken as a first approximation to the corresponding crater depth; values were taken from results of Schmidt[29], in general. This estimate can be improved by including a correction for the depth of the sediments in the mare basin. As an upper limit, Baldwin gives roughly 2 km. as the depth in question for the maria; this value was adopted for the largest mare (Imbrium) and scaled linearly with diameter for the others. Representative points determined in this manner are shown in Fig. 2 for Mare Imbrium, Nectaris, Serenitatis, Crisium and Humboldtianum. One sees that the points lie closely on the curve already determined from mensuration of Glasstone (H) and the craters of Class V.

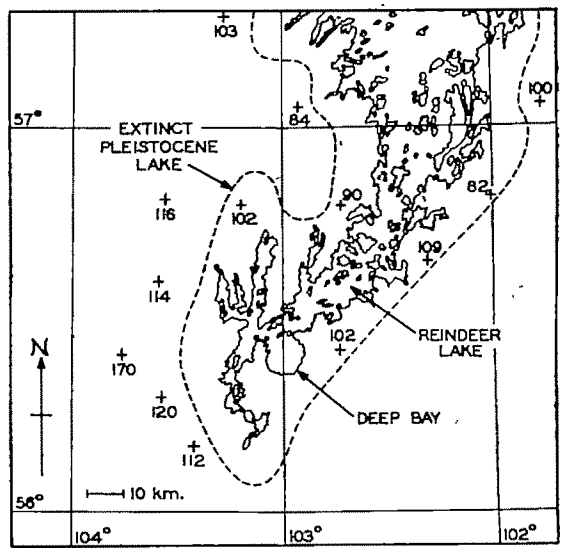

Fig. 3. Map of the southern half of Reindeer Lake, showing Deep Bay and the outline of the extinct Pleistocene lake. The crosses indicate spot elevations, with heights in metres above the present level of Reindeer Lake

As compared with the corresponding argument for the craters of Class I, the reasoning indicating that the Imbrian maria, the craters of Class V, and Glasstone (H) form one family lacks a link in the form of terrestrial meteorite craters. However, a meteoritic crater exists which one can argue reasonably must have been formed in water. This crater is Deep Bay[30], which is a nearly circular appendage of Reindeer Lake in northern Saskatchewan, Canada, as shown in the map of Fig. 3. It has not been possible to fix the geological age of this crater with any degree of certainty. However, Reindeer Lake occupies the site of an extinct Pleistocene lake of considerably larger area, as Fig. 3 shows[31]. If Deep Bay actually is of Pleistocene age, it most probably was formed in water, and the spot elevations above the level of the present lake appearing in Fig. 3 indicate a value $\mu \approx 1/2$ for the parameter of equation 4.

Deep Bay was formed in schist and gneiss, and thus in soft rock on the criteria adopted. To construct a curve for meteorite craters formed in water for a bottom of soft rock, a_1 of equation 5 was fixed by the dimensions of Glasstone (S), and the values of a_2 and n were taken as already determined from the craters of Class V. The resulting curve is shown in Fig. 2 (labelled soft rock). One notes that the point for Deep Bay lies on it closely. The bottom of Deep Bay has not been bored, but would have to

consist of roughly 1 km. of glacial debris for the representative point in Fig. 1 to fall reasonably close to the curves for craters of Class I. Such a large value is inconsistent with the fact that at least one glacier passed over Chubb but left relatively little glacial deposit in the crater; it is necessary to presume that freezing of the lake in a crater protects it from glacial filling[32]. Note that the points for both Deep Bay and the lunar maria have been fitted without making use of their dimensions in constructing the fitting function.

If the dimensions of the lunar craters of Classes II, III and IV (exclusive of V) are fitted separately in each case, the corresponding curves lie between those for Class I and the curve determined by Glasstone (*H*) and the craters of Class V, in a progression corresponding to ordinal number of the class. On the thesis of this article, this progression corresponds to formation of craters at temporal stages in the dissipation of the lunar hydrosphere, where the average water-level was below the maximum. Terrestrial analogues of these craters of intermediate type probably exist in the Campo del Cielo crater field[33] in Argentina. The meteorite fall occurred in marshland; the dimensions of one of the largest craters are known with reasonable accuracy from excavation and the corresponding point occupies an intermediate position relative to the curves of Fig. 2.

Discussion and Conclusions

It is clear that the presence of a lunar hydrosphere of the age calculated yields a direct explanation of the progression of relative dimensions of the craters in the various classes, of the origin of the maria, and of the nature of the mare floors. It is ironical that, on these views, the name mare is correct on the basis of provenance.

The considerations of this article have a direct bearing on the problem of the origin of tektites. Nininger[34] has proposed that these glassy objects are fragments of rock fused initially by meteorite impact on the Moon and ejected from the lunar surface by the force of the explosion. The second melting phase displayed by these objects then occurred during supersonic passage through the Earth's atmosphere. Objections to the possibility of a swarm of bodies from the Moon falling on the Earth in a compact cluster seem to have been disposed of recently by Baker[35]. Thus, the theory yields properly two periods of fusion, the observed flow structure and shape of these objects, and the distribution over the Earth's surface.

However, the chemical composition of most tektites is similar to that of argillaceous sedimentary rocks, and the view that such rocks could not be present on the Moon has precluded general acceptance of Nininger's idea. This objection is met fully by the considerations of this article. Erosion explains the presence of quartz particles in the lunar sediments, required to yield the lechatelierite observed in tektites. Thus the theory in question is the only one satisfying all the requirements laid down by Barnes[36].

It remains to explain the dark colour of the maria. Since only a small amount (less than 5 per cent) of organic carbon in a sediment is sufficient to yield a dark rock of low reflectivity[37], it will be postulated that a primitive form of life existed in the lunar hydrosphere. All the requirements for biopœsis were once met on the Moon[38], in view of the existence for an extended time of an atmosphere and hydrosphere. Their presence would reduce the daily range of temperature below that at present observed[6]; if the albedo of the primitive atmosphere of the Moon were comparable with that of the Earth, the mean surface temperatures would be the same[39]. The time-scale is favourable to the possibility in question, since the oldest known fossil plant (an alga) is at least $2 \cdot 6 \times 10^9$ years old[40], indicating that life began on the Earth within a period less than 2×10^9 years of its origin. This maximum span for biopœsis to occur is less by 1×10^9 years than the minimum life-time shown for water in Fig. 2. Thus, one can speculate that life originated on the Moon through the process postulated by Oparin[41]. The initial steps were the formation of fairly complex organic molecules through the action of solar ultra-violet radiation and lightning discharges on atmospheric gases, as reproduced to some extent in the laboratory[42].

A positive clue exists that life once existed in the lunar hydrosphere. As this medium dissipated, the dark coloration in the maria of Imbrian type tended to recede from the bases of the encircling mountains, as is evident in the pattern of light and dark colour in the mare basins. The retreat is most prominent in the case of Mare Nectaris, where the dark material has regressed about 100 km. from the ring defined by the arc of the Altai Mountains[43], but it appears also for Mare Crisium, Mare Serenitatis and Mare Imbrium. It is characteristic of living matter to follow the retreat of its habitat in this manner.

The inferred presence of organic carbon in the maria and adjacent craters would explain in a natural way Kozyrev's observations[44] of the Swan bands of C_2, as the result of sublimation of carbon by the heat of a meteorite impact. Accordingly, the observations can be explained without the need to invoke volcanism on the Moon, for which no visible evidence exists otherwise, on the thesis of this article.

A full account of this work will appear elsewhere.

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PROGRESS OF CANCER RESEARCH

SOME hundreds of investigations are described in the current annual report of the British Empire Cancer Campaign which in 1959 gave financial support, directly or indirectly (£750,000) to more than 1,300 investigators at numerous centres of research in Great Britain and the Commonwealth*. The 666 pages of the report demonstrate, if that were necessary, that notwithstanding the immense industry expended, we are still a long way from the solution of cancer.

The subject-matter of the report can be conveniently subdivided into three main classes: (1) researches dealing with carcinogenesis, chemotherapy, demography, hormones and allied lines of work of a more biological or biochemical nature; (2) clinico-pathology and related themes; (3) physics, radio-biology, isotopes and radio-therapeutics.

Perhaps the most interesting recent development in class 1 has been the additions to the catalogue of cancer-inducing viruses, namely, the filterable mouse leukæmia agents of Gross, and the polyoma virus studied by Stewart which evokes tumours in a number of sites in mice. Work on these viruses is in progress at several research centres: Miller, at the Chester Beatty Institute, London, found that his cell-free filtrate prepared from the leukæmic tissue of mice of the high leukæmia-susceptible strain *AKR*, when injected into new-born mice of the C_3H strain produced a low incidence of leukæmia (13 out of 169 mice developed the disease); the induction of immunological tolerance in C_3Hf mice, produced by first inoculating them intravenously at birth with healthy spleen cells from *AK* mice, did not increase the susceptibility to leukæmia by the injection of leukæmic filtrate from *AK*'s at one month of age. Miller has also prepared filtrates from Gross's own leukæmic mice (C_3Hf/GS strain); these filtrates induced leukæmia in 27 per cent of C_3Hf mice in Miller's colony, which were much less susceptible to leukæmogenic filtrates from the tissues of *AKR* mice. The deoxyribonucleic acid and ribonucleic acid prepared by Kirby's method from this very active filtrate retain some of their potency, for on injection into new-born C_3Hf/GS mice, tumours of the salivary gland developed after a few months. Thymectomy prevented leukæmia in strains inoculated at birth with leukæmic filtrates even in strain C_3Hf/GS, which gives 100 per cent leukæmia in the normal non-thymectomized litter mates.

Metcalf in Victoria points out that the thymus produces more than 75 per cent of the lymphocytes in C_3H mice, and that pre-leukæmic mice of the *AKR* strain show a 2–3 times higher daily production of lymphocytes than normal C_3H mice; when the *AKR* mice become leukæmic, the mitotic rate rises to twice as high as in the pre-leukæmic animal.

Salaman and Rowson, at the London Hospital, in work on the Gross and Stewart viruses, found that the inoculation of C_3H mice with cell-free filtrates from leukæmic tissue of *AKR* mice resulted in a high yield of tumours in less than three months; these were not leukæmias but were tumours of the salivary glands and subcutaneous carcinoma and sarcoma (40 tumours in 15 out of 23 treated mice). These tumours were similar in type and distribution to those described by workers in the United States as initiated by the '*P*' or polyoma virus; a few leukæmias appeared later, between 14 and 20 months. In further experiments some litters were found to be immune to the carcinogenic activity of *P* virus, while other litters were highly susceptible, which strongly suggested that immunity had been spreading through Salaman's mouse colony and had effected complete protection in some litters, less or none in others. He found, also in agreement with Stewart and her colleagues, that tissue cultures of *CBA* mouse embryo cells treated with cell-free filtrates from lymphatic tissue of an *AKR* mouse bearing spontaneous leukæmia gave rise to a cytopathogenic and hæmagglutinating agent; antibodies to this agent could be detected patchily distributed in his colony of mice, and the cell-free filtrates from the *P* virus-induced tumours contained antibody to the hæmagglutinating agent. Salaman observed that tumours of the salivary gland and subcutaneous tissue which had been induced in C_3H mice by the inoculation of cell-free filtrate from leukæmic tissue of *AKR* mice contained hæmagglutination-inhibiting antibody which could well account for the failure of these filtrates to evoke tumours on injection into new-born mice.

Orr and his collaborators at Birmingham have been investigating the chemical induction of ovarian and mammary tumours in mice of the 1*F* strain by painting the skin with 9 : 10-dimethyl-1 : 2-benz-

* Thirty-seventh Annual Report covering the year 1959. Part 1. The Chairman's Statement and the Accounts. Part 2: The Scientific Report of the Researches undertaken by the Central Organization and Its Autonomous Councils in the United Kingdom, and by some of Its Affiliated Organizations Overseas. Pp. liv+666. (London: British Empire Cancer Campaign, 1960.)

anthracene (DMBA). "In a recent experiment, ovariectomized mice were grafted with one ovary from a DMBA-treated mouse and one normal ovary. No ovarian tumours developed, showing that the presence of secretion from a normal ovary can prevent potentially neoplastic ovaries from developing into tumours. This falls into line with results obtained by other workers on the induction of ovarian tumours by X-rays or intrasplenic grafting, which techniques also fail in the presence of normal ovaries or adequate ovarian hormones." Tumours of the breast in male mice resulted when the skin was painted with methylcholanthrene after pretreatment of the rudimentary mammary tissue by stimulation with the injection of œstrogen together with progesterone or the subcutaneous grafting of an ovary. Progesterone secretion seems to play an important part in this type of mammary tumour; virgin females of the $C_{57}B1$ strain are much more resistant to breast tumour induction by painting of the skin with methylcholanthrene, but if the mice are kept pseudopregnant by mating with vasectomized males and painted with methylcholanthrene or 9 : 10-dimethyl-1 : 2-benzanthracene, breast tumours appear in a very short time.

Workers at the Nottingham centre and at the Royal College of Surgeons have been using the fluorescein–globulin staining technique studied by the Australians, King, Hughes and Louis, who also contribute an account of their experiments to the report; they originally found that a fluorescein–globulin complex combines with some components of the tissues to give fluorescent staining which could be observed in the microscope. It was found that "normal tissue stains but malignant tissues uniformly fail to stain and this applies to both experimentally produced and naturally occurring growths". The cytoplasm of the cells took up the fluorescein–globulin stain, while the nuclei remained free from stain; but there were some exceptions, such as the tissues of the nervous system, hæmoglobinized red corpuscles, megakaryocytes and connective tissue cells, which all failed to stain. Red blood corpuscles which still retained their nuclei (normoblasts from human bone marrow and the nucleated cells of lower animals) showed nuclear instead of cytoplasmic staining, and when the connective tissue cells enlarged and showed a considerable amount of cytoplasm these stained in the normal manner. Cells in tissue culture stained during the first 3- or 4-days growth in the normal manner, but after the fourth day failed to stain. These results show that staining capacity cannot be considered a reliable test for malignancy; the lack of staining has been put forward as the indication of a loss of some protein components in cancer tissue, but the unstainability of some normal tissues and of *in vitro* cultures of normal tissues pose questions demanding further investigation.

At the Glasgow centre, work is in progress on the lung cancer – cigarette-smoking problem. "For sixteen countries surveyed, a close relationship exists between national consumption of cigarettes 20 to 25 years ago and standardized mortality of men for lung cancer at the present time . . . an exception is the United States of America where the mortality is lower than would be expected from the apparent level of cigarette consumption." The anomaly has apparently been solved by the measurement of the mean length of butt of smoked cigarettes in Britain and in the United States . . . "on the basis of average butt lengths discarded by British and American smokers . . . it would appear that the American smoker receives approximately 65 per cent of British smoker's smoke intake" (that is, the carcinogens contained in the tar of the smoke condensate).

The incidence of cancer in Jamaica has been studied at the Cancer Registry in the University of the West Indies. Statistical analysis shows that compared with Denmark the overall incidence of cancer is approximately the same, but the sites of election are rather different. Cancer of the upper respiratory and alimentary tract and of the lip, tongue, œsophagus, liver, cervix and penis appear to be more common in Jamaica in both male and female; but gastrointestinal malignancies are less frequent.

In the field of clinico-pathology the results obtained in exfoliate cytology as a means of detecting carcinoma of stomach and prostate are of interest. Price's report from Bristol suggests that the abnormal seasonal presentation of osteogenic sarcoma of adolescents may be related to the seasonal rhythm of the growth of bone. Prof. Hou's investigation of primary carcinoma of the liver due to infestation with *Clonorchis sinensis*, suggests that the worm requires a high level of copper in its environment in order to maintain its physiological functions. The report from St. Mark's Hospital is an admirable synopsis of significant clinical and pathological features of neoplastic disease of rectum and anus; the general results of the surgical treatment of rectal cancer for the period 1928–57 have been analysed, and among other facts revealed by this investigation are the following: the operation of combined excision of the rectum and sigmoid colon, which in recent years has replaced the older one of perineal excision almost to the exclusion of the latter, does not significantly improve the results in the less-advanced cases, whereas the survival for advanced cases is almost doubled. This advance has been made possible not by better surgery, nor is the operation itself an innovation, but by the improved anæsthesia and pre- and post-operative care which modern technique has made practicable. Thirty years ago it was far more hazardous for a patient to undergo the more radical procedure. The chances of cure of carcinoma of the rectum are expressed as follows: if the operation is carried out on patients in whom there is still a reasonable prospect of cure, between 40 and 50 per cent of the operation survivors are likely to be alive five years later. Some of those who have survived five years may succumb to a recurrence, but the majority of five-year survivors are likely to be cured.

What is to be expected from tests for 'cancer'? When extensive tumour deposits are present it is only reasonable to anticipate that there will be detectable alterations in the body fluids. These may be of a purely secondary nature, such as the hypercalcuria and raised serum alkaline phosphatase which accompany gross bone involvement by tumour, or the raising of the erythrocyte sedimentation-rate associated with tumour necrosis or ulceration. But a test is very rarely specific, although malignant trophoblastic tumours and some cases of testicular tumour show a high serum and urinary level of chorionic gonadotrophin, assay of which may give a guide to the presence or not of functionally active tumour tissue in the body. Similarly, the malignant argentaffin cell tumours of the intestinal tract may be associated with a high urinary output of 5-hydroxyindole-amino-acid. In general, however, no specific

alterations in metabolism, nor the production of abnormal substances is associated with the common cancers, for example, of the lung, bowel, and primary and secondary sex organs.

In the paper from the Pharmacology Department of the University of Melbourne chromatographic tests applied to extracts of specimens of urine from 'cancer' patients and control normal subjects have suggested the presence of weak organic bases in a concentration of the order of $1/10^6$ in the urine of 'cancer' patients. These substances, isolated in milligram quantities, have been crudely characterized by infra-red spectroscopy. A mention of the criteria used in the classification of these patients would have been helpful. The use of the term 'cancer patient' is to be avoided unless qualified. The varieties and stages of development of cancer are so numerous, their patterns of evolution so different, with consequent variations in prognosis, that the term has no more significance than, say, 'infectious disease' would have in a similar context.

The special contributions made by radiation physics and applied radioactivity are now so broad, merging especially with biochemistry and radiobiology, that the task of reviewing them is difficult. Some reports in the present volume do indeed deal with purely physical problems, but in most of them the physical contribution is firmly integrated into programmes which are fundamentally biological. This must be good both for the physicists and biologists involved and is a welcome departure from the usual trend of scientific research, which is towards ever greater specialization.

In radiotherapy, the most interesting points to note are the detailed work on the problems of using electron beams for therapy; the steady growth of interest in telecæsium units; and the development by the Radiochemical Centre of cæsium-137-loaded tubes, the advantages of which as a replacement for radium are being investigated at the Royal Cancer Hospital. Illingworth's team at Glasgow has made notable advances in the technique of using yttrium-90 rods for pituitary irradiation, as an adjunct to the treatment of breast cancer. The use of unsealed preparations of radioisotopes administered parenterally for radiotherapy continues to lag as it has done for some years.

There have been no important new developments in the diagnostic use of radioisotopes, though several centres report improvements to existing techniques. Similarly, there are no new developments in isotope instrumentation; and in one important respect, the assay of tritium in biological samples, demand now outpaces supply. At least two centres report that they are working on the improvement of existing techniques, and there is no doubt that if these could be made simpler and more reliable this particularly useful tracer would be far more widely used than at present. The British Empire Cancer Campaign might do worse than devote some of its funds to a solution of this problem, thus saving the wastage brought about by divided effort.

Reading between the lines, one has an occasional feeling that, in the diagnostic and therapeutic fields especially, progress is not all it might be because various centres live too much in a world of their own. For example, it is clear from some of these reports that various hospitals have only recently begun to use the short-lived iodine-132 in place of iodine-131 for thyroid testing. Others are still improving their techniques for administering radiogold colloid; and one has not yet passed beyond the primitive stage of using a heavily shielded syringe, presumably manually operated, for this purpose, which may well involve more than 100 mc. of radiogold. Now the palliative use of radiogold for the treatment of pleural effusions has been well established for at least ten years, during which time many simple methods of remote handling have been developed and published. In view of this, and of current concern with occupational radiation protection, it certainly looks as if some centres are leaving their improvements rather late in the day—though, of course, better late than never.

As usual, it is in research that the techniques of radiation physics and radioactivity continued to find their greatest application. The main emphases are on the vexed question of the proportionality of dose to effect in causing cancer; on the similar effect of dose-fractionation; on the effects of prolonged radiation exposure; and on the relationships between oxygen-tension and tumour radiosensitivity. Many centres are at work on these problems. The results are not startling; what is more important is that they are solid and impressive. The radiation degradation mechanisms of cellular constituents continue to receive detailed investigation.

In addition to this, many useful metabolic studies are reported. At the Royal Cancer Hospital it has been shown that diethylene-triamine-penta-acetic acid is more effective than ethylenediamine-tetra-acetate in removing americium-241 from the body. The same centre has made comparative studies of the absorption of the alkaline earths from the gastro-intestinal tract, showing, somewhat surprisingly, that the degree of absorption is not related to atomic weight, but that radium is more readily absorbed than barium. The Royal Cancer Hospital also continues its valuable work on environmental radioactivity and the natural activity of foodstuffs. The Department of Biochemistry at St. Bartholomew's Hospital has continued its work on zinc metabolism, showing among other things, that erythrocyte zinc, in contrast to leucocyte zinc, is higher in leukæmic than in normal blood. These are but a few of the many examples which might be quoted; selection is really invidious.

However, mention should be made of a new development by Mitchell's team at Cambridge, because of its direct relevance to the important question of cancer chemotherapy. For six years they have been trying to produce labelled organic substances which are selectively concentrated in tumour tissue. They have now succeeded, using tritium-labelled tetrasodium - 2 - methyl - 1,4 - naphthohydroquinone diphosphate (synkavit) of very high specific activity. The therapeutic possibilities of this agent are at present under investigation.

The size and, even more so, the method of presentation of these reports combine to defeat any realistic attempt at adequate summary. This is a matter which has received adverse comment before. To some extent the problem is insoluble; there are, and must be, dozens of authors, but some of these report in a few vague lines, others in several pages; and this disparity is not always related to the intrinsic importance of the work discussed. Some further editorial—or pre-editorial—advice to contributors is indicated. A much more serious objection is that the contents of the report continue to be laid out on a geographical basis, centre by centre. This system

not only has no scientific merit, it also renders the report as a whole almost unreadable because it is so disjointed; and, in the absence of an analytical index (indeed, of any subject-index at all), nothing short of leafing through every one of its 666 pages will allow the reader to form any clear picture of what is happening in his own and related fields of interest.

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TEST TRACK FOR THE ROAD RESEARCH LABORATORY

THE Road Research Laboratory was founded in 1933. In recent years the importance of the work being done both on road materials and methods of road construction and on traffic and safety problems has been responsible for increases both in staff and the facilities needed. The Laboratory has thus long out-grown the field at Harmondsworth on which the first buildings were erected, and various other buildings within a radius of 5 miles of Harmondsworth have been pressed into service.

The first stage in bringing all the Laboratory's activities together was accomplished on October 12, when the Laboratory's special test-track was declared ready for service. This has been built on a triangular site of some 253 acres of undulating wooded country immediately north-west of the village of Crowthorne in Berkshire. This site is ultimately to house laboratories, workshops, offices, a library and a canteen to provide all the facilities required for the Laboratory work and to accommodate some 750 members of staff.

The new track has cost about £500,000 to build and will be used mainly for research into traffic problems and safety measures with special attention to the behaviour of vehicles at high speeds. The type of investigation proposed cannot be carried out on public roads with safety, but abandoned airfields have been used from time to time.

The track is some 3 miles long, and is built in the form of a figure of eight, one loop being about twice as large as the other; the larger loop has a steeply banked bend leading to a straight portion 900 yd. long. For tests on stability during braking at high speed a car can thus take this bend at 60 m.p.h. left-handed, accelerate along the straight, which has a downhill gradient of 1 in 25, and then, while the track swings away to the left, take a siding which continues the straight portion for some 200 yd. and leads to a terminal area some 300 yd. long and 80 yd. wide. A car can thus enter the terminal area at 100 m.p.h. and be braked to a standstill in perfect safety. This area will be used for investigations of the stability of vehicles in good condition and defective when performing emergency manœuvres involving steering, accelerating and braking.

Much remains to be learnt about the steering characteristics of vehicles under transient conditions. Theory and experiment need to be closely linked in this work, and the two large paved areas afford unrivalled facilities for obtaining experimental data at fairly high speeds. One of the demonstrations during the opening inspection showed an experiment of this type. A car with unbalanced brakes entered the terminal area at high speed and spun round several times before being brought to rest. The long straight section, which has been termed the 'high speed' section, is made up of six different road surfacings for skidding experiments. A storage tank containing 54,000 gallons of water has been installed on a nearby bank with pumps and pipes so that some 800 yd. of this track can be kept wet during tests. This section of the track will thus enable investigations to be made of the effect on skidding of the texture and other properties of the wet-road surface, the properties of the tyres used and the characteristics of the vehicle as regards steering, braking and general ease of control.

The track as a whole will also be used for tests on vehicle lighting both on straight and curved roads with surfaces of different colours and textures, and also for comparison of different street lighting installations under controlled conditions, both types of test being hazardous when carried out on public roads. The track will also provide a continuous circuit where driving habits and reactions can be studied in safety: a demonstration of the technique involved was given during the opening inspection. Two cars followed each other both in wireless communication with a fixed receiving station. The experiment was to determine safe following distances; the first car carried out various manœuvres, and the braking reactions, throttle position, speeds and other data involving the cars were recorded at the receiving station on a moving chart.

Where the tracks of the figure-of-eight cross, a circular centre area has been built with a diameter of 900 ft.; this is about the size of the grass area of Lords Cricket Ground. This centre area will be used to investigate large-scale problems of traffic control. Where the design of an intersection is being considered, for example, the several possible alternatives can be set up with moveable barriers and kerbs, and can be studied with actual traffic; variations in the siting and operation of traffic signals, and other aids to the flow of traffic can also be investigated.

In a complex network it may be possible to speed up the flow of traffic by a system of vehicle detectors and traffic lights controlled by a computer which adjusts the traffic controls according to the volumes of traffic signalled to it from the detector points. This central area will be available for practical tests of such systems. The track is also provided with a novel control feature. This consists of a straight wire running under the whole length, together with a series of wire loops at regular intervals. These wires can be made to emit various types of signal which can be picked up by electronic devices in the test vehicles and translated into instructions. Thus 'automatic pilots' can be used in experiments involving cars being crashed, and the loop system can be made to signal back to a driver the passage of a car over the loop in front. This system will be used to explore the possibility of providing guidance to the drivers of vehicles in dense fog.

T. Lonsdale

OBITUARY

Sir Harold Spencer Jones, K.B.E., F.R.S.

HAROLD SPENCER JONES was born in Kensington on March 29, 1890, and died there on November 3, 1960. He was educated at the Latymer Upper School, Hammersmith, and at Jesus College, Cambridge, where he was a wrangler and Smith's Prizeman and also obtained first-class honours in Part 2 of the Natural Sciences Tripos. He was elected a Fellow of his College in 1914, but a year before this he was appointed chief assistant at the Royal Observatory at Greenwich.

In 1923 he was appointed His Majesty's Astronomer at the Royal Observatory of the Cape of Good Hope. He directed this Observatory with great vigour for ten years, and interested himself personally in both the spectroscopic work, contributing full-scale studies of Nova Pictoris and of Procyon as a double star, and also the astronomical work, investigating the constant of aberration, the mass of Venus and the Moon's motion. He took the important decision to resume the Cape programme of parallax determinations, which had been set aside in favour of spectroscopic work. He, however, left the Cape before this programme was completed, and it was finished by his successor as H.M. Astronomer, John Jackson.

In 1933 Sir Frank Dyson retired from the position of Astronomer Royal, and Spencer Jones succeeded him, being the tenth person to hold the office since the appointment of Flamsteed in 1675. His major work during his first years at Greenwich was the reduction of observations made on the minor planet Eros, with the end in view of securing an improved value of the solar parallax. Eros made a close approach to the Earth in 1901, the minimum distance on this occasion being 30,000,000 miles. Observations of its position were reduced by A. R. Hinks, who found a solar parallax of $8{\cdot}807'' \pm 0{\cdot}0027''$ from photographic measures and $8\ 806'' \pm 0\ 004''$ from micrometer measures. However, it was realized that Eros would make a much closer approach to the Earth in 1931 (minimum distance 16,200,000 miles), and in 1928 the International Astronomical Union set up a commission with Spencer Jones as president to organize observations on a world-wide scale in the forthcoming favourable opposition. The circumstances of the opposition favoured observatories in the southern hemisphere, and in fact a great part of the weight of the determination came from observations at the Cape, which Spencer Jones was then directing. Spencer Jones's reduction and discussion of the work was not published until 1941; he obtained the value $8{\cdot}790'' \pm 0\ 001''$, a result which differed substantially from that of Hinks. Spencer Jones was an authority on the consequential changes in the inter-related constants of the solar system and discussed the adjustment of them with great thoroughness.

In addition to his interest in the solar parallax, Spencer Jones took a deep interest in latitude variation and in the accurate determination of time, and he ultimately replaced Dyson's Shortt clocks with quartz clocks and commissioned a newly designed photographic zenith tube to determine both latitude variation, formerly determined with the Cookson floating telescope, and time, determined with a small reversible transit telescope. The photographic zenith tube was not brought into use until after Spencer Jones's retirement in 1955; but the quartz clocks operated for many years under his direction, and he had the satisfaction of detecting with them variations in the rate of rotation of the Earth. This has important consequences on apparent motion of bodies in the solar system, which was a topic that Spencer Jones had already studied at the Cape.

Perhaps as a result of his service at the Cape, Spencer Jones was led to the view that Greenwich had become permanently unsuitable for astronomical observation, by reason of atmospheric pollution and the development of street lighting. He therefore set about persuading the Admiralty that it was necessary to move the Royal Observatory from Greenwich to a country site. Approval was obtained in 1946, and Herstmonceux Castle, with its associated estate of 372 acres, was purchased by the Admiralty: but the actual move proceeded somewhat slowly, the first stage taking place in 1948 and the move being incomplete when Spencer Jones retired in 1955. He, however, secured the building of premises outside the Castle such as to make the Royal Greenwich Observatory much better equipped than it had ever been at Greenwich and Abinger (the magnetic sub-station, at which a great deal of the time service was located), and the night sky at Herstmonceux has proved greatly superior to that of Greenwich.

Spencer Jones also realized that the want of a large modern telescope had had a crippling effect on British astrophysics, and he led the astronomical profession in representing to the Royal Society, the Admiralty and ultimately the Treasury, that a large telescope should be built. Approval was given for the building of a 98-in. reflecting telescope, to be called the Isaac Newton telescope, and to be set up in the grounds at Herstmonceaux. The diameter of 98 in. was occasioned by the gift of a 'Pyrex' blank of that size by the McGregor Fund in the United States, a blank which had been made at the time of the casting of the blank for the 200-in. reflector. Again Spencer Jones did not continue in office long enough to see the result of this move, and in fact the project was delayed for a number of reasons. It is now expected that the telescope will be put into commission in 1966.

Spencer Jones was the recipient of many honours. He was created a knight in 1943 and K.B.E. in 1955. He received the Gold Medal of the Royal Astronomical Society in 1943 and a Royal Medal of the Royal Society in the same year. He was highly esteemed in international circles, and was president of the International Astronomical Union from 1945 until 1948, and he held all the offices in the Royal Astronomical Society, being president from 1937 until 1939 and foreign secretary at the time of his death. He became secretary-general of the International Council of Scientific Unions in his retirement. His interest in horology was recognized by his being made president of the British Horological Institute, and he received its Gold Medal in 1948; and he was twice master of the Clockmakers' Company—in 1949 and 1954. Perhaps his most important service to British astronomy consisted in his moving the Royal Observatory to the country and equipping it to take on an entirely new lease of life, and as such he occupies a distinguished position among the Astronomers Royal.

R. V. D. R. WOOLLEY

NEWS and VIEWS

The Royal Society: Officers

SIR HOWARD FLOREY has been elected president of the Royal Society in succession to Sir Cyril Hinshelwood. The new treasurer of the Society is Sir Alexander Fleck, formerly chairman of Imperial Chemical Industries, Ltd., and the new foreign secretary is Sir Patrick Linstead, rector of the Imperial College of Science and Technology, London. Sir Lindor Brown, Waynflete professor of physiology in the University of Oxford, and Sir William Hodge, Lowndean professor of geometry and astronomy in the University of Cambridge, have been re-elected biological secretary and physical secretary, respectively.

Other members of Council elected were: Prof. J. F. Baker, professor of mechanical sciences in the University of Cambridge; Mr. R. P. Bell, reader in physical chemistry, University of Oxford; Dr. J. C. Burkill, University lecturer in mathematics, University of Cambridge; Prof. D. G. Catcheside, professor of microbiology in the University of Birmingham; Prof. J. E. Harris, professor of zoology in the University of Bristol; Prof. T. M. Harris, professor of botany in the University of Reading; Prof. A. F. Huxley, Jodrell professor of physiology at University College in the University of London; Sir Christopher Ingold, professor of chemistry in the University of London (University College); Dame Kathleen Lonsdale, professor of chemistry in University College, London; Dr. R. A. Lyttleton, reader in theoretical astronomy in the University of Cambridge; Dr. R. G. Macfarlane, reader in hæmatology, University of Oxford; Prof. R. A. Morton, Johnston professor of biochemistry in the University of Liverpool; Sir Alfred Pugsley, professor of civil engineering in the University of Bristol; Dr. C. J. Stubblefield, director of the Geological Survey of Great Britain; Sir Gordon Sutherland, director of the National Physical Laboratory; Prof. C. H. Waddington, professor of animal genetics in the University of Edinburgh.

Sir Howard Florey, P.R.S.

SIR HOWARD FLOREY, professor of pathology in the University of Oxford, was born in Adelaide in 1898, where he attended St. Peter's College and the University, afterwards proceeding to Magdalen College, Oxford, as a Rhodes Scholar. After holding academic posts in the Universities of Cambridge and Sheffield, he was appointed to his chair at Oxford in 1935. He is well known for his contributions to experimental pathology and medicine, and especially for his work on the isolation, structure, therapeutic use and mode of action of penicillin, for which he was awarded the Nobel Prize for 1945, jointly with Sir Alexander Fleming and Prof. E. Chain (*Nature*, 156, 564; 1945). Among his many awards he has received a Royal Medal in 1951 (*Nature*, 168, 1017; 1951), and the Copley Medal in 1957 (*Nature*, 180, 1231; 1957) of the Royal Society.

Applied Science in the University of London: Prof. B. G. Neal

PROF. B. G. NEAL has been appointed to the chair of applied science with special reference to engineering tenable at the Imperial College of Science and Technology, University of London, as from April 1, 1961. This chair was first established in 1955 with the aim of giving special attention to the common course for all engineering students at the City and Guilds College and was held by Prof. D. G. Christopherson (see *Nature*, July 2, 1955) until he resigned the chair on September 30 last. Prof. Neal had a distinguished undergraduate career at Trinity College, Cambridge, where he won the Rex Moir, Ricardo, and Seely Prizes. After the War, he carried out research at Cambridge and at Brown University in the United States; after his return to Cambridge, he held appointments on the teaching staff until in 1954 he was appointed professor of civil engineering in the University College of Swansea. His research interests lie in the properties of materials, particularly structures and welded joints, and he has published many papers on the theoretical and experimental analysis of the stresses in such structures. He is keenly interested in current problems of education for engineers, and the new expansion and development of engineering at Imperial College will doubtless afford Prof. Neal many opportunities for guiding engineering education along the right lines.

British Scientific Policy and Research Effort

IN the debate on scientific policy in the House of Lords on November 9, Lord Adrian intervened to make two points. He stressed the importance of the science teachers and their work and of associating them with the necessary re-examination of curricula in science. His other point related to the scientific societies which played an important part in any organization for both pure and applied science. While there were no serious complaints about the arrangements between the State and the scientific societies during the past 100 years, or about Government goodwill towards these societies, their finances were now seriously threatened by proposals of the Pritchard Committee, that in future societies which are now exempt from rates should be liable to the extent of half the full rateable value of their premises. Few of them had substantial financial resources, and one consequence was likely to be a reduction in the publications of learned societies. Lord Hailsham said he was aware of the position in general, but undertook to look into the question, and he suggested that Lord Adrian should induce the societies to memorialize him or the Chancellor of the Exchequer on the subject.

Referring to some of the gaps in the British research effort mentioned in the report of the Advisory Council on Scientific Policy, Lord Hailsham said that since the War the Government had financed the work of the National Institute of Oceanography, under the supervision of the National Oceanographic Council, to the extent of £1·5 million, and had recently approved the construction of a new oceanographic ship for the Institute costing about £750,000. He agreed that oceanography was essentially an international study, and he hoped shortly to have the opinion of the British National Committee for Oceanic Research, set up by the Royal Society, as to the part the United Kingdom could play. Various proposals involving international co-operation in astronomy were being considered and his office was also in touch with developments through the British National Committee on Astronomy of the Royal Society; he

thought it was important that there should be an early decision. The Government had accepted the Advisory Council's recommendation regarding the use of the telescope and equipment maintained at Pretoria by the Radcliffe Trustees, and specific proposals for additional financial help to the work at this observatory were under consideration by the Department of Scientific and Industrial Research. The recommendation relating to the establishment of seismological centres at the Universities of Cambridge and Edinburgh was in the first place a matter for the Universities concerned, and Lord Hailsham understood that they had it under active consideration. He added that he had given some attention to the matter of financing the administration of scientific departments although this was primarily a matter for the University Grants Committee.

Overseas Trainees and Students in Britain

Two recent booklets describe the increasing part being played by Britain in the education and training of students from Commonwealth and other countries oversea. The first, "Overseas Trainees in United Kingdom Industry", describes the opportunities available through scholarships provided by the British Council, Colombo Plan, Federation of British Industries Overseas Scholarships and other agencies, as well as the actual scales of assistance provided by the agencies (Pp. 16. London: Federation of British Industries, 1960. 6*d*.). The booklet has been prepared by the Federation of British Industries and shows clearly that the development of such facilities is as essential for the long-term growth of the British economy as for the benefit of participating trainees and their sponsoring countries. The second, "Overseas Students in Britain", is more concerned with what is being done by various welfare organizations to serve the 47,500 overseas students who are now in Britain (Pp. 34. London: London Overseas Dept. of the British Council, 1960. 1*s*. 6*d*. net). The booklet has been prepared by the Standing Committee of the London Conference on Overseas Students but has application throughout Britain. It may be obtained from the British Council, 3 Hanover Street, London, W.1.

Science and Technology for Commonwealth Students in Britain

In a written answer in the House of Commons on November 23, the Secretary of State for the Colonies, Mr. Iain Macleod, gave a table showing that of the 2,230 students from territories under United Kingdom administration studying technical or scientific subjects in the United Kingdom, 235 were studying pure science, 708 medicine and pharmacy, 867 engineering and technology, 43 dentistry and 96 agriculture. Many of the further 1,150 students taking courses for the Ordinary and Advanced Level examinations of the General Certificate of Education in the United Kingdom will have included science among their subjects. A parallel statement on the same day from the Secretary of State for Commonwealth Relations gave the number of science and technology students from member countries of the Commonwealth in 1959–60 as 3,125, of whom 687 were in pure science, 1,203 in technology, 942 in medicine, 109 in dentistry, 129 in agriculture and forestry, and 55 in veterinary science. For the Federation of Rhodesia and Nyasaland the corresponding figures are: 19, 14, 33, 1, 8 and 11, giving a total of 86; and for the High Commission Territories the total was 6. In addition to 4,961 students from member countries of the Commonwealth enrolled in technical colleges in the United Kingdom in 1959–60, many of the approximately 2,000 students from these countries studying in private colleges and of the 830 students in teacher-training colleges would have included science among their subjects of study.

Government Grants to University and other Students

In answering a question regarding grants to students in the House of Commons on December 1, the Minister of Education, Sir David Eccles, said that the Government has decided on the general lines of the revised scale of parental contributions. Details of the scale, which will come into force in October 1961, will be published shortly, after he has consulted the local authority associations. In addition to university students, the new scale will apply to students taking comparable courses in further education institutions and to teachers in training. No contribution would be required below £700—net scale income—and in general there would be a substantial reduction in the parental contribution. The income tax child allowance would be continued and the cost of the proposed relaxation would amount to about £10 million in a full year. The relaxation is to be without prejudice to full abolition of the means test if on examination this proved to be the right course. It is intended that all local education authorities should apply the scale uniformly, and the application of the decision to Scotland is still under discussion.

Training Nuclear Engineers and Reactor Physicists

In written answers to questions in the House of Commons on November 24, the Parliamentary Secretary to the Ministry of Education, Mr. K. Thompson, as representing the Minister for Science, said that the University of Birmingham, the Imperial College of Science and Technology, Queen Mary College, London, the Universities of Manchester and Liverpool jointly, the University of Southampton, and the Scottish universities, jointly with the Royal College of Science and Technology, Glasgow, had applied for financial grants to cover the whole cost of building a low-power nuclear reactor, to provide better facilities for training nuclear engineers and reactor physicists. Sir Edward Boyle said that the Universities of Birmingham, Durham, London, Manchester and Southampton already offered facilities for training nuclear engineers and reactor physicists, and during the period 1956–60 an average of 90 students took postgraduate courses, and about 100 students chose nuclear engineering or reactor physics as an option in their final undergraduate year.

Report of the Faculty of Fisheries, Prefectural University of Mie, 1958–59

The University of Mie publishes both a *Journal* and a report for the Faculty of Fisheries and both seem to cover similar ground. In the reports (published annually since 1951) a good balance is maintained between economic and non-economic subjects. Those of a practical application to fisheries are written in Japanese, usually with summaries in English, while the non-economic articles are, as a rule, in English. The periodical is well produced and has the support of leading Japanese scientists. In the reports for October 1958 and November 1959, which have recently become available, there are three

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papers by S. M. Shiino on Japanese copepod parasites of fish, and one on bopyrid parasites of Crustacea (3, Nos. 1 and 2. Otanimachi, Tsu, Mie Prefecture: Prefectural University of Mie). He has written very extensively in this journal and elsewhere on these two subjects and has added enormously to the Japanese fauna. T. Ito and T. Iwai have nine papers (with English résumés) on the 'Mizukawari' in eel-culture ponds. This is the study of the grazing effects of brackish-water rotifers, on the phyto- and zoo-plankton of the fish ponds, and the physical and chemical changes brought about during this season. There are also four papers by J. Horiguchi (with English résumés) on biochemical work on the shell-fish *Pteria* (*Pinctada*) *martensii* (Dunker) and *Hyriopsis schlegelii* (v. Martens). Other articles deal with algae; the fishing capacity of different nets for small trawlers operating on the Ise Bay grounds; studies on fish-meat jellies; and some ecological studies on fish.

Cryogenics

CRYOGENICS technology is no longer confined to the large-scale liquefaction of gases, nor is low-temperature research conducted solely in university laboratories. The increasing use since the Second World War of cryogenic propellants, of liquid hydrogen for deuterium separation or bubble chambers and of liquid helium for superconductive computer elements and other electronic devices, illustrates the recent intensified and varied application of cryogenic methods. A warm welcome will therefore be given to the new quarterly *Cryogenics*, since it is the first international journal to be devoted solely to all aspects of applied or basic low-temperature research, engineering and development (1, No. 1; September 1960. Pp. 64. London and New York: Heywood and Co., Ltd., 1960. Subscription rates: £5 per annum (4 issues); 15 dollars; 90 NF.). The three joint editors, Dr. K. Mendelssohn (Great Britain), Dr. R. B. Scott (United States) and Dr. L. Weil (France), are supported by eleven advisory editors, who are all well known for their high reputations as active low-temperature research workers. The contents of the first number of *Cryogenics* consist of a review article by Dr. N. Kurti on the subject of cooling by adiabatic demagnetization of nuclear spins; nine original contributions with abstracts in English, French, German and Russian; two letters to the editors and two book reviews; and a bibliography of cryogenic literature covering the period January–May 1960. A complete bibliography up to date of all papers on low-temperature research, which has been made available to the editors by Arthur D. Little, Inc., is to be published in a special supplementary issue of *Cryogenics*, and two review articles scheduled for future issues are, "New Methods of Producing Cold", by H. O. McMahon, and "Irradiation at Low Temperatures", by L. Weil.

Use of Natural Gas in Britain

MR. P. G. INNEL CLEMENT, public relations officer to the National Coal Board (West Midlands Division), has written directing attention in amplification of the facts given in the article entitled "A British Source of Natural Gas" in *Nature* of October 29, p. 373, to what is being done to tap the natural gas resources of British coal mines. The extraction of coal causes fractures in the seams and in the surrounding strata, through which the trapped firedamp escapes into the workings. The traditional way of dealing with it has been to dilute it to safe proportions in the underground ventilating current, but in some coal seams the emission of methane is so high that there is difficulty in diluting it to safe proportions. Techniques for draining methane in such circumstances as these have been developed in the past ten years. A technique now in increasing use involves drilling holes of narrow diameter, often 100 yd. long, through the strata at an angle of about 55° from the horizontal as the coal working face advances. The holes are fitted with equipment for measuring the flow and pressure of the gas, and for taking samples. The gas is extracted by exhauster pumps, and piped to the surface or to some point underground where the ventilation is sufficient to disperse it safely. In an increasing number of collieries, methane drawn from the seams is being pumped to the surface and put to practical use. Gas obtained in this way is being used at the rate of 2,700 million cu. ft. a year, most of which is being piped to the works of Divisional Gas Boards. In the North Staffordshire area of the West Midlands Division, four collieries are contributing about 500 million cu. ft. a year to the national total, and in the past month a Shropshire colliery has started to supply methane to a gas works. The effects of methane drainage are twofold: it improves working conditions underground, particularly from the safety point of view; and on an increasing scale it is putting a natural product to a practical use.

Safety Propaganda in Industry

POSTERS are widely used in the interests of accident prevention but little reliable information exists as to their efficacy. A recent report from the Human Factors Section of the Operational Research Department, British Iron and Steel Federation, published in *Occupational Psychology* (34, No. 3; 1960), suggests that appropriately chosen posters may appreciably reduce certain kinds of industrial hazard. In an experiment with specially designed posters carried out in six steel works, Dr. S. Laner and Mr. R. G. Sell have been able to show that the percentage of operations conforming with safety requirements (hooking of chain slings on to crane hooks) averaged over a six-week period after display of the posters rose very appreciably, in some cases by more than 20 per cent. No comparable improvement was noted in a similar steel works in which no posters were displayed. Interestingly, the slingers often found it difficult to recall what the posters were and many doubted their efficacy. It is suggested that the effectiveness of the posters may have derived from their relevance to a specific working situation rather than to safety in general. This point should be borne in mind by all concerned with the design of safety propaganda.

Shortage of Graduate Biochemists

EVIDENCE of a shortage of trained graduate biochemists in the United Kingdom emerged during the recent Biochemical Society colloquium on "The Organization and Financing of Research in Biochemistry and Allied Sciences in Great Britain" (see *Nature*, 188, 194; 1960). With the object of defining more closely the extent and the nature of this shortage, the views of those who employ biochemists are being sought. Information should be sent to Dr. K. S. Dodgson, Department of Biochemistry, University College, Newport Road, Cardiff.

Diseases of Wild Animals

THE part that apparently healthy wild animals play as the carriers of the causal agents of serious diseases in domestic animals and man has increasingly occupied the attention of workers in many parts of the world for many years. The effect of disease on populations of wild animals has not been so closely studied; but its importance is well known to many ecologists and others. In a mimeographed paper recently issued by the Food and Agriculture Organization (McDiarmid, A., "Diseases of Free-living Wild Animals". Pp. 91. Animal Health Branch Monograph No. 1. F.A.O., Rome, 1960), Dr. McDiarmid summarizes the information available about the diseases of wild animals and lists the recent literature up to 1955. The diseases are classified as those due to bacteria, fungi, viruses, protozoa, rickettsiæ, and neoplasms and tumours, and the author gives a brief review of what is known about each together with references to the literature. The paper is issued as a Food and Agriculture Organization "Working Paper" for circulation to veterinarians and others in the Organization interested in the subject. It is to be hoped that it may be made available also to the many workers outside the Organization who will find it an extremely useful work of reference.

Pre-History: Implements and Rock-Carvings

THE July issue of *Man* contains several articles of general interest. The mystery of A. C. Carlyle and his collections from caves in the Morhana Pahar district of India has been elucidated by G. de G. Sieveking of the British Museum. It seems that many of the finds were bought by Dr. Sturge and are now in that celebrated collection at Bloomsbury. A. D. Lacaille illustrates a number of very large British Acheulean coups de poing, and a puzzling rock-carving from the Val Camonica is discussed by Dr. Anati of Paris. The site is near where the great glacial valley debouches on to the north Italian plain, and many rock-carvings there have been known for a long time. They include animals and humans treated in a conventional manner somewhat recalling the Copper Age paintings of Las Figuras in south-west Spain. The little group in question seems to indicate either a phallic or a ritual scene. The author suggests a date for this art group somewhere towards the start of the first millenium B.C. Is not this somewhat too early? An interesting illustrated article on the Hainault scythe in England by G. E. Fussell and another on the ethnic origins of Zande office-holders are also included.

Royal Meteorological Society: Scientific Activities Fund

GRANTS from this Fund are intended to be used to assist attendance at meteorological conferences, and priority will be given to members of the Royal Meteorological Society. Applications from younger meteorologists will receive special consideration in order to give them the opportunity to present their work. Assistance may also be given in furtherance of meteorological research, or in support of a personal meteorological activity. Grants may also be made to European meteorologists who have been invited by the Society to visit Britain to give lectures or courses of lectures, or British meteorologists who have been invited to visit Europe for the same purpose. Applications, which should include details of estimated expenditure, should be forwarded to the Assistant Secretary (Scientific Activities Fund Committee), Royal Meteorological Society, 49 Cromwell Road, London, S.W.7, not later than December 15, 1960.

Announcements

THE Charles Léopold Mayer Prize for 1960 of the Société de Chimie Biologique has been divided between Prof. R. Monier, Maitre de Conférences de Chimie Biologique at the Faculté des Sciences de Marseille, and Dr. M. Beljanski, maitre de recherches at the Centre National de la Recherche Scientifique, for their work on nucleic acids and nucleoproteins. The Prize, which is awarded annually, has a value of 5.000 NF.

THE Palæontological Association is holding a discussion meeting on "Palæo-ecology" at the Department of Geology, the University of Glasgow, during December 16–17. Further information can be obtained from the Secretary to the Association, Dr. Gwyn Thomas, Department of Geology, Imperial College of Science and Technology, Prince Consort Road, London, S.W.7.

COMMENCING on January 14, 1961, Norwood Technical College is holding a course of twelve morning lectures and appropriate practical work as "An Introduction to Micro- and Semi-microchemical Methods". This course is particularly suitable for teachers, industrial and research chemists and is designed to survey the principal branches of chemistry in which small-scale methods have been successfully applied. Further information can be obtained from the head of the Chemistry Department, M. A. Fill, Norwood Technical College, Knights' Hill, West Norwood, S.E.27.

THE Bradford Chemical Society, the Plastics Institute (Yorkshire Section) and the Department of Chemical Technology of the Bradford Institute of Technology, in conjunction with the Yorkshire Council for Further Education, are jointly holding a symposium on "New Developments in Plastics" at the Bradford Institute of Technology on February 11, 1961. Further information can be obtained from the honorary secretary of the Bradford Chemical Society, R. P. Sheldon, Bradford Institute of Technology, Great Horton Road, Bradford 7.

THE University of Cambridge Physical Chemistry Summer School will be held again in 1961, during August 12–19, the general topic being "Fast Reactions". Further information can be obtained from Prof. R. G. W. Norrish, Department of Physical Chemistry, University of Cambridge.

THE first international conference on "Protozoology", organized under the auspices of the Czechoslovak Academy of Sciences, will be held jointly with the thirteenth meeting of the Society of Protozoologists in Prague during August 22–30, 1961. Further information can be obtained from Dr. Norman D. Levine, College of Veterinary Medicine, University of Illinois, Urbana, Illinois (not later than March 1), or Prof. Otto Jirovec, Charles University, Viniena 7, Prague 11 (not later than April 1).

ERRATUM: In the communication entitled "Prolonged Survival of Human Sperm in chemically defined Media at Room Temperatures", in *Nature* of November 26, p. 760, it is stated that the *p*H of the medium was initailly 7·1; this should read 7·4.

THE BRITISH ASTRONOMICAL ASSOCIATION

WORK OF THE RADIO-ELECTRONICS SECTION

IN January 1957 the British Astronomical Association formed a Radio-Electronics Section. Such a move was quite consistent with the Association's interest in all branches of astronomy. Since the fortunes of the amateur astronomer have always been of interest to the professional scientist because of the successes that amateurs have had in astronomical research, it would seem that the time is ripe for a statement on the work of this new Section and its contribution to amateur endeavours.

The great stimulus to the Section's activities was the launching of the first Soviet Earth satellite. Its members made both visual and radio observations of *Sputnik* 1 and *Sputnik* 2 which have been reported elsewhere[1]. Since then, in co-operation with the Radio Research Station (Department of Scientific and Industrial Research), an independent service has fed sixty visual observers with predictions in order to stimulate observations. Visual observations of Earth satellites are most necessary if a satisfactory prediction service is to be maintained. They are also an example of the usefulness of the amateur observer. Of recent months it has become necessary to constitute a subsection to deal with this new but major field of amateur activity. This revised policy has also caused a complete revision of the memoir on Earth satellites[2] which is to be published at the end of the year. In addition to the history of the radio observations, it will now include full details of visual observing methods, a summary of prediction methods derived from G. E. Taylor's work[3] and a generalization of prediction techniques (as yet unpublished) suitable for application to all future satellites, due to K. Fea.

Earth satellites were not intended to be the main activity of the Section. They have, however, taken up a large part of the time devoted to amateur radio astronomical activities during the past three years, and account perhaps for the not very spectacular developments in the field of amateur radio astronomy.

Nevertheless, sufficient data have been collected by members of the Section to merit a recommendation for the publication of a memoir devoted to the design, construction and operation of radio telescopes. An interesting contribution by two of the contributors contains an approach to the design of large radio telescopes; it is a combination of existing papers by Lovell[4], Husband[5] and Christiansen[6], but it is thought to be a more comprehensive introduction to the mechanical, electrical and radio astronomical research problems involved[7].

However, at the real level of amateur research, the corner-reflector type of aerial as typically described by Carr[8] for use at low frequencies has been modified, and, although of smaller dimensions, is steerable in altitude. Such aerials can be built at relatively low costs and are suitable for use as the aerial sections of low-frequency interferometers. F. W. Hyde has successfully operated a phase-switching interferometer using these aerials at 27 Mc./s. with a space of 20 wave-lengths. Other similar instruments have been operated at 50 and 36 Mc./s. Experiments are now being conducted with corner V reflectors and also large arrays of dipoles in the region of 19 Mc./s.

These experiments were initiated from a suggestion by Dr. A. Hewish, of Cambridge. He suggested that simple instruments such as these could be used to extend his own work in investigating the solar corona into the low-frequency region of the electromagnetic spectrum[9]. With the narrow spacings of the interferometer aerials, a longer period of observation is necessary to provide satisfactory results for separating the radiations of the Crab Nebula from those of the Sun, the two components being well integrated on the records. A year's continuous observations have been made at 27 Mc./s., and the operation of the instruments is now reasonably well understood. The preliminary results of these investigations suggest that useful work can be done in this low-frequency part of the electromagnetic spectrum, and the rough analysis of the observations made during the 1959 and 1960 occultations suggest a confirmation of Hewish's theory.

However, by far the most important factor has been the realization that with a network of similar interferometers operating at widely scattered points throughout the British Isles and operating on the same frequency it should be possible to assess the accuracy with which observations can be made in the low-frequency region. With each station providing similar observations, evaluations of the influence of the ionosphere and the true value of conducting research at the lower frequencies where the ionosphere plays such an important part in reception can be made. Two stations, at Beckford (Gloucestershire) and Clacton-on-Sea, are operating simultaneously on 27 Mc./s., and it is planned to build instruments operating in the region of 19 Mc./s. at both these sites.

In addition to the observations of the solar corona and the qualitative analysis of the effects of the ionosphere, it is intended to use these instruments in attempted observations of the non-thermal radiations from Jupiter. These observations will extend the information available on the continuity of storms through consecutive rotations of the planet, and since the same group of stations will be available for such observations further light should be thrown on the terrestrial ionospheric features of the emissions associated with this planet, which have been discussed by Gardner and Shain[10], and more recently in *Nature* by A. G. Smith *et al.*[11].

Apart from encouraging the beginner to construct simple radiometers for observing deflexions in the output as the aerial is pointed to Cygnus, Cassiopeia and the Sun, the Section has undertaken an unusual education programme. A portable radio interferometer operating at 200 Mc./s. (ref. 12) was designed for erection in school playgrounds. Lectures have been given to groups of schools, and several younger

members of Advanced Level (General Certificate of Education) standard have studied the history and techniques. The most interesting project has been in connexion with a project for sixth-formers. Two sixth-formers of the Salesian College, Battersea, with no previous knowledge of radio astronomy, were set a three-part project. The first part dealt with fundamentals, the second part with a simple practical project and the third was a dissertation on the two parts of the project followed by an oral examination. The boys were given only the minimum of information, and at the time of writing the first part of the work had been completed. The indications are that their work will throw considerable light on the value of project work with oral examinations being included among the methods of university selection.

Although the Radio-Electronics Section cannot possibly compete with the professional radio astronomers, it is clear that there are a number of small but valuable research projects which they can perform. The time taken for the completion of the project is admittedly long.

The other asset of the educational policy of the Section is that it has enabled a number of people to come into contact with the practice of the science and others to gain their first contact with this new science. These are important factors in a science where professionals are few and far between.

The financial support given by the Carnegie Trust, the Council of the British Astronomical Association and the encouragement of the professional radio astronomers, and of the Department of Telecommunication, Norwood Technical College, seem to justify the aims which the Section has set itself. These are aims which undertake a new responsibility for amateur science; the provision of a new type of link between the scientist and the public: the provision of a liberalization for science in its increasing specialization—a liberalization that reminds people that in all the complexity of modern technological thinking it is still possible for an outsider in his own time and at his own inclination to come to grips with the mysteries of the universe.

J. HEYWOOD

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THE TWENTY-FIRST INTERNATIONAL GEOLOGICAL CONGRESS

THE twenty-first International Geological Congress was held this year in the Nordic countries, with excursions in Denmark, Finland, Iceland, Norway and Sweden, and with meetings in Copenhagen during August 15–25. The usual excursions were in three groups: those preceding the actual meetings in Copenhagen; one-day excursions during the meetings; and longer excursions afterwards, some of which ended in mid-September. The number of geologists participating was about 2,500, coming from about a hundred various countries.

Although the possibility had been touched on in 1952, in Algiers, it was not until the 1956 meeting in Mexico that the invitation to geologists of the world to hold the Congress in the Scandinavian countries in 1960 was brought forward. After the invitation had been accepted, an organizing committee of the Congress was appointed by the geologists of the five countries. Its composition was as follows: Denmark, Arne Noe-Nygaard, Theodor Sorgenfrei and Christian Poulsen; Finland, A. Laitakari, P. Haapala, V. Marmo and H. Ignatius; Iceland, S. Thorarinsson, T. Tryggvason and G. Kjartansson; Norway, O. Holtedahl, T. F. W. Barth and J. A. Dons; Sweden, K. A. Lindbergson, N. H. Magnusson, F. E. Wickmann and E. Fromm. During the preparation period the organizing committee met from time to time in the different countries; at shorter intervals executive secretaries from each country came together (Dons, Fromm, Ignatius and Sorgenfrei). It does not minimize the efforts of the members of the organizing committee as a whole that the splendid work carried out by Dr. Sorgenfrei, on whose shoulders the heaviest burdens fell, is specifically underlined.

Of the excursions primarily offered, a few had to be cancelled for various reasons. The total number of guide booklets worked out was 42, amounting to more than 1,500 pages. As is usually the case, a considerable number of pre-sessional excursions were repeated as post-sessional tours. Of the guide booklets, Denmark was responsible for 6, Finland 6, Iceland 1, Norway 17 and Sweden 12. The seventy excursions covered an area between Iceland in the west and eastern Finland in the east, and between southern Denmark in the south and Spitsbergen in the north. The subjects covered by the various tours extended from recent volcanism and hot-spring activity in Iceland to Caledonian orogeny in Norway, from the Pre-Cambrian of Sweden and Finland to the Cretaceous and Tertiary sediments in Denmark.

The formal meeting of the Congress in Copenhagen was held under the patronage of H.M. King Frederik of Denmark. The first meeting of the Council was held on August 15. The opening of the General Assembly took place on August 16 in KB-hallen. Señor Garcia Rojas, president of the Twentieth International Geological Congress in Mexico first spoke; then the assembly was addressed by the Danish Prime Minister, Mr. Viggo Kampmann, and finally the newly elected president, Prof. Arne Noe-Nygaard, took the chair.

The following subjects had been selected for presentation and discussion, each subject corresponding to a section of the Congress: (1) geochemical cycles; (2) geological results of applied geochemistry and geophysics; (3) Pre-Quaternary absolute age determination; (4) chronology and climatology of the Quaternary; (5) the Cretaceous–Tertiary boun-

dary; (6) Pre-Quaternary micropalæontology; (7) Ordovician and Silurian stratigraphy and correlations; (8) Late Pre-Cambrian and Cambrian stratigraphy; (9) Pre-Cambrian stratigraphy and correlations; (10) submarine geology; (11) regional and structural problems in oil geology; (12) regional palæogeography; (13) petrographic provinces, igneous and metamorphic rocks; (14) the granite–gneiss problem; (15) genetic problems of uranium and thorium deposits; (16) genetic problems of ores; (17) minerals and the genesis of pegmatites; (18) structure of the Earth's crust and deformation of rocks; (19) Caledonian orogeny; (20) applied geology; (21) other subjects.

As a new feature in the arrangement of the meeting, it may be mentioned that all papers selected for presentation were printed prior to the sectional meetings and delivered to the participants on their arrival—more than 4,000 pages.

During the meeting, the following affiliated associations and societies held meetings: International Palæontological Union, Association of Sedimentary Geologists, International Association of Hydrogeologists, International Mineralogical Association, Association des Services Géologiques Africains, Society of Economic Geologists, International Commission for the Study of Clays. A joint symposium was arranged by the Geochemical Society and the Geochemical Commission of the International Union of Pure and Applied Chemistry. The Karpato-Balkanic Association also held meetings.

The following commissions of the International Geological Congress held meetings and reported to the General Assembly on the business meeting of the Congress on August 23: (*a*) International Commission on Stratigraphy, with several sub-commissions (Prof. R. C. Moore resigned, and a nominating committee for electing new officers was appointed with Dr. C. J. Stubblefield as chairman); the Commission to be continued. (*b*) Commission of the Geological Map of Europe (Prof. A. Benz and v. Gaertner); the Commission to be continued. (*c*) Commission of the Geological Map of the World, with two sub-commissions (Prof. M. F. Blondel); the Commission to be continued. (*d*) Commission on the Gondwana System (Dr. S. H. Haughton); it was suggested that this Commission be made a sub-commission to the Commission of Stratigraphy (*a*) with four members, one from each of the following regions: South Africa, South America, Australia and India. (*e*) Commission on Meteorites (report by the secretary, Dr. M. H. Hey); Commission to be continued; Prof. E. L. Krinow was elected as the new president. (*f*) Commission for the Formation of an International Geological Abstracting Service (Dr. H. M. E. Schurmann); first number of a geological abstracting journal will be issued in the beginning of 1961 by Pergamon Press. (*g*) Commission de la Croûte Terrestre (Prof. C. E. Wegmann and Prof. P. Fourmarier); it was proposed that the existing Commission be discontinued and that its functions concerning the establishment of a lexicon of tectonic terms handed over to the sub-commission on the tectonic map of the world (under *c* above) and that a new organization be formed under the title, "Commission de Coordination des Recherches Géologiques et Géophysiques", with Prof. J. Goguel as president. (*h*) Commission for the Spendiarov Prize; members elected and functioning during the twenty-first session were the following: D. V. Nalivkin, J. M. Harrison, V. Marmo, M. Roubault and Th. Sorgenfrei.

During the meetings an exhibition of geological maps, instruments and books was arranged in an exhibition building near the main site of the Congress. The Mineralogical and Geological Museum of the University of Copenhagen, also situated near the main site, was open daily during the period; more than 3,000 visitors passed the main door during the ten days.

At meetings of the Council of the Congress, traditional questions were treated in a traditional manner. Special treatment was given to the question of the formation of a Geological Union, which was prepared by the Bureau of the Congress before being presented to the Council for decision. The Council decided at its business meeting on August 23 to appoint an organizing committee for the formation of an International Geological Union. It was further decided that the organizing committee should prepare draft statutes of the Union in order to get it established in 1961. This committee consists of the following members: N. Belyaevsky (U.S.S.R.), W. Smulikowski (Poland), B. C. Roy (India), J. M. Harrison (Canada), T. B. Nolan (U.S.A.), L. Hawkes (United Kingdom), R. Laffitte (France), E. Clar (Austria), H. M. E. Schurmann (Netherlands), K. A. Lindbergson (Sweden), V. Marmo (Finland), A. Noe-Nygaard (Denmark), J. A. Dons (Norway) and T. Sorgenfrei (Denmark).

At the closing meeting of the General Assembly on August 25, Dr. Sigurdur Thorarinsson, of Reykjavik, was awarded the Spendiarov Prize for his outstanding volcanological and tephrachronological studies in Iceland. Then representatives of former host countries greeted the Congress, and Dr. Roy, from India, looked forward to seeing members in 1964, at the twenty-second Congress, in his country.

ARNE NOE-NYGAARD

POLLINATION BY INSECTS

"POLLINATION" was the subject of a symposium held during August 12–14 at Copenhagen prior to the eleventh International Congress of Entomology in Vienna. The symposium was presided over by Prof. Eric Åkerberg of the Swedish Seed Association, and the final sessions took place at the Association's plant breeding station at Svalof.

The importance of bees as insect pollinators has long been recognized in the production of fruit and seeds of insect-pollinated plant species, and it was therefore natural that the majority of papers were concerned with bees. In the seed production of red clover, it was clear that humble bees were useful pollinators in every country, but the value of honey bees varied from country to country. The special difficulties of obtaining satisfactory seed yields from tetraploid red clover, however, appeared to be due as much to abnormal pollen as to the lack of suitable pollinators.

Several speakers reported work on the habits of humble bees, and various attempts to increase the population of the humble bee were described. Danish

workers reported that certain species of humble bee had now been kept in domestication for several years, and this had enabled a much more detailed investigation of their breeding habits than had formerly been possible.

The use of 'scent direction' to improve the value of honey bees as pollinators was discussed by several contributors, but results had been somewhat varied, and it was evident that further work on this important subject is needed. Attention was directed to the varying composition of nectar between the different plant species, and the possibility that this might influence pollination was discussed. The pollination of lucerne, the subject of another session, was covered by papers describing work on this subject in North America.

At the closing session of the symposium, the following conclusions were agreed.

(1) An annual census of bumble bees would be desirable in order to identify trends in populations that could be associated with changing agricultural practices.

(2) Solution of the seed production problem in tetraploid red clover will require continued effort by plant breeders, pollination specialists and biologists.

(3) Greater effort should be given to obtaining a better understanding of the basic relationship between pollinators and flower. Identification of morphological or physiological links in those species of bees having a restricted host-range would be worth while.

(4) Pollination should be considered as one of a number of factors, and consideration should be given to them all when studying seed production. Increased effort should be given to domestication of bumble-bees. However, much more basic information needs to be developed before the full potential of this endeavour can be realized.

(5) Exchange of pollinators between countries should be encouraged. An effort should be made to provide the proper pollinator for a given crop. This can be done by growing the crop where pollination occurs naturally, or by providing the pollinator where it does not occur naturally. A survey of all known pollinating insects for clover and alfalfa is required.

(6) Honey bees should be exploited to the maximum extent possible. Information concerning this pollinator is greater than for any of the others, and should be utilized.

(7) Scent training should be studied further; but identification of the volatile products in flowers would seem to be necessary in order to advance this phase of the work.

These recommendations, with the papers read at the symposium, are to be published in due course. The secretary of the symposium was Dr. Ole Hammer, assisted by Dr. Tom Mittler, Statens Biavlsforsøg, Strødam, Hillerød, Denmark.

R. P. Hawkins
M. S. Percival

GENERATION AND APPLICATION OF ELECTROSTATIC POWER

An international colloquium, held under the auspices of the Centre National de la Recherche Scientifique, was held at Grenoble during September 24–October 1. The subjects discussed covered the generation of electrical power by electrostatic means and the applications of these machines. It is believed to have been the first international conference devoted entirely to the science of electrostatics. Due to the presence of Prof. N. J. Felici, who is the holder of the chair of electrostatics at the University of Grenoble, this was a natural meeting place, and more than 120 engineers and physicists gathered there.

Appropriately, after a description of the early days of electrostatic machines in Grenoble, given by Prof. L. Néel, the lectures were inaugurated by Prof. Felici's discussion of the types of electrostatic generator and his hopes for the next 'generation' of electrostatic machines. This, in conjunction with a talk by Prof. J. G. Trump of the Massachusetts Institute of Technology, indicated in broad outline the scope of present possibilities and the problems of the future. There were two types of electrostatic generator in current use: first, the Van de Graaff belt-type machine, and secondly, the Felici insulating transporter cylindrical machine. Both have their advantages and disadvantages. Briefly, for high voltages and very low currents the Van de Graaff is better, and for low voltages (below one million volts) and higher currents (up to 50 m.amp.) the Felici machines are better. For long-term continuous running, the cylinder machine is undoubtedly more reliable, but in its present state of development it cannot provide the very high voltages or current that may be required. Prof. Trump discussed also a further type of electrostatic generator, the disk machine. This is by no means a new development; and on show at the colloquium was a very early disk-type generator built in the late 1940's at Grenoble. However, it seems to be generally agreed that this type of design has the greatest development possibilities, particularly for space travel, where the problem of insulation is much reduced.

Several papers were presented which discussed the application of this type of electrostatic generator for ion propulsion. Considerable research is being carried out both in France and the United States on electrostatic machines for this purpose. The design of a generator delivering 1,250 kW. at 200 kV. is being investigated at the High Voltage Engineering Corporation in Massachusetts. Parallel work is proceeding in France.

The future development of the cylinder machine is being investigated to increase the currents available, and other dielectrics, including various liquids, are being studied. Questioning elicited visualized requirements in the region from 100 kV. at 100 m.amp. to 1 MeV. at 1 amp., but no concrete suggestions as to how this might be achieved were agreed. The emphasis on ion engines for space travel was supplemented by a talk on electrohydrodynamic energy conversion by a representative of the U.S. Air Force.

Engineers who have been involved in the practical problems of designing the Felici generators and producing a standard range of models for industry gave a fascinating insight into the complexities of electrostatics as opposed to the comparative simplicity

of electromagnetic machines, despite the duality which exists between them. There is no doubt that the shortage of technology on this subject is retarding the advance of the electrostatic machines. Nevertheless, an impressive array of standard machines were described, and on a subsequent visit to the factory of Société Anonyme de Machines Électrostatiques in Grenoble the members of the colloquium were able to see the ideas of Prof. Felici in concrete form. From the smallest machines for electrostatic deposition of paint to the large 600-kV. and 1-MeV. generators for accelerators and other nuclear applications, one cannot help but be impressed by the progress of this technique. When it is realized that the continuous operation of these generators for thousands of hours with negligible maintenance is regarded as commonplace, an appreciation of the status of the technique is possible.

Of particular interest on the nuclear side were the neutron generators capable of delivering fluxes of neutrons up to 10^{11} neutrons per sec. Continuous development aimed at greater fluxes with smaller machines is being carried out.

To sum up, the position of the electrostatic generators at the present time is not easy. Both the French and American experts expressed faith that the present machines are the first in a field capable of great development. Discussion gave glimpses of actual development models in course of construction at the present time. Whether certain fundamental difficulties will obstruct this advance or whether new techniques will emerge remains to be seen. Whatever happens, great resources of money and labour will have to be made available.

The remainder of the lectures dealt with the applications of electrostatic machines. Two very interesting papers were read, one by Dr. W. D. Allen (Atomic Energy Research Establishment, Harwell) and the other by Mr. F. A. Julian (Atomic Weapons Research Establishment, Aldermaston). They described the remarkable achievements of the staff of the United Kingdom Atomic Energy Authority in constructing two 12-MeV. tandem accelerators which have now been in operation for the past year. The many problems which they encountered and overcame were discussed and a résumé of the experimental work carried out, both in the design of the machines and their subsequent usage, were given.

In the more commercial field of precipitation and mineral separation, the use of electrostatic generators has, as yet, had little application apart from the deposition of paint. Demonstrations of the paint precipitation plant show the fascinating possibilities of electrostatic machines in industry. The 100-kV. unit is very small, approximately 24 in. long, 9 in. wide and 9 in. high, and completely safe. The operator may place his finger on the high-voltage terminal of the spray gun and feel very little effect. The generator is very light and easily portable. Being sealed in a high-pressure cylinder, it is impervious to all dirt and damp.

For other heavier precipitation processes, the electrostatic machine, so far, does not yet deliver sufficient current. Considerable research is going on in the United States in mineral separation, and, in Europe, on insecticidal spraying in agriculture.

Future applications in the nuclear field would appear to lie with neutron sources of higher fluxes than at present available. If fluxes of the order of 10^{13}–10^{14} neutrons per sec. could be produced economically, there would be a demand from those at present forced to use reactors for activation experiments. There is some argument as to what an economic figure might be, but there is a real hope that for an accelerator working at, say, 1 MeV., 4 m.amp. of ions in the beam of a beryllium target could produce a flux of 10^{13} neutrons per sec. From preliminary inspection it was severally agreed that the price of such a machine might be very attractive *vis-à-vis* a small reactor. A 1-MeV. accelerator and a high-current ion-source of this type was shown to the members of the colloquium.

Both Prof. Trump and Prof. Felici touched on the possibility of power generation by electrostatic means. It may seem inconceivable that the electromagnetic power generators could be superseded by electrostatic methods for the generation of electric power for the grid system. However, a strong plea by Prof. Felici for research funds to be made available throughout the world for work in this direction was made. Prof. Felici cited the considerable advances achieved so far in the U.S.S.R., and the United States. Perhaps the domination of the present technology has blinded engineers to the possibilities in this other field.

BRITISH BOOKS AND PERIODICALS FOR USE OVERSEAS

IN a written answer to questions in the House of Commons on November 7 about Government Information Services, the Chancellor of the Duchy of Lancaster, Dr. C. Hill, made a long statement about the low-priced book scheme. The first group of 23 text-books on scientific, engineering and other technological subjects, he said, is now being produced, and the books should be available during the forthcoming buying season to students and others in India at 9*s*., 12*s*. or 15*s*. a volume, depending on size, diagrams, illustrations, etc. It was expected to discuss shortly with the Pakistan authorities the possibility of operating a similar scheme for that country.

Dr. Hill gave a list of the titles which had been approved by the Advisory Committee, following consultation with the university authorities in India. The list involved more than 100,000 volumes and more copies would be produced as necessary. A further group of university text-books on these and other subjects would follow. The Advisory Committee has also recommended further categories of books, similarly aimed at helping to meet the needs of readers in developing countries in Asia and Africa. One group of titles included would help people in these countries who wished to develop their knowledge of English, or to extend their practical skills, and these volumes would be available in substantially larger numbers and at much lower prices than the university text-books. The Advisory Committee recognizes that some of its other recommendations involve books which need bringing up to date or

other adaptation and that this work requires detailed and expert study. The Publishers' Association has now recommended to its membership the establishment of a consortium of publishers familiar with the export fields concerned or otherwise interested in the low-priced book scheme, which would pool the experience and resources of the trade in Britain and, in co-operation with local trade interests overseas, might further assist the Government's programme.

Dr. Hill also stated that an encouraging increase in the flow of British publications into Yugoslavia has occurred since the agreement with the Yugoslav Government was announced on April 14, and that the text of an agreement with the Israeli Government, providing for imports up to £400,000 a year of British books, periodicals, newspapers and certain kinds of gramophone records, was laid before the House on October 25. The Government of Indonesia is considering British proposals for an agreement to facilitate the import of British publications, and steps have been taken to overcome the difficulty arising from the system of import control used in Chile, which has led to an unsatisfied demand there for British books. The British Council has undertaken a considerable extension of its library services, and of the half-million books distributed by the Council in the past 18 months to its own libraries or other institutions all over the world, by far the greatest number have gone to Africa and Asia, especially to India, Pakistan and Ceylon. The range of learned periodicals covered by these libraries has also been greatly extended and many more presentations have been made to institutions such as medical schools.

In India and Pakistan, the Council's multiple holdings of widely used text-books has been very greatly increased, and in the past four months some 45 Indian universities and colleges have begun to use this scheme; the Council's services in these countries have also been improved by recruitment of a number of professional librarians to advise locally on the choice and direction of material and to organize the reference use of the libraries. Important presentations of books and periodicals have been made to colleges and other institutions in Nigeria, Ceylon, Burma, Viet Nam, Malaya and Indonesia.

THE POST OFFICE RESEARCH STATION

SOME of the scientific and engineering work of the Post Office Research Station at Dollis Hill, London, was shown during its open days, September 22–23. This Research Station serves the telephone and radio systems of the British Post Office, and also works on the mechanization of the postal service.

The Post Office (in collaboration with the National Physical Laboratory and the Royal Observatory) broadcasts signals of standard time-interval and frequency, having precisions of the order of $\pm$ 2 parts in 10^{10}. This has required the production of quartz crystals of great precision and stability, and the development of techniques for mounting them and maintaining them in oscillation at constant temperature. Further improvement in these time and frequency standards may require the use of cæsium-beam resonators, one of which was shown working.

Transmission along wave-guides at frequencies such as 35,000 Mc./s. is a possible method of long-distance communication. The intended mode of transmission is H_{01}; all others must be suppressed since they have different velocities of propagation. Suppression can be achieved either by using for the wave-guide a close-wound helix, so that its longitudinal resistance is high, or by internal coating of a solid guide with a dielectric other than air. The first of these methods is being investigated by other workers; the Post Office is studying the use of dielectric coatings.

Parametric amplifiers operate through the variation of the electrical magnitude of some component by means of a local source of power—the 'pump'. They are particularly useful at frequencies greater than about 200 Mc./s. A parametric amplifier was shown working, based on a variable-capacitance diode, and suitable for a tropospheric-scatter system working at about 900 Mc./s.; a similar amplifier, for 960 Mc./s., had been used to receive signals from the United States by way of the balloon satellite *Echo I*.

For some years the Post Office has specialized in work on metallic magnetic materials. Samples of silicon-iron were shown in which special crystalline textures had been produced by suitable rolling and heat treatment. Methods shown for work on magnetic properties included measurement of saturation flux by reversal of the specimen itself in a stationary field—a method suggested by Ewing and apparently overlooked since his time—and an apparatus displaying the variation of magnetization with direction in anisotropic material.

For many purposes the Post Office is introducing transistors into its apparatus, but, as its need for reliability is unusually strict, it is interested in the probable life of transistors and in the causes of their premature failure. One investigation of this kind has led to the detection of leakage through seals, even when the leakage-rate is of the order of 10^{-11} litre micron per second. Improvements in thermionic valves are still being pursued, however, and gains in both performance and reliability have been achieved: a valve suitable for submarine cable systems, having a conductance of 25 mA./V., yet operating at only 40–50 V. high tension, has been produced by winding both control grid and screen grid on a single former.

The chemical laboratories have produced a range of organic phosphors, intended for making code markings in postal sorting work. They are based on cyanuric-acid-formaldehyde condensation compounds, and offer a wide range of colours. They are easily handled and can be incorporated into printing inks and other such media.

The influence of high-speed computers as an aid to physical and engineering research was clearly in evidence. Although the Research Station has no computer of its own, it hires time on other computers and has its own staff who can prepare computer programmes.

A. C. LYNCH

BIFURCATION AND OTHER IRREGULARITIES OF THE IONOSPHERIC *F*2-LAYER

By DR. E. WOYK (CHVOJKOVÁ)
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IN recent years the bifurcation and other irregularities of the ionospheric *F*2-layer have been much discussed. I have made several attempts to provide a theoretical basis of the subject, and finally I derived formula (2), which expresses the diurnal variation of the critical frequency of the *F*2-layer[2]. Incidentally, the subject is of interest in astronautics; thus the usual sort of short-wave connexion would fail on account of rareness of a planetary atmosphere preventing a pronounced maximum of electron density above the surface, so that only a local minimum of electron density—arising from the process of bifurcation—can permit the circumplanetary propagation shown in ref. 3.

My theory of bifurcation is explained in a few words as follows: the excess of energy of each ionizing photon over the ionizing potential is transformed into heat. Thus, on account of the quasi-neutrality, the rarefaction of the gas at the maximum of ionization can create a small secondary minimum of electron density there which separates the *F*-layer into *F*1 and *F*2. This secondary minimum of electron density N appears paradoxically just at the maximum of electron production q (Fig. 1*a*, *b*).

It was deduced that a layer arising from a previously un-ionized gas cannot be divided into two parts with the exception of a very rare atmosphere

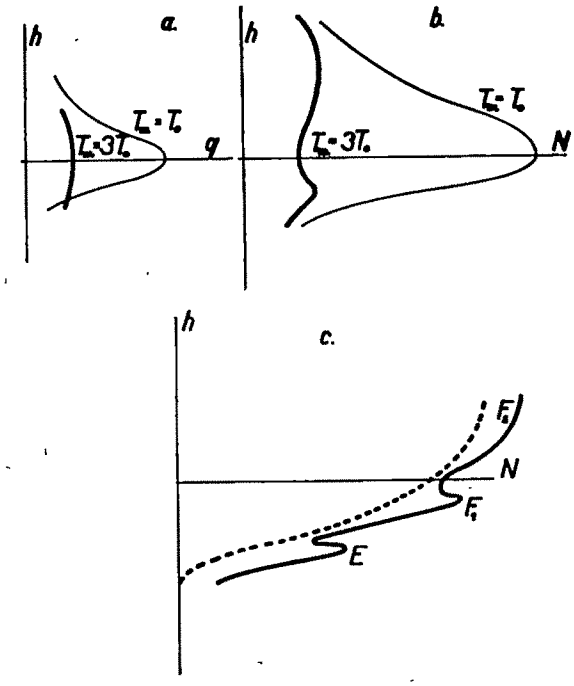

Fig. 1. Distribution with height: (*a*) the electron production q according to equation (4): (*b*) the corresponding electron density N of equation (5) allowing for no remainder of free electrons at the beginning; (*c*) allowing for a sunrise-remainder of free electrons (shown by the dotted curve)

($n \leqslant 10^{10}$ cm.$^{-3}$) and only when the temperature T_m at the maximum of ionization is at least twice as high as the temperature T_0 at the beginning of ionization. If at sunrise, however, the new ionization begins to act on a region where a considerable quantity of free electrons has remained from the previous day, it is possible that the bifurcation is produced even beyond the given limits, as shown in Fig. 1c. It appears, however, that only the *F*-layer can be separated, never the *E*-layer.

Also the strange diurnal and seasonal variation of the critical frequency f_c of the *F*-layer and its unexpected dependence on solar activity (Fig. 2) can be explained on my theory as follows[3]: the diurnal variation of f_cF2 cannot be expressed by a simple sinusoid as is the case of f_cE. It seems rather to follow a sinusoid the period of which increases linearly with time ($T = At + B$). See the auxiliary dotted curve of Fig. 2 which is expressed by:

$$\bar{f}(t) \equiv \bar{f} = c + M\left(1 - \cos\frac{2\pi t}{24a + (1-a)t}\right),$$

$$a = \frac{T_1}{24 - T_1} \qquad (1)$$

From this curve a cosinusoid was subtracted in order to take into account the rarefaction produced by ionization (Fig. 2, full curve). It was surprising to find that this cosinusoid would have to be subtracted from $\bar{f}(t)$ even after sunset, when the real course of f_cF2 had to be expressed precisely. It seems that the atmosphere, expanded during sunshine and contracting at sunset, passes over the equilibrium, oscillating about the equilibrium density with the same period as it had during daylight. Thus the resulting formula, capable of expressing any diurnal course of f_cF2, is:

$$f_cF2 = \bar{f}\left[1 - m\left(1 - \cos\frac{2\pi(t - t_1)}{\tau}\right)\right] \qquad (2)$$

The beginning of curve (2) is given by a value t_0 not differing much from that at sunrise. The time t_1 at which the oscillation starts to be subtracted need not be zero; moreover, t_1 varies with solar activity R and it is the variation of t_1 which makes it possible to express the strange variation of the f_cF2-curves with R. It is to be noted that a small increase of t_1 transforms the first curve of Fig. 2 ($R = 0$ usually characterized by a flat and late maximum) into the curve corresponding to $R = 150$ (characterized by a sharp maximum appearing just before midday). The coincidence of the theoretical curves (2) and the real ones (measured at different epochs and different points of the Earth) is further evidence for this theory of bifurcation of the *F*2-layer by photoionization. A prediction frame[4] has been constructed for satellite and telecommunication purposes, and formulæ for trajectories[5]. By the use of this frame,

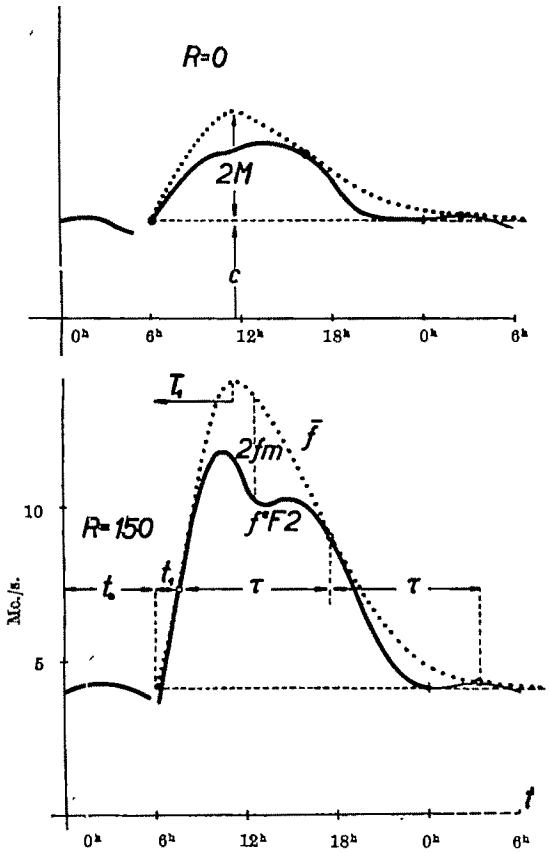

Fig. 2. Diurnal course of the critical frequency f_cF2 at middle latitudes in winter for low and high solar activity R and the explanation of symbols used in equations (1) and (2). All parameters have a fundamental physical meaning. The plotted curves are defined by $t_0 = 6{\cdot}0$ hr., $c = 3{\cdot}2 + 0{\cdot}009\,R$ (Mc./s.), $a = 0{\cdot}30$, $M = 1{\cdot}7 + 0{\cdot}022\,R$, $t_1 = +0{\cdot}1 + 0{\cdot}008\,R$, $\tau = 10{\cdot}0$ hr., $m = 0{\cdot}12$. (m depends upon latitude only; the other parameters depend also on season)

it is possible to determine easily the elements of trajectories of satellites in spite of differences in time and position. Also, on planets with a highly curved surface and a very rare atmosphere, short-wave communication would depend on whether a negligible rarefaction of electron density above the surface will allow circum-planetary propagation, analysed in ref. 3, or not.

Let us treat a relatively cold atmosphere of temperature T_0, containing only one sort of particles, on which suddenly a source of powerful radiation $h\nu$ begins to act. The mean temperature T_i of a recently ionized pair of particles follows from the mean energy of the ionizing photon $h\nu = E_i + \frac{3}{2}kT_i$, where E_i is the energy necessary for ionization. Neglecting recombination, we find that, after a relaxation time t, the tq newly ionized particles of temperature T_i mixed with the n particles of the neutral remainder of gas (having the temperature T_0) give the resulting gas temperature T:

$$T = \frac{T_0(1 + az)}{1 + tq/n} \approx T_0(1 + az) \qquad a = \frac{T_i t q_0}{T_0 n}$$

$$z = \frac{q}{q_0} \leqslant 1 \qquad (3)$$

From the gas distribution with height, $n = n_0\exp(-h/H)$ and the intensity of radiation at a height h given by $dI = AIn.\sec\zeta.dh$, we find the course of ion-production with h near $q_{max.}$ (where $dq/dh \approx 0$):

$$q = q_m \exp(1 - x - \sec\zeta \exp(-x))$$

$$x = \frac{1}{H_0}\frac{h - h_m}{1 + az} \qquad q_m = \frac{q_0}{1 + az} \qquad (4)$$

which is identical with the well-known Chapman formula[6] (where $T = T_0 =$ constant), except that the electron production q is now T/T_0 times rarer and the layer is T/T_0 times larger. The thin curve of Fig. 1*a* represents the Chapman layer, the thick one relates to equation (4) for the case in which the maximum T_m is three times T_0.

After a relaxation time t, we suppose that the ionization equilibrium is accomplished, and we put $dN/dt = 0$ into $dN/dt = q - \alpha N^2$, which gives $N_0 = (q_0/\alpha)^{\frac{1}{2}}$. The suffixes here denote values at which the increase in temperature has not yet been taken into account. From the relations $N_0T_0 = NT, \alpha \sim T^j$ and equation (3), the equation for electron distribution with height is obtained (Fig. 1*b*):

$$N = \sqrt{\frac{q_0}{\alpha_0}}\, z^{1/2}(1 + az)^{-1-(j/2)} \quad j \approx 0$$

$$\frac{q_0}{\alpha_0} = \text{constant} \qquad (5)$$

The coefficient of recombination α depends principally on the electron temperature T_e. At the moment of ionization the mean electron temperature is constant and it approaches only very slowly the gas temperature T. Consequently we can put $j \approx 0$, or at least $j > -1$, which is another condition for bifurcation.

The remainder of free electrons at sunrise already mentioned, which makes the bifurcation more pronounced, appears above a critical level (h_c) defined by a critical gas density n_c deduced from $dN/dt = \alpha N^2$ (where[7], since $T \approx$ constant we put $\alpha \sim n^{\frac{1}{2}}$) giving

$$N_{\text{night}} = \frac{N_s}{1 + N_s t\alpha_0 \sqrt{(n/n_0)}} \qquad (6)$$

where t is the time from sunset, N_s the sunset value and the zero suffix denotes values related to an arbitrarily chosen level h_0. When the second term of the denominator equals unity, we have $n = n_c$. High above n_c the gas is so rare that N_n is nearly constant during the whole night, while, below n_c, N falls rapidly to zero (Fig. 1*c*, dotted curve). h_c represents the lower boundary of the night ionosphere.

A similar mechanism[8] seems to govern also the planetary nebulæ.

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PACKING OF SPHERES

Packing of Equal Spheres

J. D. BERNAL[1] has directed attention to the importance of geometrical models to represent the structure of liquids. A random packing of equal spheres may provide a useful model for an ideally simple liquid. One of the basic parameters related to an array of spheres is the packing density, that is, the ratio of the volume of the spheres to the total volume they occupy. The present experimental work arose from a suggestion by H. S. M. Coxeter[2] that some random array of equal spheres might conceivably have a packing density higher than for regular close-packed spheres (that is, either hexagonal close-packing or face-centred-cubic packing) which is $\frac{\pi}{6}\sqrt{2} = 0{\cdot}7405$.

Several measurements have been reported on the packing densities of equal spheres made with balls poured into cylindrical containers. O. K. Rice[3] found a 15 per cent decrease in the density of random packing as compared with regular close-packing. Rice considered his result to be in agreement with a value obtained by Westman and Hugill[4], who had found a 20 per cent decrease. Neither of these results was intended to be precise, and it is likely that disturbing peripheral effects were present in both cases.

To obtain packing densities for random packing of spheres from measurements on balls poured into rigid vessels there are two basic experimental problems: (1) to establish a method of getting random packing which is not significantly disturbed by the walls of the container, and (2) to correct the measuredp acking densities for the peripheral errors so as to determine the packing density characteristic of space, that is, of infinite volumes.

The present experiments were carried out with steel balls of nominal $\frac{1}{8}$-in. diameter. Two separate batches of balls were used, the first totalling about 6,000 in number, the second about 20,000. The balls were uniform to better than 10^{-4} in. within a batch. As supplied by the manufacturer, they had a very thin protective oil coating which was not removed.

Method of packing. Early in the work it was observed that when balls are poured into a rigid container there is a range of random packings with different total volumes. For example, when the $\frac{1}{8}$-in. balls were poured into a 100 c.c. graduated cylinder up to 54·(5) c.c., shaking and tapping quickly reduced the volume to 53·0 c.c. Continued gentle shaking produced no further reduction in volume. More vigorous shaking increased the volume. On the other hand, when the vessel was tipped horizontally and then slowly rotated about its axis and gradually returned to the vertical position the volume of the balls increased to 58·2 c.c. For all the rigid containers used, a similar effect was observed, namely, there is a range of random packings lying between two well-defined limits. The limits are called here 'dense random packing' and 'loose random packing'. For the dense packing the balls in the vessel are gently shaken down for about 2 min. For the loose packing the balls fill the vessel essentially by rolling down a slope of random-packed balls. The difference in the packing densities for the two kinds of packing is about 6 per cent. The individual measurements at either of the two limits were consistent to within $\pm$ 0·2 per cent.

In both kinds of packings the balls are always rigid in the sense that a uniform pressure over the top will not alter the packing. Even small non-uniformities in the pressure will readily cause a re-arrangement which might be considered similar to the flow of liquids. It is unlikely that in these experiments the packing of the balls was significantly influenced by the frictional forces between adjacent balls either in the filling process or in the final configuration.

Small spherical containers. The first series of measurements were made with six glass flasks of roughly spherical shape ranging in diameter from ten to twenty times the diameter of the balls. The smallest flask could contain about 600 balls, the largest (about 130 c.c.) nearly 5,000 balls.

The packing densities were found by weighing the vessel when filled with balls to determine their number and hence their intrinsic volume, and then weighing the vessel when filled with water to the same level in order to find the total volume. A correction was made for the density of water depending on the ambient temperature.

For spherical containers the peripheral error of the measured packing density is presumably proportional to the ratio of surface to volume, or to the reciprocal of the radius of the vessel, or very nearly to $N^{-1/3}$, where N is the total number of balls. A plot of the packing density, ρ, against $N^{-1/3}$ will therefore be a straight line which, when extrapolated to $N^{-1/3} \rightarrow 0$, gives the packing density in space, that is, for an infinite volume, or with no peripheral error.

The validity of the above procedure for eliminating the peripheral error was confirmed by a plot of the packing density of close-packed spheres contained within a sphere. (The necessary data were obtained with the aid of a table kindly supplied by Prof. C. C. Gotlieb of the Computation Centre, University of Toronto, giving the number of integral solutions of $x^2 + y^2 + z^2 \leqslant k^2$ for integral values of k up to 142. The work on this table has now been extended and will be published elsewhere.) The packing density was plotted against $N^{-1/3}$, where N is the total number of spheres, for N up to about 48×10^6. As was expected, the graph was a straight line extrapolating to 0·7405, the density of close-packed spheres in space. Deviations of the points from the line were surprisingly large, amounting to as much as 2 per cent for N even as high as 10,000. Though with random packing the deviations should be greatly reduced, this theoretical result suggested that considerable scatter might be expected in the measured densities quite apart from experimental error.

The measurements with the small spherical flasks are shown in Fig. 1. The extrapolated values for the limiting packing densities are 0·63(4) for dense random packing and 0·59(1) for loose random packing.

Larger spherical flasks. With the second batch of balls an attempt was made to extend the measurements to larger flasks, that is, up to 500 c.c. The results gave points which did not follow the lines of Fig. 1, but the densities were slightly higher than expected. An examination of the packing of the balls at the surface of the flasks revealed that regions of near close-packing were occurring with irregular boundaries, rather like certain patterns seen in rafts of equal bubbles. No doubt the regular packing

was associated with the smaller curvature of the larger flasks. It appears that to maintain random packing throughout a vessel it is necessary to avoid even approximately flat surfaces.

A series of glass flasks up to about 500 c.c. in volume were made with dimples over their surfaces. Measurements of the packing densities were taken as in the case of the smaller flasks and the extrapolated values of ρ were found to be 0·63(5) for dense random packing and about 0·61 for loose random packing. Though these results are in reasonable agreement with the previous values, it was felt that in the larger flasks the control of the packing, particularly the loose packing, was not satisfactory.

Non-rigid containers: balloons. Three ordinary unextended balloons of different sizes (the largest 350 c.c.) were filled with balls and the density of packing determined. The volume of the balls was found from their weight, as before, and the total volume by immersion of the balloon in water in a graduated cylinder. The filled balloons could be gently 'kneaded' to produce dense random packing. There did not appear to be a simple way of studying loose random packing in a balloon. The packing density from an extrapolation of the three measured values gave 0·63, in agreement with the previous results. As would be expected, the peripheral error with the balloons was smaller than with the rigid containers.

Dimpled copper cylinders. The last set of measurements were made with a series of four copper cylinders, of diameters about 3·1, 3·9, 4·9 and 6·3 cm., and heights about three times the diameter. The largest with a volume of 500 c.c. would take up to 20,000 balls. The cylindrical shape was selected to provide easier control of the packing. The walls and bottom of the cylinders were impressed to a depth of 2 mm. with dimples about 6 mm. in radius and 15 mm. apart. Though the dimples were roughly in a rectangular array they were sufficiently irregular in size and spacing to prevent any significant regular effects on the random packing of the $\frac{1}{8}$-in. balls.

Measurements of both loose and dense random packings were made at eight or ten heights for each of the four cylinders. In a given cylinder the packing densities were plotted against $1/h$, where h is the height of the volume used in the cylinder. The graph should be a straight line, and the value at $1/h \rightarrow 0$ should correspond to the packing in a cylinder of the same diameter but of infinite length. The plot for the 6·3 cm. cylinder is shown in Fig. 2. The extrapolated values of ρ for each of the cylinders were then plotted against $1/D$, where D is the diameter of the cylinder (Fig. 3). The graph should again be a straight line

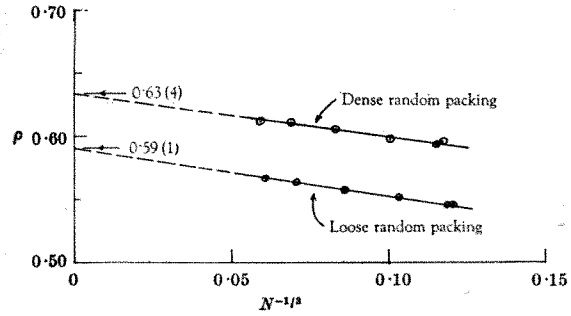

Fig. 1. Packing density for steel balls in glass flasks. Packing density (ρ) versus $N^{-1/3}$. N is the number to fill the flask

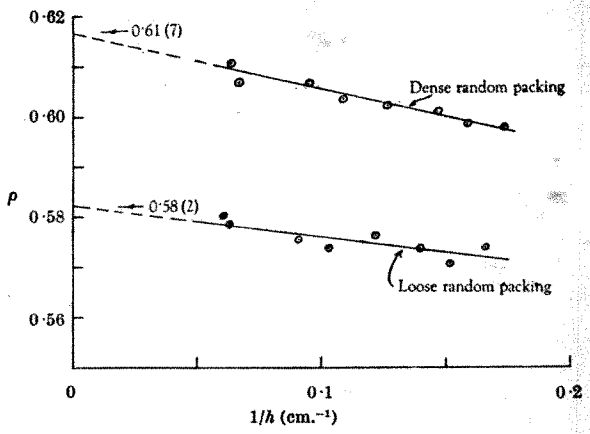

Fig. 2. Packing density of balls in a dimpled copper cylinder No. 4 (6·3 cm. diam.). Packing density (ρ) versus $1/h$. h, Depth to which balls fill cylinder

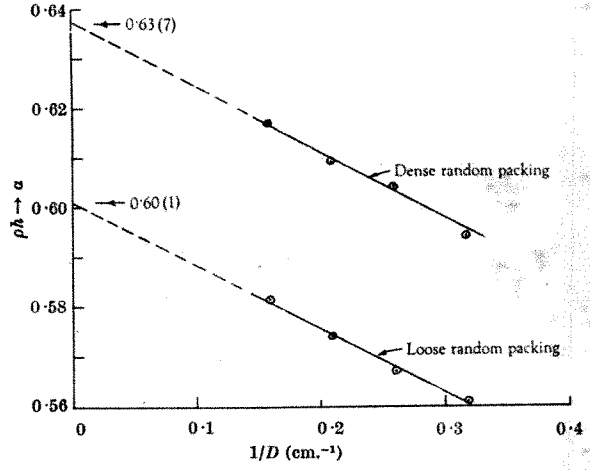

Fig. 3. Packing density in cylinder of 'infinite' length obtained from extrapolations as in Fig. 2, plotted against reciprocal of diameter. Packing density $\rho_h \rightarrow \alpha$ versus $1/D$. D is diameter of cylinder

and the value of ρ, at $1/D \rightarrow 0$, will be the packing density in space. The disadvantage of having to make the double extrapolation seemed to be overweighed by the advantages in the control of the packing. Individual measurements were reproduced to within 0·2 per cent. As seen in Fig. 3, the final values for the dense and loose random packings are 0·63(7) and 0·60(1) respectively. It is considered that these results are more reliable than the corresponding values obtained with the small flasks, relative to which they are somewhat higher.

When spherical balls are poured into rigid containers there appears to be a range of random packing densities possible, with the upper limit at 0·63(7) and the lower limit at 0·60(1). It seems unlikely that there are other stable random packing arrangements for equal spheres in space which have packing densities outside these limits.

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Co-ordination of Randomly Packed Spheres

IN following up earlier work on a geometrical model of liquid structure[1], we have been examining more closely the precise mutual co-ordination of spheres when arranged at random and more-or-less closely packed. As can be seen from Dr. Scott's communication, which came to hand during this investigation, there are at least two types of random packing: random close packing with an occupied volume of 0·64, and random loose packing with one of 0·60. The first of these packings we had already studied with wax balls contained inside a rubber balloon. Realizing, however, that the arrangement studied was liable to be distorted from that of random close packing owing to the compression, it seemed desirable to repeat the experiment with a larger number of approximately rigid spheres. Accordingly, these were now replaced with ¼-in. ball bearings, about 1,000–5,000 in number in different experiments, well shaken down and compressed by winding round with thick rubber bands. This assembly appeared to be rigid, its occupied volume of 0·62 indicated a reasonable approximation to Scott's close-packed density, considering its limited size.

Table 1. ANALYSIS OF CLOSE AND NEAR CONTACTS
(*a*) From assembly in random close packing

Total number of contacts	Number of close contacts: 0	1	2	3	4	5	Total contacts	Close contacts
3	—	—	—	—	—	—	—	5
4	—	—	—	—	—	—	0	13
5	5	0	2	—	—	—	7	72
6	12	20	5	1	—	—	38	**132**
7	31	**47**	25	3	1	—	107	**133**
8	33	**61**	**46**	13	3	1	**157**	95
9	19	**52** *	**37**	21	6	2	**137**	22
10	3	3	10	4	6	3	29	4
11	0	1	—	—	—	—	1	—
	Number of balls						476	

* Centre of distribution. The cases marked in bold type contain between them more than half the balls.

(*b*) From assembly in random loose packing

Total number of contacts	Number of close contacts: 0	1	2	3	4	Total contacts	Close contacts
3							21
4	6	1	—	—	—	7	78
5	10	10	10	—	—	30	**128**
6	17	**32**	26	8	—	83	**108**
7	17	**47** *	**45**	24	2	**135**	57
8	15	**28**	**28**	**39**	12	**122**	24
9	4	5	11	14	2	36	4
10	—	—	3	1	2	6	0
11	—	—	—	1	—	1	0
	Number of balls					420	

* Centre of distribution. The cases marked in bold type contain between them more than half the balls.

The mass of balls prepared in this way while still compressed was soaked in black japan paint. After standing for some time the paint was drained off. The object here was to mark the nature of the contacts and distinguish between them. Surface tension drew the paint to the places where the balls touched (*a*), or nearly touched (*b*), the first giving rise to a black ring with a clear centre and the latter to a black spot (Fig. 4). Careful experiment showed that the near contacts were registered by this method up to a radius of 5 per cent greater than the diameter of the ball. After thoroughly drying the paint, the mass of balls was unwrapped, with an appearance resembling caviare (Fig. 5). When broken apart they showed many of the small clusters referred to as pseudo-nuclei[2], and a certain number of holes, none of which was observed large enough

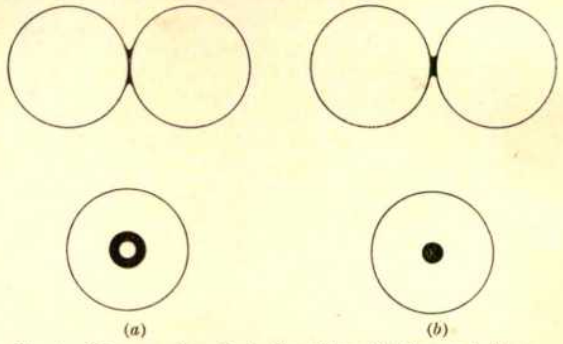

Fig. 4. Diagram of method of marking (*a*) close and (*b*) near contacts between spheres. The areas of adherent black paint are marked

Fig. 5. Portion of random close packed ball assembly showing marks of further contacts

to contain another ball. About 400–500 of these balls, taken from the centre of the sphere to avoid the surface effects noted by Dr. Scott, were separately examined and a number of close and near contacts counted. They were sorted according to the numbers of both kinds of contacts, the results being shown in Table 1 (*a*). These give effectively the distribution of co-ordination types characteristic of random packing. The distribution, as can be seen, is extensive and skew; but the modes are clearly marked and do not differ much from the mean. A modal co-ordination lies between 8 and 9, the largest number having between 6 and 7 close contacts and between 1 and 2 near contacts. The means are 8·5 total, and 6·4 close contacts.

A later experiment using the slow rolling method of Dr. Scott on a mass of ball bearings supported on a highly irregular base gave the conditions for random loose packing with an occupied volume of 0·6. The results of the sorting here give lower co-ordinations all round. The modes were between 7 and 8 for the total co-ordination and between 5 and 6 for the close contacts; the means are 7·1 total and 5·5 close contacts. In the looser random packing it was evident that there were a number of large holes, and that the co-ordinations of particular balls were highly unsymmetrical; for many of them, all the contacts being on one side, the other side facing the hole.

The meaning of these preliminary observations seems fairly clear. In any random packing we would expect each sphere to be in cose contact with at least four others, a necessary condition of stability, and at most twelve. This absolute upper limit is extremely improbable. The most probable average would seem to be six, as each sphere may be

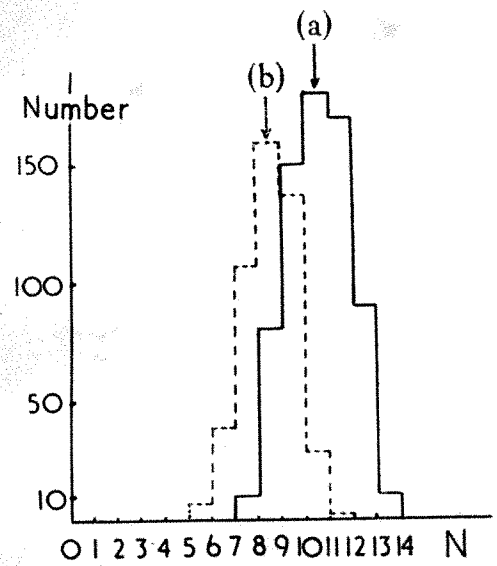

Fig. 6. Histogram of contact numbers derived (*a*) from calculated random model and (*b*) from assembly of spheres

considered in general to rest on three others and in turn to support another three. The number of near contacts, however, is not determinate, except that the sum of the close and point contacts may not exceed twelve, and is very unlikely to approach that number.

By the process of shaking and pressing, the arrangements of the spheres are progressively altered so as to give the minimum volume, and hence the largest number of near contacts. The figure for the occupied volume of random close packing—0·64—must be mathematically determinable, although so far as we know undetermined. If it is one of minimum volume, then it is also one of minimum energy, corresponding to any monotonously diminishing form of centrally attractive forces. For, by definition, any variation of this structure, while not altering the number of point contacts, must necessarily increase the distances between near contacts and thus diminish the energy.

The method used for marking near contact in the model would necessarily fail to note those between 1·05 and say, 1·25 of the minimum value, and these would to a measurable extent contribute to the total energy and should be included as physical neighbours in the sense of the first communication[1]. We may consequently take the mean physical co-ordination of random close packing to be a little more than the value of 8·5 indicated. It probably lies between 10 and 11 (Fig. 6).

The difference between random close packing and regular crystalline close packing fits very well with the observations of rare gas liquids. The increase in volume when passing from regular to irregular is almost exactly the same—16 per cent observed in argon—while the static contribution to the internal energy should correspond to a latent heat of melting between one-quarter and one-sixth of the energy of evaporation as against the observed value of 1/5·5 observed in argon.

The mathematical status of physical random loose packing is not so evident, though it may represent the approximation of the liquid at higher temperatures. The change-over would correspond roughly, on the basis of volume, to a rise in temperature of 1/5 of the interval between the melting and critical points. This will also give a configurational change of internal energy of about 0·18 c./mol. as against 0·16 observed.

Further investigations are in hand to study the statistical contribution of the angles between the contacts between the spheres and also to examine even looser aggregates which can only be obtained in the model by the use of rough or sticky spheres.

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FAILURE TO DEMONSTRATE INFECTIVITY OF NEWCASTLE DISEASE VIRUS NUCLEIC ACID PREPARATIONS

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FOLLOWING the isolation of the infectious ribonucleic acid (RNA) moiety from the tobacco mosaic virus (TMV)[1,2], infectious RNA fractions have been extracted from numerous animal viruses[3–8]. In contrast to the intact viruses, the infectivity of the extracts is ribonuclease (RNAase) sensitive, thermolabile, and is sedimented very slowly in the ultracentrifuge.

At the time that the present work was initiated no information on the infectivity of RNA preparations from the myxoviruses had been reported; however, recently Maassab[9] and Portocala *et al.*[10] described such fractions derived from influenza viruses. After repeated failures to detect infectious RNA from chick embryo-adapted influenza viruses, we made additional attempts to obtain infectious RNA fractions from Newcastle disease virus (NDV). Employing the cold phenol technique[1], the NDV extracts so prepared lacked infectivity in chick embryos. The existence of numerous variables in this type of study has become increasingly obvious from the reported results of others. Thus, exhaustive attempts were made to extract an active NDV RNA fraction by varying the conditions which are summarized as follows:

Egg-adapted strains (Iowa 23 and Calif. 11914) were used in the form of crude infected allantoic fluid, partially purified concentrated allantoic fluid,

Table 1. FAILURE TO DEMONSTRATE INFECTIVITY OF NEWCASTLE DISEASE VIRUS NUCLEIC ACID PREPARATIONS

Exp. No.	Source of virus (chick embryo)	Virus $-\log LD_{50}$	Method of extraction	Diluent for RNA extracts	Host systems tested	Demonstration of Hæmagglutinin	Demonstration of Cytopathic effect
1	CAM infected for						
	12 hr.	7·4	cold phenol	2 × conc. BME	CEF tubes	0	0
	18 hr.	11·5	cold phenol	2 × conc. BME	CEF tubes	0	0
	24 hr.	12·0	cold phenol	2 × conc. BME	CEF tubes	0	0
	36 hr.	12·0	cold phenol	2 × conc. BME	CEF tubes	0	0
2	Conc. AF	> 7·0	cold phenol	1 *M* NaCl	chick embryos	0	
3	Conc. AF	> 7·0	cold phenol	1 × conc. 199	chick embryos	0	
				2 × conc. 199	CEF tubes	0	0
				2 × conc. BME	CEF tubes	0	0
				0·9 *M* KCl + *tris*	CEF tubes	0	0
4	Conc. AF	> 7·0	cold phenol	0·1 *M* phosphate	CEF monolayers		0
				1 × conc. 199	CEF monolayers		0
				Hank's BSS	CEF monolayers		0
5	CAM	> 7·0	cold phenol	0·1 *M* phosphate	CEF monolayers		0
6	CAM	> 7·0	cold phenol	0·9 *M* KCl + *tris*	3-day-old chicks	No symptoms	
7	Conc. AF	11·3	hot phenol	2 × conc. BME	chick embryos	0	
8	Conc. AF	11·0	hot phenol	2 × conc. BME	CEF tubes	0	0
				0·1 *M* phosphate	CEF monolayers		0
9	CAM	> 8·0	urea	0·9 *M* KCl + *tris*	chick embryos	0	
				0·1 *M* phosphate	CEF monolayers		0
10	CAM	> 8·0	guanidine	0·9 *M* KCl + *tris*	chick embryos	0	

Abbreviations: CAM, chorioallantoic membranes; BME, Eagle's basal medium; CEF, chick embryo fibroblasts; AF, allantoic fluid; BSS, balanced salt solution.

and chorioallantoic membranes. Concentrated allantoic fluid pellets were re-suspended either in phosphate buffer (*p*H 7·0), 0·85 per cent saline, or in Hanks's solution minus calcium, magnesium and phosphate ions[11]. Chorioallantoic membranes were either extracted immediately or stored at − 70° C. The − log of the chick embryo LD_{50} titres of the virus preparations to be extracted varied from 7·0 to 12·0.

Many experiments employed the cold phenol method for the extraction of crude and concentrated allantoic fluid virus, and for virus from chorioallantoic membrane released by prior homogenization. Also, chorioallantoic membrane was homogenized in the presence of phenol. In addition, the following reagents were used for extraction: hot phenol[12], hot 1 *M* sodium chloride[13], 8 *M* urea[14], and 2·5 *M* guanidine[15].

In view of the reports that the ionic strength of the diluent alters the degree of infectivity of RNA preparations, the following diluting fluids were used: 1 *M* sodium chloride, 0·1 *M* phosphate (*p*H 7·0), 1 and 2 × conc. mixture 199, 2 × conc. Eagle's basal medium, 0·9 *M* potassium chloride + 0·03 *M* *tris* buffer[11], and 1 × conc. Hanks's balanced salt solution. Most of the preparations were tested undiluted, and diluted 10^{-1} with the above diluents.

Various reports suggest that the nature of the host and the route of infection might influence the RNA infectivity; that is, inactivation of infectivity presumably might be due to host RNAase in the cells or fluids. To obviate this possibility, the present work employed chick embryo allantoic and amniotic routes, chick embryo fibroblast monolayers in bottles, and chick embryo fibroblast culture tubes with cover-slips. Infectivity of the RNA extracts was ascertained by testing for viral hæmagglutinin in the chick embryo and tissue culture fluids, and by observing tissue cultures for cytopathic effects. In certain instances fluids were repeatedly passaged in chick embryos and no infectivity was detected.

The results of some of the experiments are summarized in Table 1, and a few are noteworthy of further attention. Exp. 1 (Table 1) was performed to determine whether there was a relationship between infectivity of the RNA and the period during the virus growth-cycle, since Maassab[9] reported that infectious RNA was obtained from influenza-virus chorioallantoic membranes only at the peak of virus production (18 hr.). Ten-day-old embryos were inoculated with 10^{-3} dilution of NDV, and 18 membranes were removed for each time-interval given in Table 1. For each time period membranes were stored for LD_{50} determinations and 12 membranes were extracted by the cold phenol method. Cell culture tubes were inoculated with undiluted extracts and 10^{-1} dilution of extracts in 2 × conc. Eagle's basal medium. A 60-min. adsorption period was used. After 7 days the experiment was terminated and cytopathic effects (May–Grunwald staining of cover-slips) and hæmagglutinin determinations failed to show virus activity, although the chorioallantoic membranes harvested after 24- and 36-hr. incubation had LD_{50} titres above 12·0.

In view of the repeated failures reported in Table 1, infected chorioallantoic membranes were extracted with 8 *M* urea according to the method of Frazer *et al.*[14]. The urea extracts failed to show infectivity in either chick embryos or in chick embryo fibroblast monolayers. Similarly, virus released from chorioallantoic membranes was extracted with 2·5 *M* guanidine and 0·005 *M* versene[15]. An alcohol-precipitable material of the guanidine extract was not infectious for chick embryos.

In additional experiments concentrated NDV allantoic fluid suspensions and infected chorioallantoic fluid were extracted by heating to 95–100° C. in a water-bath in the presence of 1 *M* sodium chloride for 35 sec., according to the method of Kaper and Steere[13]. The resulting extracts, untreated and treated with RNAase, produced cytopathic effects and hæmagglutinin in chick embryo fibroblast culture tubes, and plaques in monolayers. Apparently the intact virus particles were able to survive the extraction procedure. The period of heating in 1 *M* sodium chloride was extended to 1, 3, and 5 min., and the extracts obtained from a concentrated allantoic fluid virus (LD_{50} = 11·0) and from chorioallantoic membranes (LD_{50} = 12·0) were non-infectious. Although infectivity was not detected in any of the sodium chloride extracts, ultra-violet absorption and chemical analyses revealed the presence of nucleic acid.

Considering the relative complexity of the myxoviruses, attempts were made to 'reconstitute' the virus by mixing cold phenol extracts with either a protein fraction of the virus or with the *Vibrio*

cholerae receptor-destroying enzyme. The protein fraction was obtained by extraction with 67 per cent acetic acid[16] and was added to phenol extracts. In another attempt, 5,120 units of receptor-destroying enzyme were added to various dilutions of phenol extracts. None of these preparations produced detectable infectious units in the chick embryo. It was noteworthy that the reagents and techniques used in this work were efficacious in producing infectious RNA from poliovirus.

No direct proof was found that RNA is the unit which initiates the formation of new infectious virus material or hæmagglutinin from NDV preparations in the systems studied. The failure to isolate an RNA fraction from the myxoviruses which is infectious for chick embryos is not unique. Such observations have been confirmed by others[17–19], who during the course of our investigations were unable to establish infectivity of myxovirus RNA preparations in embryonated eggs. Definitive evidence to explain this failure had not been given, although the presence of RNAase in the embryonic millieu had been suspected. This implication might not be valid, since RNA fractions of Western equine encephalomyelitis virus[12] and Type I poliovirus[20] infect embryonated eggs. Similar to our findings, Schäfer was not able to obtain an infectious RNA from fowl plague virus after phenol treatment[19]. Also, Schäfer kindly reported to us that he was unable to demonstrate infectious RNA fractions from either NDV or from influenza virus employing the extraction procedures which were used in the present work. We attest to Schäfer's views[19] that possibly the RNA of NDV is relatively unstable, or that, in contrast to TMV and to other animal viruses, 2 units of RNA are needed for the formation of new infectious particles; one for the production of the *g*-antigen, and the other for the production of hæmagglutinin. Indeed, myxoviruses might be considered to be more complex than the other viral agents which have been studied.

In view of Maassab's[9] findings, we had fully expected to demonstrate infectious NDV RNA in cell monolayers. Perhaps the most obvious explanation would be lack of sufficient viable particles in the material used for extraction; however, this is unlikely. The NDV suspensions had titres of approximately 10^9 $TCID_{50}$/ml. and some with chick embryo LD_{50} titres greater than 12·0.

Pertinent to this study is the report by Portocala[21] that only freshly isolated filamentous forms of influenza virus yielded infectious RNA, and that no active RNA was obtained from chick embryo-adapted virus. The significance of this finding remains to be determined in consideration of the reported successful isolation of infectious RNA from chick embryo-adapted influenza virus[9]. In this connexion, Portocala[10] treated influenza virus with ether before phenol extraction, a procedure which is known to disrupt the nucleoprotein.

Finally, the NDV RNA might produce only non-infectious units or *S*-antigen (*g*-antigen), and no hæmagglutinin and infectious virus. Although we have no evidence, Schäfer informed us that he was unable to demonstrate this possibility.

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BINDING OF HÆMATIN BY HUMAN SERUM ALBUMIN

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METHÆMALBUMIN was identified by Fairley[1] as a complex of serum albumin and ferriprotoporphyrin. Although a number of workers[2–4] have studied certain of its properties, little information is available concerning the nature of the protein-hæmatin linkage. Keilin[2] postulated for the reduced complex that the linkage is with the porphyrin and not with the iron. O'Hagan[4], who observed that human serum albumin combined with proto- and meso-hæmatin but not with ætiohæmatin, concluded

that the propionic acid groups of the porphyrin were involved in the formation of the complex. The present article presents evidence concerning the protein groups involved in the binding of human serum albumin with hæmatin.

We have investigated the binding behaviour of a number of chemically modified derivatives of human serum albumin. A commercial preparation of human serum albumin (Cutter Laboratories) was used, and the following values for the albumin were taken in making the calculations: molecular weight 69,000 (ref. 5); (E) 1 per cent/cm. at 280 mμ = 5·3 (ref. 5); histidine residues per molecules, 16 (ref. 6). A change in the binding behaviour of human serum albumin was observed qualitatively as a change from the normal absorption spectrum of methæmalbumin which, as reported by Rosenfeld and Surgenor[3], had absorption maxima at 623, 540 and 500 mμ. Quantitative measurement of such a change was accomplished by determination of the optical density of the Soret band (400 mμ). Experiments with this human serum albumin showed that absorption at this wave-length was proportional to the protein concentration when the ratio of the molar concentration of the protein to hæmatin was between 0 : 2 and 1 : 2.

Our work has indicated that modification of the free amino-groups of human serum albumin does not appreciably alter the ability of the protein to form a complex with hæmatin. Three different samples of human serum albumin which had been acetylated roughly 50 per cent[7] (determined by the ninhydrin method[7]) showed a decrease of only 0–22 per cent in their optical density at 400 mμ when compared with a solution of native human serum albumin of identical protein and hæmatin concentration. Similarly, two different preparations of guanidinated human serum albumin[8] showed, when assayed in the same fashion, no decrease in the intensity of the Soret band. These two latter preparations had 54 and 44 per cent of their free lysine groups guanidinated as determined by their yield of ε-dinitrophenyl lysine after hydrolysis of the guanidinated protein which had been treated with fluorodinitrobenzene[9].

We have, however, obtained some evidence which indicates that the histidyl groups of the protein are important for the binding of iron porphyrin. Since Gurd and Goodman[10] have shown that zinc ions can become bound to the imidazole residues in human serum albumin, experiments were carried out to determine the effect of zinc on the complexing of human serum albumin with hæmatin. For these experiments, unbuffered protein solutions containing hæmatin, 0·15 M potassium nitrate, and zinc chloride were used. All solutions were adjusted to pH 6·0. Spectra of such solutions showed that zinc ions, when added at a final concentration of 0·005 M, prior to the hæmatin solution, completely prevented development of the characteristic visible absorption spectrum and caused a decrease and broadening in the Soret band of methæmalbumin.

Experiments using fluorodinitrobenzene also have implicated histidine in the binding of hæmatin with human serum albumin. Although fluorodinitrobenzene is known to react with amino, sulphydryl, phenolic and imidazole groups, these acetylation studies and the following observations make it appear that it is the imidazole group the modification of which is significant in the work with fluorodinitrobenzene reported here. Preliminary experiments indicated that the visible spectrum of hæmatin plus human serum albumin which had been exposed to the following reagents failed to show any major change from that of normal methæmalbumin: (a) 0·02 M iodoacetate (at pH 8·5, 5·5, and 3·0); (b) p-mercuriphenylsulphonate[11] (two-fold amount of molar concentration of the protein); (c) iodine[12] (34-fold amount of molar concentration of the protein).

Human serum albumin which has reacted with limited amounts of fluorodinitrobenzene does not form, in the presence of hæmatin, the typical absorption peak at 620 mμ of methæmalbumin. Although the dinitrophenyl-protein derivative itself has appreciable absorption at 400 mμ, a decreased absorption in the Soret region can also be demonstrated as a result of the reaction of the protein with fluorodinitrobenzene.

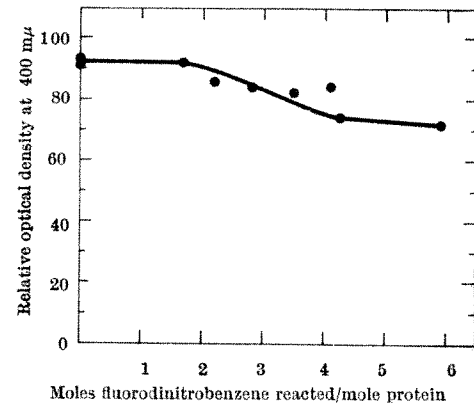

Fig. 1. Relative optical density at 400 mμ for the complex between hæmatin and acetylated human serum albumin which has reacted with varying amounts of fluorodinitrobenzene. Absorption is expressed as per cent of that observed for the control complex of acetylated human serum albumin and hæmatin

Fig. 1 indicates such a decrease resulting from the reaction of acetylated human serum albumin with varying amounts of fluorodinitrobenzene. For this work an amount of 0·04 M fluorodinitrobenzene (in 95 per cent ethanol) equivalent to a 14-fold amount of the molar concentration of protein was added to $2·9 \times 10^{-5}$ M acetylated human serum albumin (57 per cent acetylated) in 0·3 M bicarbonate buffer, pH 9·3. This solution was incubated at room temperature, and at the end of the appropriate time intervals aliquots were removed for analysis. The moles of fluorodinitrobenzene which had reacted were calculated from the difference in its concentration at the beginning and at the end of the reaction[13]. For spectrophotometric measurements, a 1-ml. aliquot was added to 5 ml. of 0·2 M phosphate buffer, pH 7·4, containing $5·8 \times 10^{-5}$ mM hæmatin and a second was added to phosphate buffer only. The absorption at 400 mμ of the latter solution was considered as the absorption of the dinitrophenyl derivative of the protein and was subtracted from the absorption at the same wave-length of the first solution. This corrected reading was then expressed as a percentage of that of a control solution prepared from the protein which had not been treated with fluorodinitrobenzene. Fig. 1 shows that only a few moles of fluorodinitrobenzene per mole of protein was required to react with the acetylated human serum albumin before a noticeable decrease occurred in the Soret band of the protein-hæmatin complex. What

protein groups reacted with fluorodinitrobenzene in this experiment have not been established. However, since many of the free amino-groups were protected by acetylation and since their modification does not appreciably affect complex formation in any event (see above), it is possible that the effects resulting from the reaction with fluorodinitrobenzene were a consequence of a modification of the histidyl moiety of the protein.

Further evidence for the involvement of histidyl groups in the protein-hæm linkage comes from work on complex formation between hæmatin and human serum albumin which has been photo-oxidized. Weil and co-workers[14-17] have demonstrated that for a number of crystalline proteins, photo-oxidation in the presence of methylene blue resulted in a rapid decrease in the histidine and tryptophan content of the protein and a more gradual decrease in the tyrosine, methionine, and cystine content on prolonged oxidation. We have found a similar rapid decrease in the histidine and tryptophan content and a much slower decrease in the tyrosine content of human serum albumin photo-oxidized under the same conditions. Histidine was estimated colorimetrically after acid hydrolysis and separation by paper chromatography[18], and the tyrosine and tryptophan were determined by the methods of Bernhart[19] and Shaw and McFarlane[20] respectively.

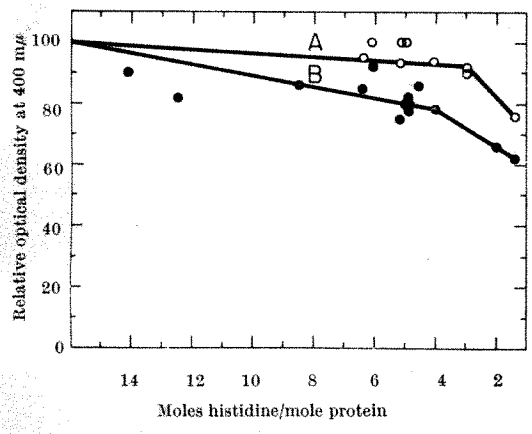

Fig. 2. Relative optical density at 400 mμ for the complex between hæmatin and human serum albumin photo-oxidized to varying degrees. Curve *A* observed with human serum albumin oxidized in the presence of hæmatin, and curve *B* observed with human serum albumin oxidized in the absence of hæmatin. Absorption is expressed as per cent of that observed for the control complex of native human serum albumin and hæmatin

The photo-oxidation of 1 per cent human serum albumin in phosphate buffer, *p*H 7·4, was carried out in a Warburg respirometer at 30° according to Weil's procedure[21]. Three different incubation conditions were employed: (*a*) incubation in the light with a two-fold molar amount of hæmatin; (*b*) incubation in the light with no hæmatin; (*c*) incubation in the dark. Condition (*c*) resulted in no oxygen uptake, and was used as a control for the spectrophotometric studies and for the histidine determinations. The number of moles of histidine oxidized was proportional to the number of moles of oxygen uptake and for a given number of moles of oxygen consumed the disappearance of histidine was identical for both conditions (*a*) and (*b*). At the completion of the photo-oxidation all the flasks were placed in the dark, hæmatin was added to the flasks incubated under conditions (*b*) and (*c*), the methylene blue was removed by 'Norite' (activated charcoal), and aliquots appropriate for spectrophotometric or amino-acid analysis were removed from the filtrate.

Fig. 2 indicated that the absorption in the Soret region for the complex between hæmatin and human serum albumin which had been photo-oxidized fell regularly with a decrease in the histidine content of the protein. It is also evident that human serum albumin when photo-oxidized in the presence of hæmatin showed a greater degree of complex formation than did a sample which had the same histidine content but which had been photo-oxidized in the absence of hæmatin. This observation could be explained by the supposition that hæmatin, when complexed with human serum albumin, protected certain histidine groups of the protein which were essential for complex formation. The possibility remains, however, that the effects observed are a consequence of the involvement of more profound changes in the structure of the molecule than just a loss of histidine content. Brake and Wold[22] have reported that photo-oxidation of enolase resulted in some heterogeneity of the enzyme as observed in the ultra-centrifuge.

Although none of the evidence presented above is conclusive by itself, when the results from the work with zinc, fluorodinitrobenzene, and photo-oxidation are considered together, we believe that they represent fairly strong evidence for considering that histidyl groups are involved in the binding of hæmatin with human serum albumin.

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NUCLEAR STRUCTURE OF HUMAN SPERMATOZOA

THE recent communications by Shettles[1,2], claiming that discrete chromosomes could be demonstrated in dried unstained smears of human spermatozoa and that *X*- and *Y*-bearing types could be morphologically distinguished, and the comments by Rothschild[3] and Bishop[4] induce me to join the discussion. Rothschild, not accepting Shettles's claims, asks for an explanation of what, in reality, has been observed. In my opinion there cannot be the slightest doubt that Shettles has misinterpreted a number of optical artefacts. Special reference should be made to the work of Oettlé, who investigated the effects of varying conditions in phase-contrast systems, including exact measurements of phase-retardation in dried unfixed human spermatozoa[5], and the occurrence of optical artefacts[6].

Objects that are not completely flat, exert a focusing action like tiny lenses[7]. In the case of spherical particles, an image can be produced of another object at some distance without much distortion, whereas in the case of structures of cylindrical or irregular curve-bounded shapes, any image produced will be highly distorted. If the diffraction images produced by a number of structural details exerting lens-like action overlap, highly intricate interference patterns can be produced that do not bear any morphological relationship to either the structure producing the image or to the more distant object[8]. In phase-contrast, structures with focusing action can produce images of the phase-diaphragm below the condenser. With a population of structural details at different planes along the optical axis, the plane of optimal focus for one part of the structure may coincide with that in which other out-of-focus details produce a spurious image[5]. If heavy aberrations are introduced into the optical system, such as spherical aberration and coma, produced by neglecting tube-length correction with high-power dry objectives and by faulty alignment of the optical components, blurring of the total image occurs which may render the spurious effects more difficult to recognize.

All these effects are present in the photomicrographs published by Shettles. Since I have investigated thousands of human spermatozoa with a large number of different techniques[9-12], including several types of phase-contrast (both with annular and cross-shaped phase stops) and interference microscopy, I am not at all unfamiliar with the way in which such artefacts may be produced. The round heads of Fig. 1 of Shettles's first communication most clearly show a spurious image of the annular phase-stop, whereas the longer ones show heavy optical membranes around an unsharp central image, probably of a head in side or semi-side view, closely conforming to the types of optical artefacts analysed by Oettlé[6]. His Fig. 2 also shows very heavy optical membranes, a clearly recognizable image of the phase annulus in the round sperm head, and an overall blurring due to spherical aberration and coma, the optical system being out of alignment as proved by the one-sided dark shades. Shettles's Fig. 3 shows the same phenomenon in reversed contrast; in the round sperm head the spurious image is even a perfect circle, which should have made every observer suspicious, since generally cell structure does not conform so perfectly to a geometrical shape, whereas in the longer head, optical distortion of this image has occurred owing to the rather different shape of the specimen.

Neither do the photomicrographs supplied in the second communication support his case. Fig. 1 has been produced with the optical system admittedly out of alignment "to show third dimension" (*sic*). This photograph shows very heavy haloes around the heads and one-sided interference fringes along the tails, whereas the shadows inside, erroneously interpreted as 'chromosomes', result only from the eccentric illumination; if the condenser system is brought in alignment, such shadows are shifted to the centre of the cell. The final clue is given by Shettles's second Fig. 2, which far from proving his claims, definitely settles the account, so far as physical optics are concerned. The 'chromosomes' most certainly result from an interference pattern produced by out-of-focus details both in the specimens and outside.

In the background of the picture to the left a number of interference patterns is shown, in which the shape of the phase annulus can still be recognized. The superposition of such patterns, further modified by light scattering and diffraction, may easily explain the production of the final image, which is completely out of focus with respect to the specimen itself! The same holds true for the long head, where there are at least as many 'chromosomes' to be seen outside the sperm head and surrounding it as inside, the only difference being that the outside interference pattern shows less contrast and is situated in a different focal plane, as is only to be expected, the specimen modifying the wave-front by lens-like action. The optical section in this specimen being approximately spindle-shaped, lens-like action along the longitudinal axis is much less than across the stronger curved transverse axis, thus explaining why the interference pattern here shows a mainly longitudinal array, while in the round head a circular pattern prevails. If instead of an annular phase-contrast system a cross system, as manufactured by Messrs. Baker, is used, similar interference patterns are obtained if the microscope tube is lowered after optimal focusing, however, with the difference that instead of a circular basic pattern, a rectangular pattern is produced; if, on the other hand, the tube is raised above the position of optimal focus, a bright image of the cross diaphragm of the substage appears, thereby proving the artefactual nature of the phenomena.

Finally, it should be emphasized that with the kind of phase-contrast employed (Zeiss positive *PH*), if the specimen appears dark against a lighter surround, any chromosome should appear dark, too, and not bright, as in Shettles's second Fig. 2, since phase-retardation of chromosomes is always higher

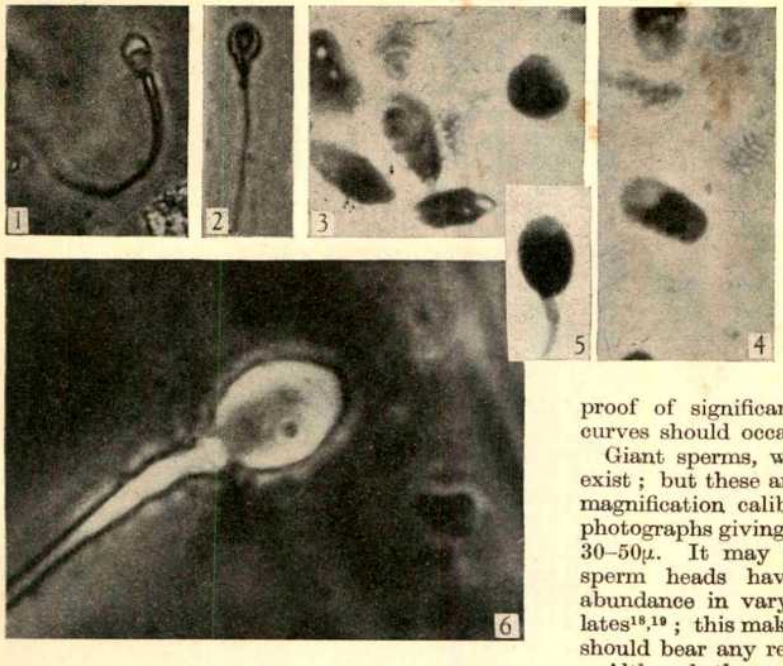

Fig. 1. Living human spermatozoon, photographed with Zeiss phase-contrast system while swimming, showing well-defined nucleus. Normal specimen; no evidence of spurious effects (× 1,000)

Fig. 2. Dried, unfixed and unstained human spermatozoon, dry mount. Photographed with ordinary transmitted illumination with dry objective *N.A.* 0·65 (× 1,000). Normal specimen, showing well-defined nucleus and extension of midpiece into the head. No evidence of spurious effects

Fig. 3. Heads of human spermatozoa showing positive Feulgen reaction (dark) after treatment with concentrated acetic acid. Resin mount, photographed with Zeiss annular phase-contrast oil-immersion system. The round head to the right clearly shows a similar optical artefact to those depicted by Shettles and interpreted by him as an *X*-chromosome. The artefact nature of the phenomenon is clearly demonstrated by the same image, with exactly the same dimensions, appearing outside the specimens in the background. The two heads near the bottom do not show distinct spurious effects (× 2,670)

Fig. 4. Same slide as 3, showing similar artefact inside and several times outside the sperm head. If the centre of the artefact image should have shifted just past the border of the head, the head would have shown optical artefacts of similar shape as shown by Shettles in his photographs of 'male' sperm heads (× 2,670)

Fig. 5. Feulgen reaction applied without pretreatment; ordinary transmitted illumination. Black area, positive test; grey, counterstain (× 2,000)

Fig. 6. Human spermatozoon in dry mount without any further preparation, photographed with annular phase-contrast oil-immersion system, demonstrating that the optical artefacts can be as easily obtained with immersion objectives as with dry ones, but with much better definition, greatly facilitating recognition of artefacts. Spurious effects shown: images of phase diaphragm both inside and outside the sperm head, corresponding to the artefactual structures called *X*-chromosomes by Shettles; heavy optical membranes; interference fringes recognizable up to the third order. No detectable effects of spherical aberration or coma; optical system in good alignment as shown by symmetry of interference fringes (× 4,000)

All photographs by the author

than that of other nuclear components and cytoplasm, whereas exact measurements with interference microscopes show that phase shift is not yet sufficient to produce contrast reversal with the phase plates used in the Zeiss *PH* system. I may add that with properly adjusted phase-contrast optics there is no difficulty at all in observing dried unstained spermatozoa with oil-immersion objectives; any structure that is really present must, if it can be observed with a dry objective, also be observable with oil-immersion.

Now the problem remains of the presence of two distinct populations of different shape and size. If this should be the case, a bimodal size-frequency distribution must be expected, and also a bimodal distribution of nucleic acid. Thus far, bimodal size distributions have never been found, either in normal spermatozoa or in pathological specimens[15,16], and the same holds true with respect to nucleic acid, arginine and total dry mass[14–16]. To prove this part of his claims, Shettles should supply extensive biometrical data (size-frequency distributions and mathematical proof of significance if any tendency to bimodal curves should occasionally be observed).

Giant sperms, with heads more than 8μ long, do exist; but these are definitely abnormal[17]. Shettles's magnification calibration remains at fault, his new photographs giving head-length values of the order of 30–50μ. It may be incidental, but both types of sperm heads have been observed previously in abundance in varying amounts in abnormal ejaculates[18,19]; this makes it even more unlikely that these should bear any relationship to sex ratio.

Although the arguments of physical optics and of biometry must in themselves be considered as final, it is only fair to add some cytological data, since it is to this part of my own work that Prof. D. W. Bishop[4] especially refers. Contrary to the condition in somatic interphase nuclei, chromosomal material in the sperm nucleus is not highly hydrated and therefore the possibility of optical differentiation cannot be excluded *a priori*. However, since no method of microscopical observation, not even the most sensitive methods of interference microscopy, has revealed any such structural detail in the living specimen, it is concluded that any chromosomal material must be highly compressed, a condition

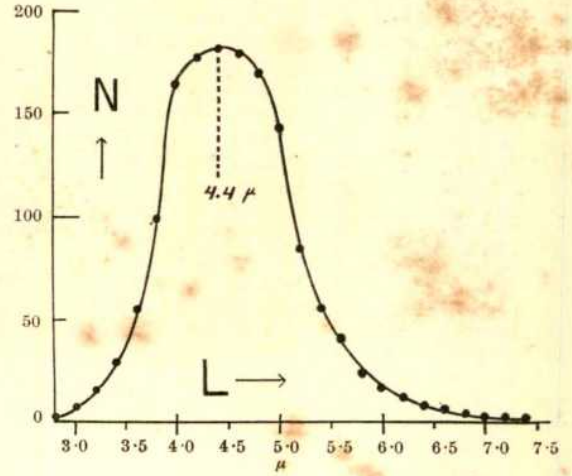

Fig. 7. Size frequency distribution curve (ref. 12) of 1,500 human spermatozoa from donors of proved high fertility, measured with phase-contrast in the living state. *L*, length of head; *N*, absolute number. The curve follows the mathematical equation

$$N = N_{max.} \exp\left(-k\left(\ln\frac{L}{L_m}\right)^2\right)$$

and demonstrates complete absence of any bimodality. Modus, 4·4μ; mean, 4·5μ

which again produces optical homogeneity. There is no reason why, in such a colloid-chemical system, simple drying should produce any effect other than shrinkage of the gel as a whole, so optical differentiation cannot be expected in this case either, contrary to experience with somatic cells. If simple drying should produce separation of discrete chromosomes, these should also be demonstrable by electron microscopy, which even with the most advanced techniques has not been the case[20,21].

Shettles[2] claims that the Feulgen test, being positive in the centre of the head, should support his views. In fact, this is not so. Apparently, to support the idea of distinct chromosomes being present, these structures should be demonstrated by the Feulgen reaction itself on observation with ordinary bright-field microscopy, phase-contrast pictures of dried and stained unmounted specimens obviously being equally liable to optical artefacts as unstained ones. Although differentiations that may point to demonstration of chromosomal structure have been obtained in the form of Feulgen-positive material remaining after an extractive treatment with concentrated acetic acid[11,12], consistent results obtained without rigorous chemical pretreatment, with the Feulgen reaction[12,14-16], Robinow staining[12] and staining (including vital) with methyl green[12], all confirm that in the native sperm nucleus the chromatin material is in a condensed karyosome form, contraverting Shettles's statements.

From a purely cytological point of view the final argument may be raised by asking why chromosomes in a 'female' spermatozoon should appear more or less globular and in the 'male' sperm elongated, while it is known that no such differentiation is found in autosomes and neither in the ovum, and why the individual forms, even in the same types of sperms, should not show reproducible shapes, which conflicts with all we know about chromosomes.

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BRIGHT-LIGHT microscopy has been used for more than thirty years and phase-contrast microscopy for ten years, the latter in studies of more than two thousand human oocytes and ova. If these methods are not used properly by one who knows what he is observing, many errors can be made.

Thin, dried smears of normal spermatozoa from more than 200 men of proved fertility have now been studied. In each individual the two populations of spermatozoa already reported[1,2] concerning nuclear morphology have been seen (Figs. 8 and 9). The

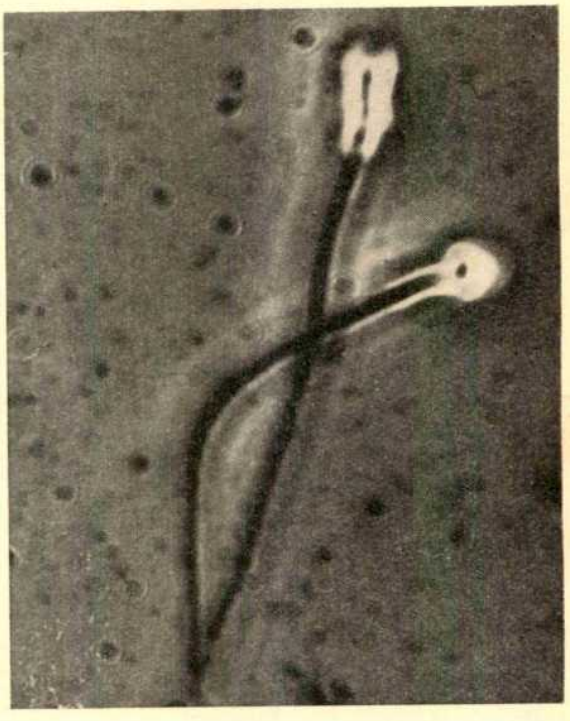

Fig. 8. Unstained, dried human spermatozoa. Phase contrast (× *c.* 430). Rounded and elongate heads

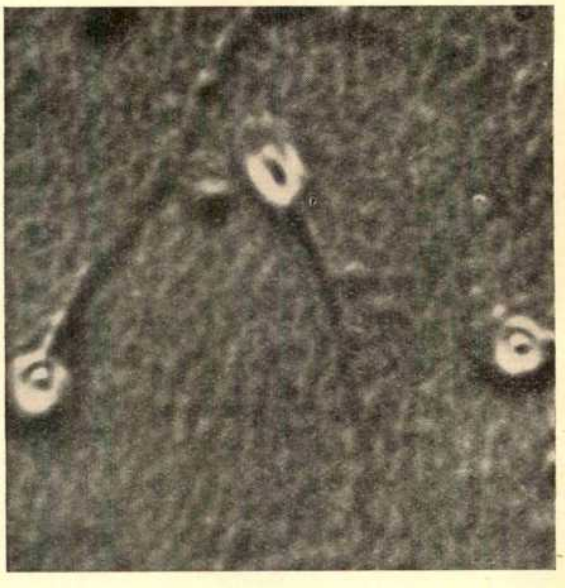

Fig. 9. Unstained, dried human spermatozoa. Phase contrast (× *c.* 430). Light adjusted to show third dimension

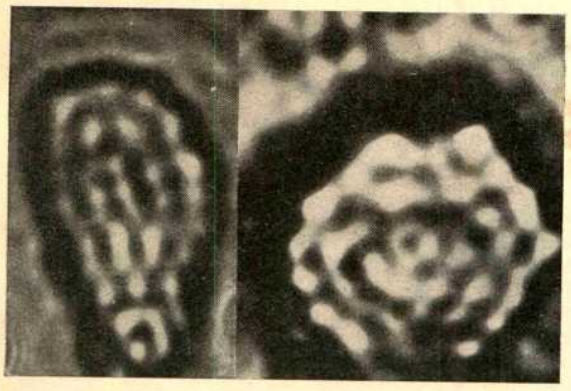

Fig. 10. Chromosomal patterns in the rounded and elongate types of spermatozoan heads. Front views. The Feulgen-positive chromosomes are dumb-bell-shaped and touch end-on like pearls of a necklace. Phase contrast (× c. 860)

chromosomal patterns in the two types of heads are shown in Fig. 10. The chromosomes are dumb-bell in outline and touch end-on like pearls of a necklace. In some spermatozoan heads sufficiently flattened, all 23 chromosomes have been seen. On breaking the thick membrane of the spermatozoan head, the Feulgen-positive, discrete, separate, dumb-bell-shaped chromosomes are easily and readily observed. In every man there has been the exact pattern of the Feulgen-positive, concentrically arranged chromosomes around the most central, rounded chromosome in the smaller, rounded type of head, and an ovoid pattern in the more elongate type (Fig. 10).

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PHOTO-ASSIMILATION OF ACETATE BY GREEN ORGANISMS

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Acetate Flagellates

FORTY years ago the senior author[1] published a paper showing that for a colourless flagellate *Polytoma uvella* acetate is a specific nutrient. Up to this time it had only been known that these organisms live in a complex mixture of so-called putrefaction products. Although it seemed surprising at the time, this result attracted little attention then. Acetic acid is now known to play a prominent part in the metabolism of most organisms.

Polytoma deposits starch as a reserve which it is unable to produce from glucose, whereas acetate is readily transformed into starch.

Lwoff[2] showed that there are more colourless and also green flagellates, not all closely related to *Polytoma*, which produce body material and polysaccharides, and gain their energy from fatty acids in the dark much in the same way. These flagellates were therefore called acetate organisms[3].

The impression that acetate as a nutrient is of considerable importance was strengthened by the observation that some chlorophyllous organisms were greatly assisted in multiplication by acetate in the light. *Euglena gracilis* and *Chlorogonium elongatum*, for example, are able to live by photosynthesis but grow poorly without acetate. Others, like some colonial Volvocales, though green, cannot grow at all without acetate, even under conditions favourable for photosynthesis[4]. The facility with which these live on acetate in the dark varies from organism to organism.

Chlamydobotrys and its Nutrition

Organisms with a complex and variable nutrition did not prove suitable for elucidating the way acetate and light work together in the metabolism of green flagellates. By testing numerous forms[4] we came across a genus of colonial Volvocales, *Chlamydobotrys*[5], which, though distinctly green, is quite unable to live by photosynthesis in the absence of acetate, which, however, is not sufficient to cause it to grow in the dark.

Ten strains were isolated from material collected in widely separated localities. Some, which multiplied faster than the rest, proved suitable for experiments because of their multiplication at relatively high temperatures. All of them require acetate, the vitamins thiamin and cobalamin and an organic source of nitrogen in addition to inorganic salts, including trace elements. The medium ought to be neutral or slightly alkaline. Optimum temperature is 25–30° C. and light intensities 2,000–5,000 lux. Acetate cannot be replaced by other organic acids or by sugar or alcohol. For most experiments a mixture described in our laboratory as *Euglena gracilis*-solution was used. The composition is: sodium acetate 0·1 per cent, 'Difco' tryptone 0·2 per cent, 'Difco' yeast extract 0·2 per cent, beef extract 0·1 per cent.

The inability of *Chlamydobotrys* to multiply unless both acetate and light were provided required an explanation. There were several possibilities: (1) Light may be required not as a source of energy but because some 'photomorphotic' influence is essential for growth. Green and blue light was not effective, but red was, and there are further reasons (ref. 5, Chap. 4) why this explanation is not satisfactory. (2) Normal photosynthesis might not be sufficient to support growth, a situation known in a few faintly pigmented flagellates. Supplementation by another source of energy, acetate in this case, would therefore be required. However, this explanation is again not satisfactory. First, *Chlamydobotrys* is quite green, and secondly, the pale organisms, referred to above, grow in darkness. (3) It may be assumed that both an organic substrate and light energy are necessary because of a photochemical reaction in which acetic acid is involved and which takes place in the chromatophores[6]. If so, 'normal' photosynthesis would not be involved and consequently carbon dioxide would not be required nor would oxygen be produced.

This hypothesis was tested in various ways.

Culture Experiments

Independence of carbon dioxide for the growth of *Chlamydobotrys* with acetate in the light was investigated:

(1) Cultures in test-tubes with cotton-wool plugs and containing acetate medium were kept under an air-tight bell jar. Carbon dioxide was removed by potassium hydroxide solution absorbed on filter paper covering a glass cylinder. This increased the effective absorbing surface exposed to the gas. Growth was the same as outside in air.

(2) Absorption of carbon dioxide might have been too slow because of the large volume of the jar. Cultures as above were therefore grown in small test-tubes individually enclosed in larger ones. Each rested on a short length of glass tubing so that the lower portion of the outer tube could be filled with potassium hydroxide up to the bottom of the culture tube. Growth was normal. *Chlorogonium elongatum*, two strains of *Euglena gracilis* and *Chlorella vulgaris* were also found to multiply under these conditions.

(3) A medium of *Euglena gracilis* solution as in (1) and (2) with 0·5 per cent agar was melted, boiled in test-tubes to remove dissolved gases, cooled to 42° C., inoculated, stirred by repeated pouring backwards and forwards in sterile tubes, and eventually solidified in cold water.

Green colonies developed throughout the 10-cm. high agar column. There was no difference in size between the colonies at the bottom and those near the surface. *Euglena gracilis* behaved in the same way, while several other green flagellates in contrast showed a denser growth near the surface than in the depth.

(4) A possible objection to the previous experiments is that some carbon dioxide might still have been left or produced by respiration. Cultures were therefore prepared through which air, freed from carbon dioxide by potassium hydroxide, was continually bubbled. One washing bottle with barium hydroxide was inserted in the gas line and one behind the cultures.

Growth took place as usual, and only a very slight production of carbon dioxide was detected. *Euglena* and *Chlorogonium* also multiplied.

A further objection might be that respiration could have occurred with the production of carbon dioxide which was immediately consumed in photosynthesis. Anaerobic growth with acetate in the light was therefore believed to be worth testing. *Chlamydobotrys* grows in putrid conditions as well as in the depth of pure cultures[6] and in an agar column.

(5) By excluding oxygen along with carbon dioxide the absence of normal photosynthesis could be established unambiguously. Cultures mounted as in (2) were therefore prepared with pyrogallic acid added to potassium hydroxide solution so that both carbon dioxide and oxygen were absorbed.

Growth was unimpaired compared with cultures in contact with the air (through the cotton-wool plug), and so was that of *Euglena* and *Chlorogonium*.

(6) Instead of air, nitrogen free of carbon dioxide and oxygen was bubbled through the cultures. As in all these tests the pressure inside the culture vessels was slightly greater than atmospheric. Complete absence of oxygen was established by using wash-bottles with pyrogallol in potassium hydroxide. As an indicator, and to make certain that no trace of oxygen was left, Wittingham's[7] anthraquinone-2-sulphonic acid in alkaline solution was used in wash-bottles inserted in the gas stream before and after the culture tubes.

Growth was again normal.

(7) To ensure anaerobic conditions sodium sulphate was added to the medium. Two kinds of experiments were performed.

(*a*) To 23 ml. portions of nutrient solution with acetate 2, 4 and 6 drops of 1 per cent sodium sulphide solution were added. Each medium was distributed into test-tubes with screw tops and soft washers. In the light the *Chlamydobotrys* strains, *Euglena*, *Chlorogonium* and *Chlorella* grew in the normal way. They are therefore not hampered by a hydrogen sulphide concentration in excess of that required to bind all free oxygen.

(*b*) Sodium sulphide solution was added to liquefied agar medium with acetate which had been inoculated with the same organisms at 41–42° C. and solidified. Green colonies developed down to the bottom without difference in size, except in the case of *Euglena* and *Chlorogonium*, which showed denser growth near the surface.

These tests established the fact that *Chlamydobotrys* multiplies in the absence of carbon dioxide and oxygen when acetate and light are provided. Since growth is no slower in these conditions than in control tubes, initial carbon dioxide production by respiration with following photosynthesis is ruled out.

Our culture experiments, though instructive in respect to living conditions and nutritional requirements, were not deemed sufficient to elucidate the peculiar metabolic features which *Chlamydobotrys* appears to have. Moreover, experiments with some other green organisms known to live heterotrophically on acetate had shown that *Euglena gracilis*, *Chlorogonium elongatum* and *Chlorella* (strain 211/11*h* Beijerinck) can live likewise, multiply anaerobically with acetate in the light, although they are also capable of normal photosynthesis.

The culture experiments were therefore supplemented with measurements of gas exchange and *p*H shifts with and without acetate and light respectively. Again five strains of *Chlamydobotrys* and the three other algae were used.

Experiments on Metabolism

Two kinds of experiments on the metabolism of our organisms were undertaken: (1) Measurement of gas exchange with the Warburg technique; (2) the following of acetate consumption by measuring the rise of *p*H and titration with hydrochloric acid to constant *p*H.

In these experiments the temperature was 25° C. The living material was grown in 300-ml. tubes through which air with 5 per cent carbon dioxide was bubbled. Neutral *Euglena gracilis* solution was mixed with the same volume of a dilute inorganic nutrient solution with trace elements and ethylenediamine tetraacetic acid. The density and dry weight of the cultures was less in the case of *Chlamydobotrys* than in *Euglena* and *Chlorogonium* but satisfactory. The living material was centrifuged off, washed twice in neutral *M*/100 phosphate buffer containing inorganic nutrients without nitrate and ammonium and for the measurements transferred into the same buffer solution. Acid and alkaline solutions were harmful and could not be used. The healthy state of the delicate living material was ascertained after the experiments.

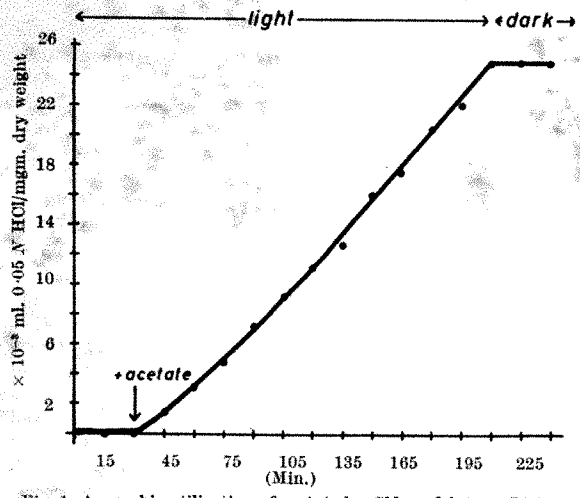

Fig. 1 Anaerobic utilization of acetate by *Chlamydobotrys*. Light, 14,000 lux; temperature, 25° C. The uptake of acetic acid was measured as amount of 0·05 *N* hydrochloric acid needed to keep the *p*H constant

(1) In the five *Chlamydobotrys* strains oxygen consumption in the dark in a medium without energy substrate was low, on the average 2/3 that of *Chlorogonium*, a little higher than that of *Chlorella* and 1/2 that of *Euglena gracilis*. With acetate added, oxygen consumption of *Chlamydobotrys* was increased by 40 per cent and that of *Euglena* by 70–80 per cent, while that of *Chlorogonium* became four times and that of *Chlorella* ten times that without. Glucose had only negligible influence on the respiration of the three flagellates, which are also unable to utilize it for growth, while that of *Chlorella* increased six times.

Photosynthesis at 14,000 lux measured as oxygen production in air with 5 per cent carbon dioxide was also low in *Chlamydobotrys* (in three strains almost nil) while the other organisms gave quite a good response. With acetate added there was no production but a consumption of oxygen by *Chlamydobotrys*, though less than in the dark, no doubt owing to a feeble photosynthesis. In *Chlorogonium*, *Euglena* and *Chlorella* oxygen was produced by photosynthesis in the presence of acetate; but it was appreciably reduced by its addition.

These photosynthetic experiments were supported by measuring the production of oxygen with the dropping-mercury electrode[8]. The relative quantity of oxygen produced showed the same relation between the various strains.

(2) Acetate-consumption in the dark and in the light was estimated by Clayton's[9] (1955) technique[10]. A specially devised glass vessel was provided with a magnetically activated stirrer. A glass electrode was immersed in the medium for measuring *p*H, and titration with hydrochloric acid was used to keep the *p*H constant. The experiments were done under anaerobic conditions (nitrogen atmosphere). The vessel was kept at a constant temperature of 25° in a water-bath, which also protected it from heat accompanying the strong external illumination.

We measured the influence of illumination and of addition of acetate on the hydrogen ion concentration. With acetate in the solution, turning on the lamp resulted in an immediate rise in *p*H, while in the dark it remained constant. With the light on, addition of acetate resulted in an instant increase of *p*H, while it remained constant (Fig. 1) in the dark.

The very rapid influence of the addition of acetate shows that it took almost no time for the molecules to penetrate through the cell wall and protoplasm into the chromatophores. It also renders improbable a long chain of intermediate metabolic processes to be passed before acetic acid is converted into a non-acid compound with the help of light energy. The quantity of acetic acid consumed was about the same in four of the strains of *Chlamydobotrys*, while in the fifth it was 50 per cent higher. In *Chlorogonium* it was about three times as much as the average of *Chlamydobotrys* while *Euglena* had the lowest consumption.

We conclude that the same process of anaerobic photo-assimilation of acetic acid as in *Chlamydobotrys* also takes place in *Euglena*, *Chlorogonium* and *Chlorella*, which in addition are endowed with normal photosynthesis which in *Chlamydobotrys* is negligible.

It is proposed to call the new reaction photo-assimilation of acetate as opposed to the photo-assimilation of carbon dioxide, which in itself is not a 'synthesis'. The investigations are being continued.

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TRANSLOCATION FROM LEAVES OF RYE

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THE filling of the cereal grain is accomplished as a result of the assimilatory activity of the top leaf and sheath on each tiller, together with that of the ear itself[1]. During this time, however, there may be up to five green leaves on a single tiller from which photosynthate could be translocated. Movement of material from such leaves has now been examined in the rye plant by supplying single leaves with carbon-14 dioxide and determining the distribution of radioactivity in materials soluble in ethanol and in water (mainly sucrose and fructose polymers) throughout a tiller after assimilation of the carbon-14 dioxide followed by a period in air and light.

Petkus winter rye was grown in the open in pots. Five plants were selected at the time of anthesis, when the stems were fully extended and the top

(flag) leaf was approaching full expansion. An amount of carbon-14 dioxide equivalent to 5·5 mgm. of hexose was supplied to one leaf of plants exposed to bright sunlight. The lowest leaf (1) was yellowing and was not included in the sequence of leaves (numbers 1–5, bottom to top) receiving carbon-14 dioxide. Assimilation of carbon-14 dioxide was complete in 2–2½ hr., and the plants were then left in air and light for a further 2 hr. In a further experiment, in which the third leaf from the bottom was exposed to carbon-14 dioxide, the plant was left under normal conditions for three weeks, by which time the ear had reached its maximum dry weight. The amount of radioactivity in the soluble material of each part of the tiller was estimated, and in the last experiment in both soluble and insoluble fractions. The results are summarized in Table 1.

Table 1. Distribution of Radioactivity in the Soluble Material* of Tiller Parts of Rye, following Assimilation of Carbon-14 Dioxide by a Single Leaf

Carbon-14 dioxide (total activity 360 × 10^3 c.p.m., amount = 5·5 mgm. hexose) was assimilated in 2–2½ hr. Plants then kept in light and air for a further 2 hr.

Leaf receiving carbon-14 dioxide numbered from tiller base	2	3	4	5	3	
Leaf fresh weight (mean of 4 in mgm.)	269	362	275	106	250	
Time after start of exposure to carbon-14 dioxide			4–4·5 hr.		3 weeks	
	Percentage of total activity supplied in carbon-14 dioxide					
					Soluble	Insoluble
Whole tiller (by addition)	83	76	46	50	2	5
Treated leaf	80	39	26	26	1	2
Sheath of treated leaf	3	17	1	5	1	
Stem internodes	0	15	19	15	1	2
Ear	0	4	—	5	1	1

There was no activity in untreated leaves and only traces in some sheaths. Roots were slightly radioactive in all plants.

* Each part extracted successively with 80 and 50 per cent ethanol, and then three times with cold water. Extracts combined.

The range of distribution through the tiller, after 4 hr., of carbon-14 from a single leaf was limited. No activity appeared in leaves other than those receiving carbon-14 dioxide, and only traces in leaf sheaths. In stems, activity was mainly in two internodes, one above and one below the insertion of the sheath of the treated leaf.

The proportion of radioactive material in soluble form in the whole tiller and in the treated leaf depended on the position of the leaf on the tiller. There was little translocation from the oldest leaf treated (leaf 2), for, at the end of the 4-hr. period, 80 per cent of the carbon-14 assimilated was in the extract from this leaf. With leaf 3, 37 per cent of the carbon-14 was in the extracts from the leaf sheath and stem internodes, and 39 per cent remained in the leaf extract, so that 76 per cent was in soluble products. Only a small fraction of the activity reached the ear (4 per cent). With the two upper leaves (4 and 5), 50 per cent of the assimilate remained in the soluble form after 4 hr., of which about half was in the treated leaf, 17 per cent in the stem, and about 5 per cent in the ear. In the plant left for three weeks after treatment of leaf 3, only 7 per cent of the initial activity persisted anywhere in the tiller. More than half this amount was in the insoluble fractions of leaf 3 and the stem internodes, and less than a third (less than 2 per cent of the initial activity) in the ear. Qualitative observations showed a small amount of activity in adjacent tillers, and rather larger amounts in roots. These amounts, together with respiration losses, presumably accounted for the disappearance from the tiller, over the period of grain filling, of about 90 per cent of the carbon-14 previously assimilated by leaf 3. These results certainly support the view that assimilation by lower leaves on cereal tillers does not contribute materially to the growth of the grain.

Paper chromatograms (propanol/ethylacetate/water) prepared from samples of the tissue extracts were sprayed with benzidine to show the distribution of saccharides and radioautographed to show the distribution of radioactivity. In all parts of the tiller there was present, in addition to sucrose, fructose and glucose, an array of fructose polymers which appeared on the paper as a sequence of spots above sucrose extending to the starting line (cf. ref. 2). In extracts of the leaves which had received carbon-14 dioxide, although most of the activity was in sucrose, all the fructose polymers were radioactive. In sheaths and the stem internodes, however, activity was confined to sucrose. It is remarkable that no trace of activity was found in the large array of soluble fructose polymers present in these tissues.

By combining all the ethanol/water extracts, an estimate of the proportion of the activity in sucrose and in the fructose polymers of the leaves was obtained after fractionation of the saccharides on a charcoal column. The radioactivity was distributed between six fractions eluted respectively by water, 5, 20, 30, 50 and 80 per cent ethanol. Water removed 13 per cent of the activity from the column, presumably in hexoses. 5 per cent ethanol removed 82 per cent, of which all but 1 per cent was sucrose; this small fraction, which was eluted after sucrose, yielded only fructose and glucose on hydrolysis, and its position on a paper chromatogram suggested that it was a trisaccharide.

There remained a further 5 per cent of the activity incorporated into oligosaccharides. Four-fifths of this amount was eluted by 20 per cent ethanol. This material was resolved into three fractions by paper chromatography, the two faster-running substances being radioactive and probably tri- or tetra-saccharides. These substances also yielded only fructose and glucose on hydrolysis. Material eluted by higher concentrations of ethanol contained only traces of activity and did not move from the starting line on paper chromatograms. At the time of grain filling, therefore, synthesis of fructosans from newly assimilated carbon was virtually confined to formation of tri- and perhaps tetra-saccharides in the leaves, for at least 4 hr. following photosynthesis.

If sucrose is assumed to be the precursor of the fructose polymers, these results suggest that the transfer mechanism in leaves only slowly builds up the well-known series of fructose polymers. Furthermore, fructose polymers do not move out of the leaf with sucrose, and consequently accumulation in sheaths and stems must result from new synthesis from incoming sucrose. The amounts formed are known to depend in part on the nutritional status of the plant—and especially the nitrogen supply[3]. Since no labelling appeared in fructosans of the stems and sheaths in 4 hr., little new synthesis can occur after the time of anthesis, when in fact the overall amounts are falling (see ref. 4).

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LETTERS TO THE EDITORS

COSMOLOGY

Interpretation of Co mology

RECENT correspondence by McCrea[1,2] and Davidson[3] has been concerned with distinguishing between steady-state and evolutionary type cosmologies. In particular, McCrea[1] has suggested that there is a fundamental inability to distinguish experimentally between the two types, and that this fact should be built into any satisfactory cosmological theory. It is shown here by considering a gravitational formulation of Mach's Principle that it is possible to incorporate this indistinguishability directly into cosmology.

Gravitational formulations of Mach's Principle[4,5] assume that the dynamical properties of a body are due to the gravitational interaction of the body with the matter composing the rest of the universe. The resulting gravitational potential of the body becomes a function of its velocity, so that the existence of kinetic energy and other dynamical characteristics are readily explained. Discussions of the advantages of such treatments have been published by Sciama[4], Bastin[5] and Burniston Brown[6] and are too long to be given here in detail. It is noted, however, that, as well as accounting for the dynamical properties of bodies, the treatments give quantitative explanations of the existence of rest mass energy, the equivalence of gravitational and inertial mass, and the non-rotation of the 'fixed-star' directions with respect to inertial frames.

The properties of a universe of variable radius R but of constant mass M will now be examined. The gravitational form of Mach's Principle will be assumed, but, apart from this, physical mechanisms will be assumed independent of R. Thus the fundamental quantities (e, h, c and G) will be assumed to remain unaltered by a variation in R. In order for the variation of R to have a meaning, we must further suppose the existence of an invariant scale measuring distance and an invariant clock measuring time.

If R_0 is the present value of R, then expressions for the kinetic energy E and momentum p of a particle in a universe of radius R (see, for example, Bastin, ref. 5, sections 3 and 4) are:

$$E = \frac{1}{s} \cdot \frac{1}{2} mv^2 \tag{1}$$

and

$$p = \frac{1}{s} \cdot mv \tag{2}$$

where $s = R/R_0$ and will be called the dilation parameter. Equations (1) and (2) may also be inferred from the treatment given by Sciama[4] in which (section 4 (iii)) it is shown that the contribution of distant matter to the inertia of a body falls off inversely as the distance of the distant matter.

Some implications of equations (1) and (2) are at once clear. For highly condensed cosmological conditions (low s), the energy and momentum of a particle (of given mass and velocity) are high. For low-density conditions (high s), the values of energy and momentum are correspondingly less. This is in fact what would be expected qualitatively if the energy and momentum of a particle are considered to be the result of gravitational interaction of the particle with the rest of the universe.

Consider now a hydrogen atom in a universe of dilation parameter s (that is, radius $R = sR_0$). Using the normal Bohr treatment:

$$\frac{e^2}{r^2} = \frac{1}{s} \cdot \frac{mv^2}{r} \tag{3}$$

where r is the radius of the electron orbit. Quantization of action gives:

$$\frac{1}{s} \cdot mv \cdot r = \frac{nh}{2\pi} \tag{4}$$

So that from (3) and (4):

$$r = \frac{sn^2h^2}{4\pi^2me^2} \tag{5}$$

The corresponding expression for the energy change during an atomic transition becomes, from equations (2)–(5):

$$E = h\nu = \frac{2\pi^2me^4}{h^2}\left(\frac{1}{n^2_1} - \frac{1}{n^2_2}\right) \cdot \frac{1}{s} \tag{6}$$

Equation (5) shows that the radius of the hydrogen atom bears a constant ratio to the radius of the universe R. The same would be expected for more complex atomic systems, so that any measuring rod would also vary in length in the same way. Since the invariant scale which was postulated is experimentally unrealizable, an observer will only be able to measure the ratio R/r which will be constant for all time. Thus whatever the radius R measured by the hypothetical (but unrealizable) invariant scale, the observer will always measure R_0. It is thus impossible at any time in the past or future to measure any value for the radius of the universe other than the present one of $\sim 3 \times 10^{27}$ cm.

The analysis also shows that no indication of variation of R may be obtained from time-dependent measurements. Thus from equation (6) the period of atomic clocks is proportional to the dilation parameter s (and a similar result may be simply shown for a macroscopic mechanical clock). The linear dimensions of an atom, a measuring rod or the universe will also be proportional to s, so that the time measured by the observer's clock for light to traverse any of these objects will be independent of s and hence independent of the radius R.

When certain types of experiment are considered, the application of orthodox physics does not give the indistinguishability suggested by McCrea. Suppose, for example, a measurement of Hubble's constant is made at some particular time. Suppose further that this result is stored for a time which is an appreciable fraction of the parametric cosmical time ($\sim 10^9 - 10^{10}$ years) when a second measure of the Hubble 'constant' is made. According to orthodox physics, we should expect the two values of the 'constant' to be the same if a steady-state model is correct, whereas a

definite difference of the 'constant' would imply an evolutionary type cosmology. The experiment could thus distinguish between the two types of model. If, however, the idea of gravitational inertia is accepted, then the two values of the Hubble constant are necessarily the same, as has been shown above.

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ASTROPHYSICS

Magnetic Field of Jupiter

RECENT radio observations of Jupiter, in the frequency-range 14–27 Mc./s., have suggested the presence of an ionosphere and a magnetic field on the planet. If the magnetic field is regarded as being due to a dipole situated at the centre of the planet, with its axis along the axis of rotation, a value for the polar field intensity of 7 ± 1 gauss can be found from the radio observations.

Radiation appears to be emitted from one or more localized regions on Jupiter[1]. The radiation from these sources is emitted within a limiting angle, and this has been interpreted[2] as indicating the presence of an ionosphere in the upper atmosphere of Jupiter. Observations by Franklin and Burke[3], Smith and Carr[4] and Gardner and Shain[5] have shown that a number of the noise bursts appear to be right-handed elliptically polarized when viewed along the direction of propagation. This polarization has been observed from both the northern and the southern hemispheres of the Earth. It is evidently not an effect of the terrestrial ionosphere, although further observations are necessary to establish this conclusively. Franklin and Burke[3] and Barrow[6] have explained the observed polarization as being due to internal reflexion, in the upper atmosphere of Jupiter, of one of the two components formed when the radiation passes through the Jovian ionosphere in the presence of a magnetic field.

The propagation of electromagnetic radiation in an ionized gas in the presence of a magnetic field has been fully discussed in the magneto-ionic theory of Appleton[7]. Most reflexion takes place at points where the refractive index tends to zero. In the presence of a magnetic field H the conditions for zero refractive index (if possible, collision effects are neglected) may be written as:

$$\frac{4\pi Ne^2}{m} = p_0^2 = (2\pi f_0)^2 \qquad (1)$$

$$f_0^2 = f_x^2 - f_x f_H \qquad (2)$$

$$f_0^2 = f_x^2 + f_x f_H \qquad (3)$$

where N is the electron density, e and m are, respectively, the charge and the mass of an electron, f_0 and f_x are, respectively, the critical frequencies for the ordinary and the extraordinary waves, and f_H is the gyrofrequency ($f_H = He/2\pi mc$). The condition (1) is independent of the magnetic field and refers to the ordinary wave. Conditions (2) and (3) apply to the extraordinary wave and they depend on the magnitude of the magnetic field although they are independent of the direction. Two cases arise as $f_H < f$ or $f_H > f$.

Consider a source of radiation at some point on Jupiter. Both mixed and polarized bursts have been observed on a number of occasions at 22·2 Mc./s. and we may, therefore, conclude that 22 Mc./s. is the approximate value of either f_0 or f_x.

If $f_H < 22$ Mc./s. reflexion of the extraordinary wave must occur at the lowest level of electron density, specified by (2). Signals have been received down to 14 Mc./s. so we can say that $f_0 < 14$ Mc./s. and $f_x \simeq 22$ Mc./s. The maximum electron density is evidently not great enough to give rise to reflexion conditions (1) and (3) for 22 Mc./s. waves. Fourth condition reflexion of the extraordinary wave, if it occurs, will be a subsidiary effect as it would take place, for all inclinations of H to the direction of propagation, at electron densities between limits specified by (1) and (2).

A little consideration will show that it is not possible to explain the observed polarization at all if $f_H > 22$ Mc./s.

It seems probable, then, that when we observe an elliptically polarized burst on the Earth it is essentially the ordinary wave which is being received. If this radiation is observed to be emitted within a limiting angle λ, from a point having latitude φ on Jupiter, then it can be shown[6] that:

$$\cos \frac{\lambda}{2} = \frac{f_0}{f} \sec. \varphi \qquad (4)$$

Franklin and Burke[3] give $\lambda = 60°$, for their 22 Mc./s. observations of the principal region emitting the radiation, whence $\varphi > 43°$ if $f_0 < 14$ Mc./s.

To find the value of the polar magnetic field H_p, we note that:

$$H_p = \frac{2\ H}{\sqrt{(1 + 3 \sin^2 \varphi)}} \qquad (5)$$

Combining (2), (4) and (5), we find that:

$$H_p = \frac{f_x\,[1 - (\cos \lambda/2\ .\ \cos \varphi)^2]}{1{\cdot}4\ \sqrt{(1 + 3 \sin^2 \varphi)}} \qquad (6)$$

taking $f_H = 2{\cdot}8H$ if f_H is in Mc./s.

H_p varies relatively slowly with the lower values of f_0 and it can be seen that for $0 < f_0 < 14$ we have, using $f_x = 22$ Mc./s. and $\lambda = 60°$:

$$6{\cdot}0 < H_p < 7{\cdot}85 \text{ and } 90 > \varphi > 43$$

An average value of $H_p = 7 \pm 1$ gauss is indicated. This implies a critical frequency of about 10 Mc./s. for the ordinary wave and an approximate source latitude of 57°.

The above value of H_p is somewhat lower than that which follows from the estimate, given by Smith and Carr[4], of about 7 gauss for the magnetic field intensity in the ionosphere at the point of propagation. This figure is obtained from their average, experimentally observed polarization ratio, assuming f_0 to be 17 Mc./s. and the source latitude to be 20°. The field intensity is then calculated from the Appleton–Hartree polarization formula. The corresponding value of H_p is about 12 gauss.

On the face of the experimental evidence, any method of calculation is going to lead to the general

conclusion that f_H is something between 13 and 22 Mc./s. However, the method outlined here avoids any specific assumption as to the latitude of the source and might well form the basis of a more accurate determination of H_p in the future.

Field[8] has proposed a cyclotron-like model of the radiation sources on Jupiter on the basis of decimetre wave-length emission. This model requires a polar field intensity of at least 1,200 gauss, and it is difficult to reconcile these two contrasting orders of magnitude for the polar field.

The radio observations of Gardner and Shain[5] and of Franklin and Burke[3] have cast some doubt on the hypothesis that the restricted angle of radio emission from Jupiter is due to ionospheric effects on the planet. However, in considering these results, it must be remembered that, as the method of interpretation is statistical, the fact that 27 Mc./s. radiation has been received so infrequently, compared to radiation in the 18–22 Mc./s. range, is liable to give misleading conclusions if the limiting angle is taken from a histogram compiled in terms of 'number of occurrences'. There is the further possibility that the spectral distribution is such that 27 Mc./s. signals only rarely reach an intensity which is detectable on the Earth. This could be the case if the radio emission is due to plasma oscillations. Zheleznyakov[9] has shown that the main features of the radiation can be explained in terms of a plasma oscillation mechanism, and Rishbeth[10] has shown that sufficient ionization for such a mechanism could be produced by solar radiation. Certainly the ionospheric hypothesis cannot be rejected on the experimental data available at present.

Future observations of polarization at two or three different frequencies may support or disprove the ionospheric theory. It is hoped to make these observations at this University in 1961.

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PHYSICS

Direct Measurements of Proton Mobilities in Protonated Ice

PROTON mobilities in ice have been calculated previously only on the basis of indirect experimental evidence. Eigen and DeMayer[1,2] have estimated from discharge experiments that in ice of pure water proton mobility is in the range 0·1–0·5 cm.^{2} sec.$^{-1}$ V.$^{-1}$. Conway and Bockris[3] calculated from conductivities of ice of pure water that proton mobility is 0·19 cm.^{2} sec.$^{-1}$ V.$^{-1}$. Some theoretical estimations[4] yield proton mobilities in ice of 0·11 cm.^{2} sec.$^{-1}$ V.$^{-1}$. These mobilities are all extremely high when compared with

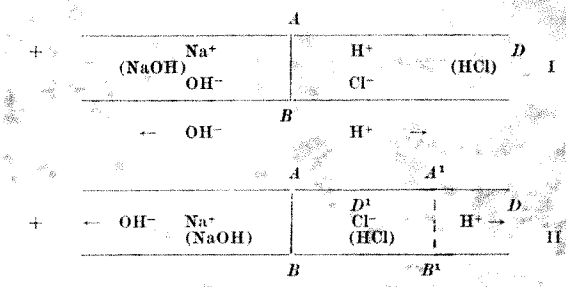

Fig. 1. A sketch for proton boundary movement (hydroxyl ion boundary movement is not considered here). Dye (D) used, malachite green; D, yellow (frozen) for 0·1 M hydrochloric acid; D^1, blue after proton depletion; AB, initial boundary; A^1B^1, migrating proton boundary; $AB - A^1B^1$ region is blue; I, boundary positions initially; II, boundary positions after electrolysis

the mobilities of protons in liquid water (3×10^{-3} cm.$^{-2}$ sec.$^{-1}$ V.$^{-1}$).

Protonated ice is a relatively good electrical conductor (Heinmets, F., unpublished results) which suggests that direct measurements of proton movement by the boundary method could be made. Prerequisities for such measurements are the establishment of a sharp moving proton boundary in ice and a proton concentration indicator-molecule to follow the boundary movement. After extensive exploratory work, the conditions for obtaining a suitable boundary have been established and an indicator-dye (malachite green) has been found which exhibits colour change in ice at a suitable proton concentration. I have made such direct measurements of proton mobilities in protonated ice.

Ice was obtained by freezing supercooled 0·1 M hydrochloric acid solutions. A U-type conductivity cell (length 30 cm.) was used in which one vertical section was plastic (diameter 1·2 cm. and wall-thickness 0·03 cm.). This facilitated sawing up the tube for sectional analysis. A stable proton boundary, suitable for mobility measurements, is obtained when a boundary is established between hydroxylated and protonated ice (Fig. 1). Half the plastic cell was first filled with 0·1 M hydrochloric acid solution (containing indicator dye) and was frozen. Afterwards a layer of 0·1 M sodium hydroxide solution, containing also a dye for better boundary indication, was poured on top of the ice and frozen. Some experiments were carried out in the presence of gelatin, since a visually sharper boundary is maintained during the electrolysis. The procedure here was as follows. Half the plastic section was first filled with 0·1 M hydrochloric acid solution, containing a proton indicator and 2 per cent gelatin, which gelled and was afterwards frozen. A layer of 0·1 M sodium hydroxide solution containing 2 per cent gelatin and metacresol purple was poured on top of this and frozen. This in turn was topped with a non-freezing electrolyte containing a 1 M sodium hydroxide solution in 50 per cent glycerol. For the other U-arm a 1 M hydrochloric acid solution, also with glycerol, was used. A d.c. potential was applied by means of platinum electrodes. To avoid warming the ice, current values were kept low. The initial boundary of yellow 0·1 M hydrochloric acid and purple sodium hydroxide was clear. Shortly after the application of a potential a blue boundary appeared between the purple-yellow interphase, and the blue zone gradually widened. The positions of the boundaries were determined at various time-intervals by switching the current off while the cell

was lifted from the bath and the boundary position measured rapidly. During electrolysis at constant voltage, the current value diminished because the blue-zone represents a proton-depleted ice region and its resistance increases with time. In my experiment the current was kept constant by increasing the potential. However, the increase of resistance is not too rapid, since all protons do not migrate out of the region immediately. Apparently all hydrochloric acid molecules are not dissociated in ice and protons migrate only after dissociation. In gel-ice it takes several hours before the resistance in the proton-depleted zone gets very high; during that time the boundary has moved several cm. After completion of boundary measurements, the cell was put into powdered dry ice. Using a duplicate cell, the electric field strength in the hydrochloric acid region was determined for selected current value. Then various sections of plastic cell were sawn off, melted and conductivity and *p*H determined. A thin section between sodium hydroxide–hydrochloric acid interphase was discarded. In Table 1 the result of a typical experiment is presented. Zone *A*-1 represents the proton-depleted region. During 180 min. at 1 m.amp. the displacement of the boundary was 1·1 cm. In the blue *A*-1 zone the *p*H value was 1·1 before and 3·3 after electrolysis. This was reflected also in resistance increasing from 4,000 ohms to 26,100 ohms. Both measurements reveal a large reduction of proton concentration in *A*-1 zone. In two control sections (*A*-2, *A*-3) at the front of the boundary there was no significant change in either the *p*H or the resistance value, nor was there a change in colour. Additional control experiments with hydrochloric acid solutions and malachite green revealed that the change in colour corresponds to the reduction of the proton concentration. This proton-depleted zone is shown in Fig. 2, which is a black-and-white copy of a colour photograph. All available evidence indicates that the blue zone in ice represents a proton-depleted region, and proton mobility is calculated from the length of the zone. Results are presented in Table 2. Since the conductivity of protonated ice decreases when temperature is lowered, it is expected that proton mobility is also reduced. The results in Table 2 confirm this phenomenon.

Table 1. Resistance, *p*H and Colour of Various Sections before and after Electrolysis

Length of section (cm).	Resistance (ohms)		+ *B* ↑ OH^- NaOH	*p*H		Colour of ice	
	Before	After		Before	After	Before	After
	—	—		—	—	*P*	*P*
1·1	4,000	26,100	HCl ¹ ↓ H^+	1·1	3·3	*Y*	*B*
1·5	4,000	3,850	²	1·1	1·1	*Y*	*Y*
1·5	4,000	3,750	³	1·1	1·1	*Y*	*Y*
			A −				

Current of 1 m.amp. applied for 180 min. Temperature was kept at −15°. Electric field strength, 0·5 V./cm. *A*, 0·1 *M* hydrochloric acid, 2 per cent gelatin and malachite green; *B*, 0·1 *M* sodium hydroxide, 2 per cent gelatin and metacresol purple. *P*, Purple; *Y*, yellow; *B*, blue.

Table 2. Velocity of Protons as a Function of Temperature

Experiment No.	Composition of ice	Temperature (° C.)	Velocity (cm.²) / sec.–volt.
1	0·1 *M* HCl+H_2O	−30	$2·0 \times 10^{-5}$
2	0·1 *M* HCl+H_2O	−25	$8·1 \times 10^{-5}$
3	0·1 *M* HCl+H_2O + 2 per cent gelatin	−22	$2·4 \times 10^{-5}$
4	0·1 *M* HCl+H_2O + 2 per cent gelatin	−15	$2·2 \times 10^{-4}$

In these experiments potential applied at the electrodes varied in the range 200–800 V. The velocity of proton was calculated as follows:

$$V^- = \frac{d}{e \times t}; \text{ in example at } -15^\circ \; V^- = \frac{1·1}{0·5 \times 180 \times 60} = 2·2 \times 10^{-4} \text{ cm.}^2 \text{ sec.}^{-1} \text{ V.}^{-1}$$

where *d*, boundary displacement (cm.); *e*, electric field strength (V./cm.); *t*, time (sec.).

Temperatures reported here are those of bath; ice temperatures are slightly higher due to the passage of current. Electric field intensity for each experiment was determined by d.c. conductivity measurements in a duplicate cell. Same current values were used for conductivity measurements and for electrolysis.

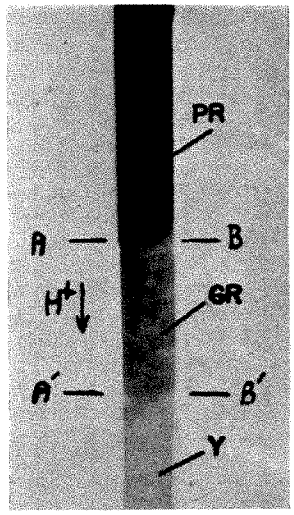

Fig. 2. Proton boundary in ice. *PR*, Purple zone, 0·1 *M* sodium hydroxide plus metacresol purple; *GR*, blue zone, part of '*y*' zone whence protons have been removed by electrolysis; depletion of protons changes colour of ice from yellow to blue; *Y*, light yellow zone, 0·1 *M* hydrochloric acid plus malachite green (ice is yellow); *A*—*B*, initial proton boundary position; A^1B^1, final boundary position
This black-and-white print has been prepared from a colour slide

It can be questioned how much diffusion contributes to movement of the proton boundary in the ice. A rough estimate of this has been made on the basis of measurements with a control cell which was stored at −28° C. for six months. Approximate velocity of diffusion boundary was 1×10^{-7} cm./sec. It appears that diffusion displacement of proton boundary is insignificant in experiments lasting only for a few hours.

It is evident that proton mobility in protonated ice is about three orders of a magnitude smaller than previously estimated[1,3]. This raises the question whether previous indirect estimations and calculations are based on uncertain assumptions or whether, in the ice of pure water, a different mechanism is operating for the proton transfer process. Further work is required to elucidate this point. Unfortunately, moving-boundary methods cannot be used at very low proton concentrations. My experiments were carried out under conditions where current and temperature were regulated manually, and experimental error may be considerable, but the accuracy is

definitely better than an order of magnitude. Experiments are in preparation with automatic current and temperature control in order to obtain more accurate proton mobility determinations.

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Electrostatic Attraction between a Liquid Surface and a Needle Height-Gauge

WHERE the height of a liquid surface needs to be measured accurately, it is customary to use a needle height-gauge. In a typical gauge a needle point is slowly lowered by a micrometer screw until the point just touches the liquid surface. The instant of contact is detected either visually or electrically, and the micrometer reading at that instant gives the height of the liquid surface. Such gauges are regarded as accurate to within $\pm 0 \cdot 001$ in. It has been found, however, that with a non-conducting liquid that has become electrically charged, errors of $0 \cdot 025$ in. can easily occur.

A laboratory needle gauge was being lowered towards a surface of mineral oil in a 'Perspex' vessel, when it was observed that, when the needle was held at a height of about $0 \cdot 05$ in. above the oil surface, a rhythmic disturbance of the surface occurred immediately below the needle. The frequency of this disturbance was usually of the order of 1 c./sec.

Subsequent investigation revealed that the 'Perspex' vessel had become electrostatically charged when it was being cleaned immediately before being filled with oil, and that this was the cause of the disturbance. When an earth wire was brought into contact with the oil at the site of the disturbance, the disturbance ceased at once, only to start again (but with diminished vigour) when the wire was withdrawn.

When the oil was replaced by de-ionized water, which has a much lower resistivity than the oil, the phenomenon did not occur. After the oil had been allowed to stand exposed to the atmosphere for a few days, only very slight disturbances could be produced. This was due to the absorption of atmospheric moisture by the oil and the consequent decrease in resistivity; the oil was afterwards dried by prolonged agitation in a vacuum desiccator, and immediately it became possible to produce the disturbances again on the same scale as when the oil had been fresh.

Evidently the cycle of events is as follows: (1) When the oil is put into the charged container the charge slowly spreads across the surface of the oil. (2) When the needle is brought close to the oil, the charged oil immediately below is attracted towards it, thus producing a hump in the surface, in which the combined effects of gravity and surface tension are balanced by the electrostatic attraction. (3) The needle, being earthed, acts like a lightning conductor and the hump is rapidly discharged. (4) The hump collapses suddenly. (5) The electrostatic charge on the surrounding area spreads slowly over the discharged area, and the cycle begins again.

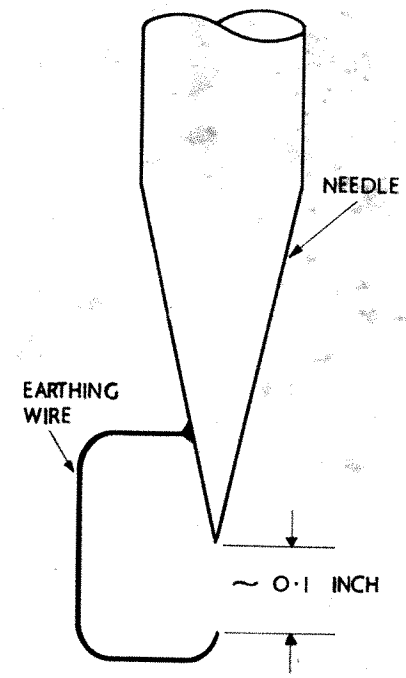

Fig. 1

Once started, this cycle of attraction and collapse is likely to continue for hours before the charge is completely dissipated.

When the needle is lowered closer to the surface of the liquid, a point must obviously be reached when the hump in the surface comes into contact with the needle. Contact once having been made, it is maintained permanently by surface tension. In the experiments described above, contact usually occurred when the needle was between $0 \cdot 020$ and $0 \cdot 025$ in. above the level of the surface.

There is thus a serious risk of erroneous readings when a needle gauge of the normal design is used to measure the level of a non-conducting liquid. This risk may be eliminated very easily by adding an earthing wire to the needle, as shown in Fig. 1.

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Finely Ground Quartz: Evidence against a 'Disturbed' Layer

BRISCOE *et al.*[1] discovered that the rate of solution of a finely ground quartz powder decreases slowly from an initially high value to a much smaller steady value. Kitto and Patterson[2] concluded that the effect could not be accounted for on the basis of particle size alone and attributed it to edge effects and the presence of a 'Beilby layer', presumably of amorphous silica. Further evidence of an amorphous layer has been reported by various authors using X-ray diffraction[3,4], electron diffraction[5], differential thermal analysis[6,7], rate of solution[8,9], and density[8,9]

measurements. Some, not wishing to commit themselves as to its exact nature, have called it a 'disturbed' layer. Estimates by a variety of methods[3,5-9] put the thickness of the layer at between 300 Å. and 1,500 Å.

Doubt was cast on the existence of an amorphous or non-quartz layer by the electron diffraction observations of Finch, Lewis and Webb[10] and of Heavens[11], and by the discovery that a similar decline in the rate of solution occurs in the case of vitreous silica[9].

Taking into account all the experimental results, King and Nagelschmidt[12] adopted a model of the quartz particle composed of a central core considered to be highly crystalline quartz, surrounded by a transitional layer about 300–600-Å. thick in which the highly crystalline structure of the core is supposed to change gradually to an effectively amorphous state near the surface. The surface itself is supposed to consist of a monolayer of silicic acid.

We were led to doubt the validity of this model by the ease with which electron diffraction patterns are obtained from finely ground quartz. The following observations were made as a test of the model.

(1) The electron diffraction patterns of numerous untreated ground quartz particles of diameter 1–5μ were compared with those of similar particles after leaching in 20 per cent hydrofluoric acid for 5 min. Collodion films, on which the electron beam was incident normally, were used to support the particles. The diffraction patterns of the untreated particles differed from those of the treated quartz in having a higher background, more intense haloes, and in many cases weak spotty rings. In other respects they were similar. The strong individual spectra were commonly observed to show marked asterism (Fig. 1 (inset)). Examination of a large number of patterns revealed no tendency for the asterism to be more pronounced normal to the radii joining the spectra to the zero order spectrum than in other directions. It was concluded that the effect was due to refraction of the electrons on entering and leaving the particles, and not to lattice strains or other crystal imperfections which would have caused arcing of the spectra normal to the radii.

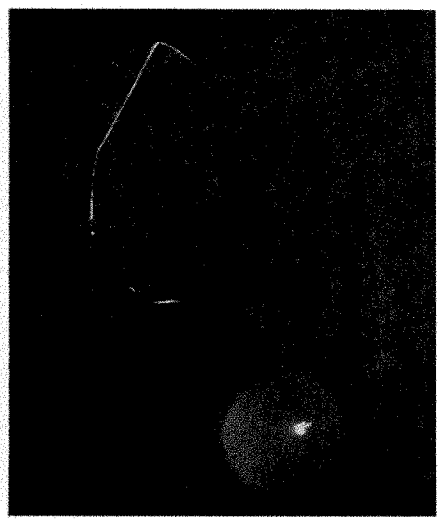

Fig. 1. Dark-field image of a quartz particle formed by one diffraction maximum (inset). The asterism of the diffraction maximum is due to refraction of the electrons

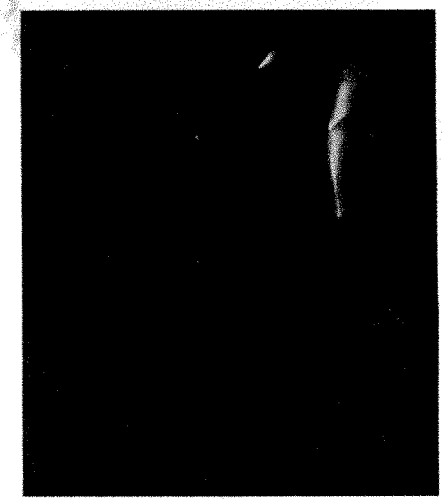

Fig. 2. Dark-field image of a particle treated with hydrofluoric acid, after shadowing with silica

(2) Dark-field images of the diffracting particles were formed in an electron microscope by using an eccentric objective lens aperture so as to accept only one diffraction maximum. The images show that the diffraction patterns are produced by transmission through thin edges of the particles (Fig. 1). Images of the untreated and of the treated quartz were found to be equally distinct. Shadowing the untreated quartz with silica at 45°, producing a layer of silica about 150 Å. thick in a direction normal to the plane of the supporting film, resulted in marked diminution of the clarity of the images, these becoming blurred in one direction (Fig. 2). This is believed to be due to inelastic scattering of the diffracted electrons in the silica layer. The effect was observed in nearly all cases where the particles had been coated with silica, but in no case was it observed with untreated quartz particles.

(3) Kikuchi N and L patterns from thin layers of quartz near the surface of the particles were observed. This was achieved by making carbon surface replicas of the particles using an etching time of 10 min. which resulted in some of the particles being incompletely removed from the replicas. Many remnants thin enough for the observation of N or L patterns were found. No differences of any significance were found between the patterns of the untreated quartz and those of the treated quartz. Twenty patterns of each were observed, and in no case were any rings or any arcing of the spectra observed.

In the light of the above observations the King-Nagelschmidt transitional layer or a 300-Å. layer of purely amorphous silica seems unlikely. A gradual transition from a crystalline core to an amorphous surface layer would presumably imply a reduction in the sizes of the crystallites and an increase in the disorder of their orientation with increasing distance from the core. A layer of this type would be expected to cause the following:

(*a*) pronounced arcing of the spectra, or rings of varying intensity along their length;

(*b*) an increase in the intensity of the background and of the haloes; and

(*c*) a marked diminution of the clarity of the dark-field images of the diffracting edges.

Effects (*a*) and (*c*) have not been observed. Rings have been observed in the diffraction patterns described in (1), but the intensity is roughly uniform along their length and not greater in the vicinity of the strong spectra, which would be the case if the above model were correct. We consider it more likely that the rings are produced by the numerous small particles which have been observed to cling to the surfaces of the larger particles[13]. Effect (*b*) has been noted in the observations (1) but could equally well be due to the numerous adhering particles which are thin enough to transmit electrons but are not orientated for Bragg reflexion.

We are of the opinion that the numerous small particles which are always found adhering to the larger particles of ground quartz, and which are extremely difficult to disperse, offer a plausible explanation of all the effects usually ascribed to an amorphous or 'disturbed' layer. This will be discussed in a more detailed account of this work to be published elsewhere.

We wish to thank Mr. P. H. Kitto for many valuable discussions and the Transvaal and Orange Free State Chamber of Mines for permission to publish this communication.

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Electrical Resistivity of Nickel Ferrite

UP to the present the only systematic investigation published on the semiconducting behaviour of ferrites is a study of cobalt ferrite, $CoFe_2O_4$, by Jonker[1]. In the case of other ferrites insufficient information of the basic structure of the material has impeded an understanding of the electrical properties. In the case of nickel ferrite it is known that these properties are closely related to a small deficiency, δ, of oxygen (a few tenths of 1 per cent) which occurs when the ferrite is formed in the sintering process. This may be represented by $NiO + Fe_2O_3 \rightarrow Ni^{++}Fe^{+++}_{2-2\delta}Fe^{++}_{2\delta}O^{--}_{4-\delta} + \frac{1}{2}\delta(O_2)$. The creation of iron ions with two valencies in the crystal lattice is known to lead to a marked lowering of activation energy of conduction electrons[2], and the resistivity of nickel ferrites therefore depends on the temperature and atmosphere of the sintering process and on the rate of subsequent cooling. To produce high-resistivity nickel ferrite it has been found desirable to sinter at relatively low temperatures (below 1,300° C.) in an oxygen atmosphere[3,4]; but it is very doubtful if a nickel ferrite with electrical properties representative of the stoichiometric material has so far been produced.

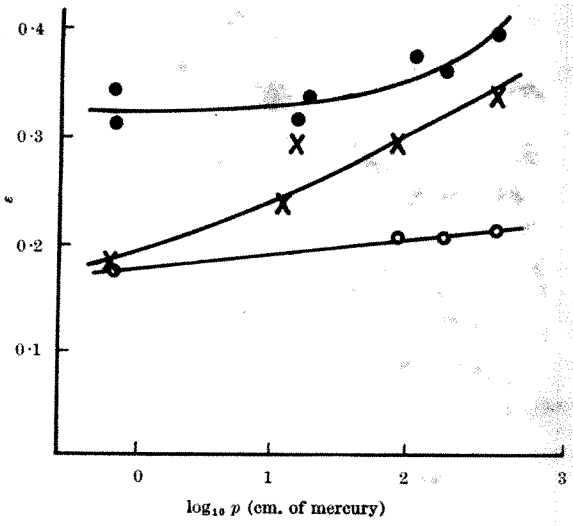

Fig. 1. Activation energy against $\log_{10}$ oxygen pressure for stoichiometric nickel ferrite. ●, 1,100° C.; ×, 1,150° C.; ○, 1,200° C. firing temperature

In order to investigate the influence of oxygen pressure during sintering on the electrical properties, a closed system was constructed which allowed specimens to be sintered in a quartz tube under various oxygen pressures. It was found that a pressure of up to about 6 atmospheres could be maintained at temperatures of 1,250° C.

A stoichiometric mixture of spectroscopically pure nickel monoxide and ferric sesquioxide was ball-milled for 24 hr., pre-fired at 800° C., milled again and then pressed into specimens which were fired under various oxygen pressures at 1,100° C., 1,150° C. and 1,200° C., respectively. Specimens were then slowly cooled (2 deg. C./min.). Firing times in each case were sufficiently long for the reaction to have been completed. This was judged from measurements of both magnetic moment and from the fact that a further period of firing did not alter the electrical resistivity. After surface grinding, resistivity measurements were made at d.c. and at frequencies of up to several Mc./s. and no significant dispersion was observed. The temperature dependence of resistivity could be expressed by the usual semiconductor equation[3] $\rho = A \exp \varepsilon/KT$. A was found to be in the range of 0·1–1 ohm cm. in each case and values of ε are plotted in Fig. 1 against the logarithm of oxygen pressure. Measurements of thermo-electric power showed that all specimens had negative Seebeck coefficients of about 2 to 3 × 10^{-4} V./deg. C. indicating n-type conductivity.

Specimens were also prepared from a mixture containing a nickel oxide excess which may be represented by $NiO + (Fe_2O_3)_{0\cdot95}$. The corresponding relationships of activation energy and sintering pressure are shown in Fig. 2. Thermo-electric measurements showed that in every case the conductivity is n-type on the low-pressure side of the peaks (Fig. 2) and p-type on the high-pressure side. Measurements of saturation moment were carried out with an accuracy of 1 per cent and showed that no detectable amount of nickel excess had entered the ferrite crystal lattice, this being in complete agreement

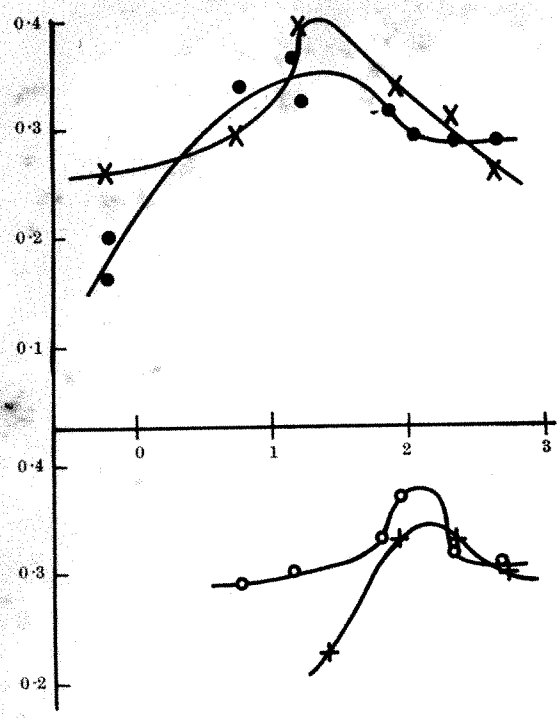

Fig. 2. Similar to Fig. 1 for nickel excess ferrite + 1,250° C. firing temperature

with the results of Derry *et al.*[4]. The magnetic measurements do not, of course, preclude a concentration of excess nickel ions in the ferrite lattice of less than 1 per cent, and indeed the most plausible interpretation of the results is that a small concentration of the excess nickel oxide has indeed been dissolved in the ferrite lattice giving rise to Ni^{+++} ions. Under high sintering pressure the ferrite loses an insufficient amount of oxygen to reduce all the excess nickel ions to a valency of two; the dominant conduction mechanism is now by nickel positive holes[1]. At sufficiently low sintering pressures more oxygen is lost than that needed to remove all trivalent nickel ions and some of the electrons released by the oxygen create divalent iron ions; specimens of this type are therefore n-type conductors. The peak in activation energy corresponds to a change of p- to n-type conduction and represents the condition where the number of oxygen atoms lost during sintering is equal to half the number of excess nickel atoms dissolved in the ferrite. As in the case of Jonker's results for cobalt ferrites, it is likely that the theoretical peak value in activation energy is somewhat greater than that shown in Fig. 2 on account of imperfect compensation and submicroscopic inhomogeneities in the specimens.

The results presented here lead to the following conclusions. In the process of nickel ferrite formation some loss of oxygen occurs even at 1,100° C., which is only slightly inhibited by the application of pressures up to 6 atmospheres. By introducing excess nickel into the ferrite lattice and by suitable adjustment of sintering pressure an approximately compensated nickel ferrite can be prepared in which the intrinsic activation process comes into effect. The systematic shift of the peak in activation energy to the higher-pressure region indicates that the loss of oxygen increases with sintering temperature.

We wish to express our gratitude to Prof. E. R. Andrew and Dr. D. Wooller for their encouragement in this investigation.

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VOLCANOLOGY

Drilling into Molten Lava in the Kilauea Iki Volcanic Crater, Hawaii

THE November 1959 eruption at Kilauea Iki, Hawaii, produced a lava lake more than 300 ft. deep containing about 45 million cubic yards of lava. An experiment was conducted to obtain knowledge of the problems encountered when drilling through the crust of the lake into molten rock, and to obtain as much volcanological data as possible.

On July 25, 1960, after drilling 19 ft., the crust of the lava lake was pierced, making possible temperature measurements of the molten rock, collection of gas samples emanating from the melt, and direct sampling of molten lava.

The experiment clearly demonstrated that it is possible to drill into hard rock at temperatures up to 850° C. with standard core-drilling equipment, using compressed air to cool the rock and to remove the cuttings. By using water to cool the rock and drilling with water periodically injected into the compressed air line, it is possible to drill with standard equipment into rock that has been at temperatures exceeding 1,050° C.

The first 14 ft. of the hole was drilled to 3·5 in. in diameter and cased to seal off possible communication with the surface. Vibration as a result of air drilling limited core recovery and diamond bits were badly damaged by heat and inadequate air circulation; otherwise, drilling proceeded rapidly. The remainder of the hole was left uncased and drilled to a 2-in. diameter. Drilling progressed more slowly due to the high temperatures encountered and also an increase in the rock density. At 15·5 ft. silver solder on the bits melted and core recovery was poor. Binding of threads on the drilling tools caused considerable difficulty; however, powdered graphite as a lubricant cured this trouble. At 16·8 ft. water was used to cool the hole and was periodically injected into the compressed-air line for additional cooling during drilling. This worked very well, and the drilling increased from 1·5 ft. in 8 hr. to 3·5 ft. in 3·5 hr. Core recovery remained poor, but there was little damage to the drill bit.

The crust-melt boundary was encountered at about 19 ft., and the melt was quite fluid at 20 ft. The air-and-water-vapour drilling coolant quenched a protective crust between the bit and the melt and further drilling did not cut this crust, but pushed it into the melt. At 19·5 ft. the bit and tools dropped

slowly in the hole of their own weight. A core of melt was then taken by cutting off circulation, allowing the silver solder to soften and the teeth on the bit to close inward. Circulation was restored and about 2 in. of melt was trapped in the bit. Sulphur from the outgassing melt was also deposited on the bit.

Gas samples were afterwards collected by John Naughton of the University of Hawaii, Wayne Ault of the U.S. Geological Survey, and me. It was also found that melt samples could be obtained by attaching a 'shoe', a tapered cylinder, to the drill rods and driving this into the melt by hand. The core melt thus obtained could then be tapped out of the shoe. At 20·4 ft. further removal of melt by sampling did not deepen the hole. In less than two days the lava had risen from 20·4 ft. to 18·7 ft. deep in the hole. The hole was then sealed with a capped stainless steel pipe. A platinum–platinum 90 per cent rhodium 10 per cent thermocouple package was installed in the pipe to study the cooling history at three points in the lava lake crust.

Difficulties were encountered in obtaining temperature data as the hole was drilled. Fig. 1 is a plot of the most reliable measurements. These measurements are preliminary and require further evaluation. The peak temperature of 1,064° C. was obtained with an optical pyrometer and is probably a little low due to some gas in the hole.

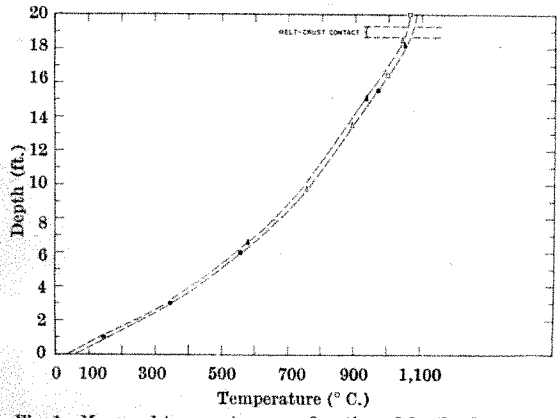

Fig. 1. Measured temperature as a function of depth of the hole. ●, Chromel-alumel thermocouple; △, platinum–platinum 90 per cent rhodium 10 per cent thermocouple; □, optical pyrometer; ▲, platinum–platinum 90 per cent rhodium 10 per cent 18 days after completion of hole

It is planned to run complete chemical and petrographic analyses on the core and melt samples. The gas samples will be analysed, oxygen-16 : oxygen-18 ratios will be determined on the water and carbon dioxide gases, and the deuterium and tritium content of the water will be measured. These will be compared with local rain and ocean water to determine whether they are primary gases or not. The hydrogen–water ratio of the gases and the ferrous oxide : ferric oxide ratio of the melt and crust samples will also be determined. Thermal conductivity will be measured on the crust samples, making possible a calculation of thermal conductivity of the crust material as a function of temperature and a calculation of heat-flow through the crust.

This work was conducted as part of the Plowshare Program supported by the U.S. Atomic Energy Commission. Details of the experiment, the results of the forthcoming analyses, and their implications will be published elsewhere.

Thanks are due to Dr. G. C. Kennedy of the University of California at Los Angeles, Dr. G. H. Higgins, and others at the Lawrence Radiation Laboratory for their interest in the investigation; Dr. G. A. Macdonald of the University of Hawaii and W. P. Bennett from this Laboratory for their participation; members of the Hawaiian National Park Service and the U.S. Geological Survey Volcanological Observatory for their kind co-operation; and the drilling contractor, Nat Whiton from Honolulu, Hawaii.

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GEOLOGY

Occurrence of Hydromagnesite in Sediments in South Australia

A prominent feature of the South Eastern Province of South Australia is the system of lagoons associated with a long narrow arm of the sea, the Coorong, formed by a receding and partly resubmerged coastline. In some of these lagoons, as well as in the shallow waters at the closed end of the Coorong, dolomite-calcite sediment is forming, apparently by direct precipitation from saline waters[1,2].

Recently, C. von der Borch examined the sediment in a lagoon which lies within a few hundred yards of the eastern edge of the Coorong from which it is separated by a belt of low sand dunes. Macroscopically the sediment closely resembles other fine-grained carbonate sediments of the region but was found in its surface layers to consist essentially of aragonite and hydromagnesite in approximately equal amounts. The proportion of hydromagnesite decreases with depth and has not been detected below about 9 in., at which level the sediment is essentially aragonite. Calcite then appears, and the proportion of aragonite diminishes to zero, after which dolomite makes its appearance. At a depth of 2 ft. the sediment consists essentially of calcite and dolomite.

This mode of occurrence of hydromagnesite appears to be unusual, and is of particular interest in South Australia where the origin of sedimentary magnesite associated with dolomite of Proterozoic age has presented a problem. These rocks occur mainly in the Flinders Ranges and have recently been described by B. G. Forbes[3]. They show sun-cracks and ripple marks, and may have been formed by sedimentary processes similar to those in progress in the shallow lagoon in the South Eastern Province to-day.

Work on the geochemistry and mineralogy of the hydromagnesite sediment is proceeding.

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OCEANOGRAPHY

Occurrence of *Calanoides carinatus* (Kröyer) in the Plankton of the Gulf of Guinea

THERE are fairly regular fluctuations in the temperature of the water of the Guinea Current off the coast of tropical West Africa between Cape Palmas and Lagos[1,2]. Minimum temperatures are usually observed during the months of July–October. The fall in temperature is most pronounced in the coastal waters between Accra and Lome. Observations carried out by Howat[2], from June 1943 until September 1944 at a station about 1½ miles from the shore off Accra, showed that the variation in the temperature of the surface water exceeded 10 deg. C., with minima of 19·0° C. during August 1943 and 19·8° C. during August 1944. This colder water was rich in phosphate and its appearance was accompanied by a flowering of diatoms.

During 1952, the R.V. *Cape St. Mary* made a series of exploratory fishing voyages in the coastal waters between Cape Verde and Fernando Po for the West African Fisheries Research Institute. During these surveys the opportunity was taken to obtain information on the quantity and composition of the zooplankton. Hydrographic and plankton sampling was carried out along a series of transects running from the coast to the edge of the shelf. At each station water samples for temperature and salinity determinations were taken at standard depths, and plankton samples were collected with 18-in. diameter plankton nets (20 meshes per cm.) hauled vertically from the bottom to the surface.

The stations worked included seventeen between Fernando Po and Lagos, during July, and twenty-five between Lagos and Cape Three Points in August. The distribution of surface temperature during the survey is illustrated in Fig. 1*a*. There was a decrease in temperature from east to west with a maximum of 27·8° C. between Fernando Po and the mainland and a minimum of 22·1° C. close to the coast off Cape Three Points. Greatest quantities of zooplankton were found along the edge of the shelf in the region where the surface temperature was less than 25° C. These higher zooplankton displacement volumes were mainly due to large numbers of the large copepod, *Calanoides carinatus* (Kröyer), the distribution of which is shown in Fig. 1*b*. The majority of individuals were stage V copepodites; but a few adults were also observed at most stations. In contrast to the usual colourless appearance of preserved copepods from tropical regions, these specimens of *C. carinatus* contained orange globules of oil.

Table 1. MEAN NUMBERS OF THE MORE COMMON SPECIES OF COPEPODA IN THE SAMPLES FROM VERTICAL HAULS TAKEN FROM 100 M. TO THE SURFACE

	Cape Three Points to River Volta	River Volta to Lagos	Lagos to Fernando Po
Calanoides carnatus (Kröyer)	3,879	11	—
Nannocalanus minor (Claus)	13	10	7
Undinula vulgaris (Dana)	3	3	16
Eucalanus pileatus Giesbr.	137	303	12
Eucalanus monachus Giesbr.	196	413	+
Paracalanus aculeatus Giesbr.	97	74	24
Paracalanus parvus (Claus)	1,416	288	57
Clausocalanus arcuicornis (Dana)	174	53	+
Clausocalanus furcatus (Brady)	41	442	23
Euchaeta marina (Prestand.)	3	15	19
Centropages chierchiae Giesbr.	239	379	7
Centropages furcatus (Dana)	41	442	23
Temora stylifera (Dana)	1,027	591	42
Temora turbinata (Dana)	1,968	1,965	+
Lucicutia flavicornis (Claus)	22	8	10
Oncaea venusta Phillipi	784	935	36
Corycaeus africanus F. Dahl	—	74	15
Corycaeus giesbrechti F. Dahl	300	735	62
Total Copepoda	10,709	7,191	575
Total zooplankton	11,602	8,973	769

+, Present.

Table 1 illustrates the relative abundance of the more common copepod species in hauls taken from 100 m. to the surface along three sections of the shelf. *C. carinatus* was the dominant copepod between Cape Three Points and the Volta, but was not recorded between Lagos and Fernando Po where the

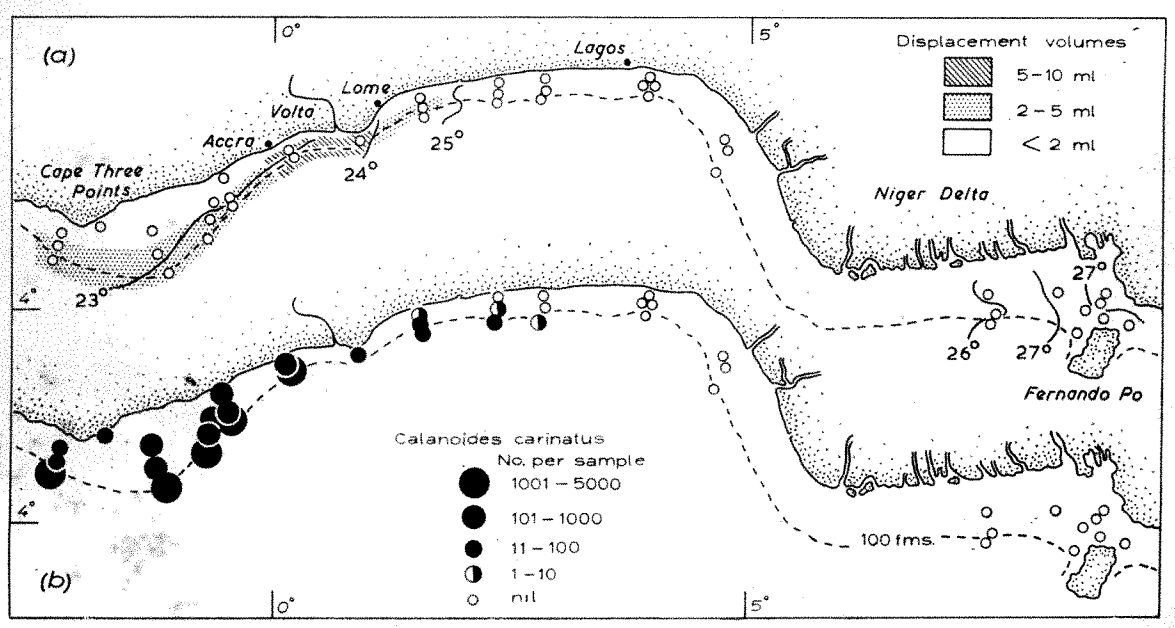

Fig. 1. *a*, Stations, surface temperature and zooplankton displacement volumes; *b*, distribution of *Calanoides carinatus*

zooplankton was sparse and no species clearly dominant.

In the Atlantic, *C. carinatus* is widely distributed between 47° N. and 37° S., although it is by no means a common species[3]. It was not recorded by Scott[4] in his monograph on the Entromostraca of the Gulf of Guinea collected during the cruise of the *Buccaneer* in 1886 although this expedition covered much the same area as that sampled by the *Cape St. Mary* sixty-six years later. However, the results of this latter survey suggest that the distribution of the species is, in some way, related to colder surface water. The cruise of the *Buccaneer*, between Cape Three Points and Lagos, took place during January and February and Scott's records showed that surface temperatures at this time exceeded 27° C.

The distribution of zooplankton along this coast is of interest in connexion with the fishery for *Sardinella aurita* Valenciennes. This fish is rare in Nigerian waters but abundant off the coast of Ghana[5], where high landings correspond closely to the period when the surface temperature is below 25° C. (ref. 6). Recent work on *S. aurita* has shown that its chief food groups are copepods together with other planktonic Crustacea, and that aggregations are often closely related to the available food supply[7,8].

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Internal Waves and Waves of Sand

A DESCRIPTION has been given of some large sand waves on La Chapelle Bank which lie parallel to the general direction of the edge of the continental shelf[1]. They occur within a zone about 10 miles wide, have a mean separation of 2,800 ft. and are up to 40 ft. high. Berthois[2] believes them to be fossil ridges while Cartwright[3] has shown in some detail how they could be formed by stationary waves, which develop in the thermocline as the tidal streams, moving landwards, feel the constraining influence of the shelf. These would be equivalent to lee-waves found on the down-wind side of a mountain.

Internal waves (not necessarily stationary) of similar amplitude and wave-length to the sand waves are the only possible explanation of the abnormal oscillation of a scattering layer shown in Fig. 1. The pattern was recognized on August 15, 1959, and on August 3, 1960, when R.R.S. *Discovery II* passed over the bank using a 36-kc./s. narrow-beam echo sounder. The new information appears to support Cartwright's theory, and adds interest to the study of the internal waves in the western approaches to the English Channel.

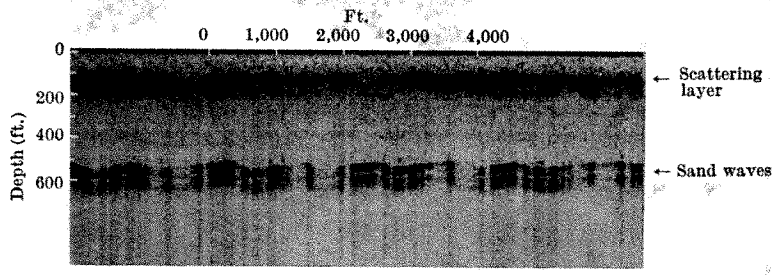

Fig. 1. An echo sounder record over La Chapelle Bank, showing internal waves (revealed by a well-developed scattering layer) overlying sand waves of similar size. The record was taken approximately at right-angles to the crests of the sand waves and its mid-point is situated about 8 miles from the oceanward side of the bank. (The vertical white stripes are due to defective recording paper)

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METALLURGY

'Intrinsic Stress', σ_0, in the High-Temperature Behaviour of Metals

THE governing relation between strain ε and stress σ for the behaviour of metals at temperatures above about half the melting point seems to be of the form :

$$\frac{d\varepsilon}{dt} = \frac{1}{E}\frac{d\sigma}{dt} + M \sinh \frac{\sigma}{\sigma_0}$$

where E is the elastic modulus and M is a function of temperature[1]. The quantity σ_0, which has the dimensions of stress, is a constant for a metallurgically stable material and is independent of temperature. Its value does, however, vary considerably, depending on the presence of impurities or of alloying material.

The constancy of σ_0 with temperature has been a mystery, but a recent paper[2] has perhaps thrown some light on the matter. In this paper the authors relate creep to the presence in the metal of so-called 'bad sites' which impede the free movement of dislocations. These bad sites are provided by crystal imperfections, impurities, and alloying elements. At these sites there develops a stress concentration which is relieved by diffusion of matter in the vicinity of the site. Such a movement of matter permits the activation energy for creep to be rationally identified with the activation energy for self-diffusion in agreement with experimental observations.

The authors, who call σ_0 an 'intrinsic stress', have attempted to compute its value on the basis of the postulated material with its bad sites. They find that :

$$\sigma_0 = \frac{nk\theta}{v}\varphi^2$$

Table 1. COMPUTED VALUES OF φ

Material	θ (° K.)	V (c.c.)	$\bar{\sigma}_0$, psi	c	b	$\sigma_0 = \bar{\sigma}_0 (1 + cb)$, psi	$\sqrt{\frac{V}{\theta}\sigma_0}$	σ	Reference for value of σ_0
Gamma iron (0·44 per cent carbon)	420	7·1	835		0	835	3·75	0·0625	3
Low carbon steels (up to 0·2 per cent carbon)	420	7·1				1,300	4·68	0·078	4
Lead (coarse-grained)	88	18·8	96		0	96	4·52	0·0752	3
Aluminium (99·987 per cent)*	390	10·0	382		0	382	3·12	0·0520	3
Aluminium (99·987 per cent)†	390	10·0	250		0	250	2·53	0·0421	2
Aluminium plus 1 per cent magnesium	390	10·0	250	140	0·01	600	3·92	0·0653	2
Aluminium plus 2 per cent magnesium	390	10·0	250	140	0·02	950	4·94	0·0825	2
Aluminium plus 2·32 per cent zinc (7075 alloy)	390	10·0	250	700	0·0232	4,300	10·5	0·1745	1

* Annealed 30 min. at 733° K.; mean grain diameter, 0·21 mm. † Mean grain diameter, 0·25 mm.

where n is the order of the highest vibrational level which is sufficient to avoid holding up a dislocation (since this communication is concerned with elevated temperatures, n is taken as 3); k, Boltzmann's constant, $1 \cdot 37 \times 10^{-16}$ erg/sec.; θ, the Debye temperature, ° K.; v, the volume per atom (c.c.); φ, the mol fraction of bad sites.

For computational purposes it is convenient to replace v by:

$$v = \frac{V}{N}$$

where V is the atomic volume and N is the Avogadro number, so that:

$$\sigma_0 = \frac{3Nk\theta}{V} \varphi^2$$

For a given material, the intrinsic stress from this formula is thus independent of temperature and varies only with the concentration of bad sites. (It may be noted that σ_0 as defined above is not a stress as such, but is thermal energy per unit volume.)

It is known experimentally that σ_0 increases linearly with concentration of alloying element, at least for small concentrations (see, for example, Fig. 8 of ref. 2). Thus one may write:

$$\sigma_0 = \bar{\sigma}_0 (1 + cb)$$

where $\bar{\sigma}_0$ is the value of σ_0 for the pure metal; b is the concentration of the alloying element; c is a constant.

In recent years, enough values of σ_0 have become known for various materials with sufficient accuracy from phenomenological observations of creep and related behaviour at elevated temperatures to enable these values to be used with confidence in calculations. For the purposes of this communication, these values of σ_0 are considered as known.

The question therefore presents itself in the form: Are the values of φ required to account for these known values of σ_0 reasonable in magnitude? On solving for φ, the mol fraction of bad sites, it is found that:

$$\varphi = \sqrt{\frac{V}{3Nk\theta} \bar{\sigma}_0 (1 + cb)} = 0 \cdot 01665 \sqrt{\frac{V}{\theta} \bar{\sigma}_0 (1 + cb)}$$

with $\bar{\sigma}_0$ expressed in lb./sq. in. and V in c.c.

Table 1 shows some computed values of φ. In the case of the lightly alloyed metals, the values of V and θ used were those for the pure metals.

Thus for 'pure' metals, out of 15–20 sites, one will be 'bad'. Note that the concentration is about the same for gamma iron and for lead, two widely different metals. The process of alloying aluminium with 1 per cent of magnesium increases the number of bad sites by about 50 per cent over the number for the original pure metal, while the addition of 2 per cent magnesium doubles the original number of bad sites. For a practical aluminium alloy like 7075 which uses 2·32 per cent zinc, the number of bad sites is apparently as high as one in every six.

It is noticed that at the temperature-range under discussion, the dislocation locking force by chemical interaction of the solute and solvent atoms accounts for a large portion of resistance to dislocation movement (ref. 5). It is known that this locking force is strongly dependent on concentration. Thus it appears that φ may be an expression of the effectiveness of this locking force.

The explanation by the authors of ref. 2 thus seems to furnish a rational picture of the nature of the 'intrinsic stress' σ_0.

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CHEMISTRY

Liquid Chromatographic Separation of Mixtures of Polymers and Mineral Oil

Porath and Flodin[1] have shown that macromolecules in aqueous solutions may be separated from low molecular weight compounds by liquid chromatography using a cross-linked dextran ('Sephadex') as the stationary phase, and water as the mobile phase. It has now been found in these laboratories that polymers dissolved in mineral oil can be separated by a similar chromatographic technique. Small pieces of thin vulcanized natural rubber latex are used as the stationary phase, and a light paraffin hydrocarbon as the mobile phase.

The column used was 21 mm. in diameter, and an 82 cm. length was packed tightly with small pieces of rubber; for convenience pieces of surgeons' finger-cots ('London' brand, supplied by Osborne Garrett and Co., Ltd., 51/55 Frith Street, London, W.1) were used. The area of the pieces of unswollen

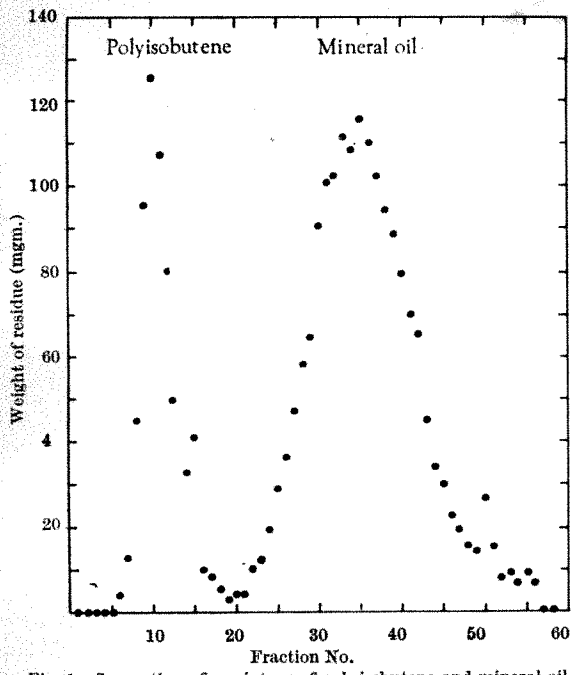

Fig. 1. Separation of a mixture of poly*iso*butene and mineral oil by liquid chromatography using rubber as the stationary phase and *n*-heptane as the mobile phase

rubber varied from less than 1 to about 200 sq. mm., the average size being about 15 sq. mm. The rubber was washed with *n*-heptane before being placed in the column, *n*-heptane being also used as the mobile phase. Under a head of 10 cm. of solvent the flow-rate was about 50 ml. an hr. The sample (about 250 mgm.) dissolved in 5 ml. of *n*-heptane was placed on top of the rubber packing. After all the sample had passed into the packing, further solvent was added, and the flow-rate adjusted to 10–15 ml. an hour. Fractions of 6 ml. were collected, the solvent being evaporated from each fraction and the residue weighed. A graph showing the separation obtained with a mixture of poly*iso*butene (average molecular weight = 18,000) and mineral oil is shown in Fig. 1. The weight per cent of poly*iso*butene found was 25·0 compared with 21·9 found by another method; 98·2 per cent of the material placed on the column was recovered. The rubber is slightly soluble in the *n*-heptane; about 0·2 mgm. is found in a 6 ml. fraction.

The separation is presumably due to the swollen rubber acting as a type of molecular sieve. The relatively small mineral oil molecules are able to diffuse into the rubber and are thus delayed during their passage through the column. This explanation is supported by Hill and Munsell's[2] observation that mixtures of polymers and mineral oil dissolved in light paraffin hydrocarbons can be separated by dialysis using a rubber membrane. Other types of polymers in solution in mineral oil have also been separated.

The Directors of Esso Research Ltd. are thanked for giving permission to publish this communication.

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Decomposition of Water by Light

We wish to direct attention to two simple cases in which the decomposition of water (or some other oxidation-reduction reaction) can be effected by light of practically any wave-length, and which may play some part in Nature[1,2].

The experimental details of these arrangements have already been described[3,4]. A novel aspect of these experiments is that an organic crystal acts as a photovoltaic and a photoconductive device. In our case, an anthracene crystal was placed between, and separated, two 1 *M* sodium chloride solutions, which acted as transparent electrical contacts to each face of the crystal. These solutions were then connected to each other by an external wire. A current flowed in the external circuit when the crystal was illuminated on one side by 3650 Å. light, as a result of the production of a photo-voltage.

If the crystal had merely been immersed in the salt solution, with no external wires, there would still have been a flow of current through the salt solution, producing in this case hydrogen at the illuminated face and oxygen at the unilluminated face. In other words, the suspension in a salt solution of material capable of exhibiting a photovoltaic effect, and the subsequent illumination of this material alone will lead to the decomposition of the water into hydrogen and oxygen. The wave-length at which this will occur will depend entirely on the action spectrum of the photovoltaic material.

This decomposition of water is, of course, simply an electrolysis, which will take place even at voltages much smaller than the decomposition potential of 1·7 volts, a fact which is sometimes overlooked. More important is the fact that in our case no special photovoltaic device containing a *p–n* junction or special electrodes was necessary for such a decomposition. The pure material, in contact with water, and exposed to strongly absorbed light, will develop a photovoltage, a current, and consequently will decompose water. This voltage is produced by an internal concentration gradient of charge carriers, which is brought about by the inhomogeneous excitation of the organic material. The light is practically completely absorbed in a thin layer adjacent to the illuminated side of the organic material. No special layers and no asymmetrical electrodes are required. This is the first process to which we wish to direct attention.

The second process we envisaged is quite different and uses a chemical reaction plus light. If the electrodes in the arrangement described above are asymmetric, as would be the case if the composition of the electrolyte were different on both sides of the organic material, or if the two faces of the crystal were different from each other, an electrochemical potential would be set up across the crystal; but only an extremely small current would flow in the dark as long as the organic material is non-conductive. If now the organic material is illuminated with light that is either uniformly or inhomogeneously absorbed and thus become photoconductive, a current will flow driven by the electrochemical voltage, and this current would decompose the water. Here the effect of the light is only to make the organic material conductive. Of course, both the photovoltaic and the conductive effects could occur in the same unit and the respective currents produced could either add or subtract, depending on the relative polarity of the photovoltaic and electrochemical potentials.

The fact that a pure organic material suspended in water can decompose the water under the action of strongly absorbed light should be an important consideration in those theories which propose the intervention of an electronic mechanism in the early stages of photosynthesis[6]. It would be expected, of course, that in Nature the photosensitive material would be more highly adapted and efficient than in our laboratory experiment.

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The Concerted Mechanism in Acid-Base Catalysis

THE velocity, v, of reactions which exhibit general acid-base catalysis in carboxylate buffers is generally assumed to conform to the equation:

$$v = k_W[H_2O] + k_H[H_3O^+] + k_{OH}[OH^-] + k_{HA}[HA] + k_A[A^-] \quad (1)$$

where the various catalytic constants, k, are differentiated by their subscripts. However, Dawson and Spivey[1] reported in 1930 that the quantitative description of the rate of enolization of acetone, as measured by its iodination in acetate buffers, required an additional cross-term $k_X[HA][A^-]$. The experimental result was substantiated in 1953 by Bell and Jones[2], who also found similar cross-terms, which may account for up to 20 per cent of v, for trimethylacetate and glycollate buffers. These data are widely considered to be the sole evidence[3,4] for the occurrence in aqueous solution of a catalytic mechanism, which requires the simultaneous presence of an acid and a base in the transition state complex. The process has been variously described[3,4] as 'concerted', 'synchronous', 'push-pull', 'ternary' (with reference to the hypothetical number of species in the transition state) and 'bimolecular' (with reference to the hypothetical number of catalytic molecules).

Although Dawson and Spivey[1] appreciated that the kinetic data are consistent with the formation of the hydrogen diacetate ion, HA_2^-, in aqueous solution, the possible existence of this species has been repeatedly discounted[4–6]. Preliminary reports[7] of the existence of the hydrogen diacetate ion and three homologues in a 3 *M* sodium ionic medium at 25° C. have been given elsewhere. Values of the association constants for the relevant reactions:

$$H^+ + A^- \rightleftharpoons HA \quad K_{11} \quad (2)$$
$$HA + A^- \rightleftharpoons HA_2^- \quad K_{12} \quad (3)$$
$$H^+ + HA_2^- \rightleftharpoons H_2A_2 \quad K_{22} \quad (4)$$

under these conditions are given below.

Acid	log K_{11}	log K_{12}	log K_{22}	
$HOCH_2CO_2H$	3·920 ± 0·005	−0·53 ± 0·02	3·16 ± 0·03$_5$	(J. D. E. Carson)
$MeCO_2H$	5·014 ± 0·009	−0·34 ± 0·03	4·63 ± 0·01	(D. L. Martin)
Me_3CCO_2H	5·327 ± 0·005	~ −0·14	~ 5·33	(J. J. Clarke)

The original potentiometric evidence for the above equilibria in the acetate system has now been substantiated by calorimetric titrations, and the enthalpies and entropies of association have been calculated[8]. The analogous equilibria have also been characterized potentiometrically in eleven other monocarboxylate buffer systems[7,9].

As the concept of an inert ionic medium[10], which effectively controls activity coefficients, has not been generally accepted, it may be noted that dimerization constants, referring to the conventional thermodynamic standard state in aqueous solution, have also been reported[11] for seven monocarboxylic acids. If our general conclusion that the first acid dissociation constants of the monomeric and dimeric acids are of the same order of magnitude be accepted, then it may readily be confirmed that appreciable concentrations of HA_2^- ions do indeed exist in concentrated buffers.

Accordingly, there is no unambiguous experimental evidence for the concerted mechanism in aqueous solution. Dawson and Spivey's original hypothesis[1] that HA_2^- ions are catalytically active is simpler than the hypothesis of a bimolecular catalytic process and a ternary transition state complex.

The term k_X may readily be shown to equal $k_{HA_2}K_{12}$. On the reasonable hypothesis that the secondary salt effect is zero for reaction (3), we may combine our values of K_{12} with Bell and Jones's catalytic constants[2]. We find 10^6k_{HA}, 10^6k_A, $10^6k_{HA_2}$ to be 5, 15, 44 for acetate; 4·4, 25, 64 for trimethylacetate; and $10^6k_{HA_2} \approx 35$ l.mole^{-1} min.$^{-1}$ for glycollate at an ionic strength of 0·2 and 25° C. Hence, the proton *bis*monocarboxylate ions appear to be more effective catalysts than the monomeric acids and carboxylate ions in enolizing acetone. Bell and McCoubrey[12] have reported that the iodination of acetone is also catalysed by the analogous ion, HF_2^-, which they consider to function as an acid catalyst. Correlations of the available data suggest that the HA_2^- ions are functioning as base catalysts. However, they are more effective than would be expected on the basis of the Brönsted relationship for the monomeric bases A^-. It may well be that they are really polyfunctional catalysts, and that the transition state complex has the cyclic structure proposed by Swain and co-workers[3].

Finally, it may be stressed that equation (1) can only be valid for very dilute buffers. For concentrated buffers, (1) might be expected to contain not only the cross-term under discussion, but also a further term $k_D[HA]^2$. The concentrations of the dimeric monocarboxylic acids H_2A_2 in concentrated buffers with a high ratio of acid to salt are of comparable magnitude to the concentrations of the HA_2^- ions in 1 : 1 buffers. The dimers are, moreover, in the open form in aqueous solution and not cyclic[7,8]. A complete analysis of more extensive and precise

kinetic data would follow the principles outlined elsewhere[13].

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Spectra of Tetrahedral Inorganic Complexes

IN the course of work on the spectra of tetrahedral inorganic complexes we have obtained two important types of information, both of which are specially significant for the interpretation of the physical properties of these complexes. The first is the magnitude of the ligand field appropriate to these complexes, and the second is the nature of the inorganic complex–solvent interactions.

Following the recent work of Gill and Nyholm[1], it is now possible to obtain authentic simple tetrahalogeno-complexes of manganese, iron, cobalt and nickel. These have been shown[2] to be essentially tetrahedral except possibly for some slight distortions which are not important to this communication. It proved, however, somewhat more difficult than anticipated to obtain the spectra of these complexes because of the large solvent–complex interactions which were observed in different supposedly 'inert' organic solvents such as nitromethane, dimethylformamide (DMF), dimethyl sulphoxide (DMS) and dimethylacetamide (DMA).

Even nitromethane solutions of the $CoCl_4^{2-}$ ion (with the triphenylmethyl arsonium cation) show departures from Beer's law which are due to the presence of such species as $CoCl_{4-n}X_n$, X being a solvent molecule, and for solutions of the $NiCl_4^{2-}$ complex the degree of solvation is very large. Not only tetrahedral species occur, however, for in dimethylformamide as solvent there is an octahedral–tetrahedral equilibrium which lies almost entirely on the octahedral side for solutions of the $[NiCl_4]^{=}$ complex and on the tetrahedral side for the analogous manganese, iron and cobalt complexes. In dimethyl sulphoxide the nickel complex is present entirely as the octahedral form.

The complexing power of these solvents is such that we have been able to isolate complexes of many types, including $[M(DMF)_6](ClO_4)_2$ and $MCl_2(DMF)_2$, and, by studying the effect of chloride ion addition to the octahedral perchlorate, we have been able to determine the extent of solvation. This has previously been done in alcoholic solutions[3,4], and recently some complexes with dimethyl sulphoxide have been isolated[5], but the equilibria in non-hydroxylic solvents have not previously been understood.

Briefly, on addition of triphenyl methyl arsonium chloride to $[Co(DMF)_6](ClO_4)_2$, the latter is at first transformed into the species $CoCl_3DMF^-$ without any other detectable intermediates; and addition of further chloride, up to a molar excess of about 10 : 1, converts a large part of this into $CoCl_4^{2-}$.

The behaviour of $[NiCl_4]^{2-}$ in dimethylformamide solution (and dimethylacetamide and dimethyl sulphoxide) is much more complicated, since nearly all the solute is present as an octahedral form in the absence of excess chloride. The equilibrium is strongly dependent on temperature, higher temperatures favouring the various, presumably tetrahedral but perhaps square, species; there are at least three and possibly four of these which occur in the solution, together with at least two octahedral complexes. Complete analysis of the spectrum is very difficult, however, because the spectra of the two stereochemical species overlap one another considerably, as do also the various tetrahedral spectra. Even in nitromethane, which is found to be the least solvating medium, the $\varepsilon_{max.}$ values of $[NiCl_4]^{2-}$ solutions are increased by nearly 30 per cent when excess chloride ion is added and a spurious band is eliminated at the same time.

The above synopsis emphasizes the need for caution in ascribing absorption bands of complexes in solution to any particular species, unless the absence of solvation has been clearly demonstrated.

The spectra of the tetrahedral species yield very interesting information concerning the magnitude of $\Delta(= 10Dq)$ for tetrahedral halide complexes, and in Table 1 we have summarized the results found for the chlorides of manganese[14], cobalt and nickel.

Table 1

Config. of free ion	Complex	Absorption maxima (cm.$^{-1}$) Experiment	Absorption maxima (cm.$^{-1}$) Calculated	Δ in cm.$^{-1}$
d^5	$MnCl_4^{2-}$	21650 22520 23200 23420 26550 27330 28090 35550 37100	21850 22350 23150 (23420) 27500 27200 (28090) (35550) 35730 36450	2650
d^7	$CoCl_4^{2-}$	?5800 14415 14965 15580 15745 16295	3250 (5850) 14900	3250
d^8	$NiCl_4^{2-}$	? 7550 14180 15170 16255	4000 (7500) 14200	3650

Note. In Table 1 the figures in brackets are used as parameters to calculate the other frequencies. Also, except for manganese, all the transitions listed are spin allowed. It will also be noted that only one visible band is listed instead of many for the cobalt and nickel complexes. The other bands are usually (ref. 6) assigned as partner spin-orbit components of the main band, but for cobalt there are too many of them, and in both cases they are too far apart (ref. 7) to be due simply to this, so that there are still features requiring explanation.

Some rough estimates of Δ for tetrahedral halides of manganese, cobalt and nickel have been given previously[10–13], but these have been based either on incomplete experimental evidence or else upon spectra which have been erroneously ascribed to the assumed species.

Thus we have been unable to confirm the usually quoted[10,11,15] value of 6,300 cm.$^{-1}$ for the $^4T_1(F) \leftarrow {}^4A_2(F)$ transition in $CoCl_4^{2-}$. The infra-red spectrum has been examined in this region by Dr. C. Barraclough, who finds a very broad band with its maximum in the range 5,800–5,500 cm.$^{-1}$, but at least below 6,000 cm.$^{-1}$. Such a value leads to a notable

reduction of Δ from the 3,750 cm.$^{-1}$ provisionally estimated by Orgel[10] and the 3,500 cm.$^{-1}$ used by Ballhausen and Jorgensen[11]. The molecular extinction coefficients given by Orgel[10] are also too large by a factor of five.

We have also been unable to confirm the spectrum claimed[12] for $NiCl_4^{2-}$, which was based on bands found in the spectrum of a complex melt; we consider that the melt spectrum belongs to some other (perhaps essentially square or tetrahedral) species of nickel halide, since it closely resembles a spectrum we obtained when anhydrous nickel chloride was dissolved in dimethylformamide, dimethylacetamide or dimethyl sulphoxide. The spectrum of the $NiCl_4^{2-}$ species in a 'Nujol' mull has one broad band with a maximum between 7,500 and 7,600 cm.$^{-1}$, and on simple crystal field theory it is impossible to account for a band at that energy unless a value of Δ larger than 4,000 cm.$^{-1}$ is used. From other compounds this seems too large, and it can be reduced to about 3,650 cm.$^{-1}$ if the complete treatment including spin-orbit interaction[7] is used for the calculations. Even this value seems large, and it may be that there are relatively large non-cubic components of the perturbing field in this molecule because of departures from a perfectly tetrahedral structure.

The values of Δ for cobalt and manganese are close to one-third the value of Δ(octahedral) for the hexahydrates. If, as has been suggested[9], the *Dq* for Cl^- is only 75 per cent that of water, then the theoretical ratio of 4/9 between the octahedral and tetrahedral Δ values would be well supported by experiment.

A complete report of this work is now being prepared for publication.

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BIOCHEMISTRY

A Possible Biochemical Mechanism for Memory

IN a recent paper[1], Leo Szilard has shown that a system consisting of an enzyme, an enzyme-forming apparatus and a repressor may be able to exist in two stable states, provided the combining energies between the various components of this system lie within certain ranges of magnitude. The two stable states which can exist contain either high or low concentrations of the enzyme. If the concentration of the enzyme or the repressor is changed by external manipulation, the system returns to one or the other of the stable states. Such a system was termed 'para-constitutive' by Szilard, and its possible biological significance in differentiation and antibody formation[2] was suggested by him.

I should like to direct attention to another possibility, namely, that a para-constitutive system, the components of which are at this time beyond conjecture, may constitute the unit of memory in the brain. A change from one to the other of the two stable states would correspond precisely to the binary memory components used in computors. Since a human brain cell may contain as many as 10^6 genes, as estimated by Szilard for other human cells, a very large number of binary units per brain cell seem possible. It appears conceivable that one might obtain experimental information on the existence of such systems by the careful analysis of brain constituents as a function of the number of memory impulses to which the brain was exposed. A brain exposed to a large number of sensory stimuli would be expected to have different concentrations of the components of the postulated system from a brain carefully shielded from such stimuli.

I should like to suggest that 'para-constitutive' systems may have numerous other biological applications, and that the recognition of their existence appears to be one of the most important biological hypotheses made in recent times.

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Heterogeneity of Fatty Acids from Royal Jelly

THE presence of hydroxy fatty acids as the major component of the lipid portion of royal jelly was indicated many years ago by Townsend and Lucas[1] and was confirmed recently by Butenandt and Rembold[2]. The latter authors characterized the major component as 10-hydroxy-2-decenoic acid. A *trans* configuration has been assigned to the double bond[3,4]. This unusual fatty acid has been found also in the food of worker bee larvæ[2] and in the mandibular glands of worker bees[3,5], but appears to be absent from pollen and other bee food. Unusual biological activity has been ascribed to the substance by Blum *et al.*[6] and by Townsend *et al.*[7].

Several chromatographic methods have been employed in our Laboratories for a careful examination of the chloroform-soluble portion of lyophilized royal jelly. The results have revealed that the lipid portion is a mixture which is resolved with difficulty and is somewhat more complex than has been previously supposed. A large fraction of the royal jelly lipids consists of free fatty acids. Chromatography of the chloroform extract on a silicic acid adsorption column separated the major acidic components into three fractions. The first of these consists of decandioic acids, the second consists of several monohydroxy monocarboxylic acids, and the third consists principally of dihydroxy monocarboxylic acids. Each fraction was separated further by silicic acid partition chromatography, paper chromatography, and chrom-

atography of the methyl esters in the vapour phase employing a silicone stationary phase.

The decandioic acid fraction consists of roughly equal parts of two acids that were separated by partition chromatography using 1 *M* citrate buffer, *p*H 5·75, on silicic acid as the stationary phase and a gradient of butanol-1 in chloroform as the moving phase. The methyl esters were also separated by vapour-phase chromatography. One of these compounds had chromatographic properties and melting point identical with those of sebacic acid. The other compound had properties identical with those reported for 2-decen-1,10-dioic acid. On reduction with hydrogen in the presence of platinum it gave sebacic acid. This confirms the work of Brown and Freure[4], who also reported the presence of these substances in royal jelly.

The hydroxy acid fraction contained at least six components, as judged by vapour-phase chromatography of the methyl esters. A major component that constitutes at least 80 per cent of this fraction was obtained in a fairly high state of purity (95 per cent or greater homogeneity, judged by vapour-phase chromatography) by careful chromatography on silicic acid. This material melts at 61·5–62° C. (corrected) and on reduction with platinum and hydrogen gives more than 80 per cent yield of 10-hydroxydecanoic acid (m.p. 73·5–74·5° C., mixed melting point with authentic compound 73·5–75° C.). Mixtures of this acid, which is assumed to be 10-hydroxy-2-decenoic acid, with the other naturally occurring constituents of the hydroxy acid fraction melt in the range from 53° to 60°.

A second component, comprising about 5 per cent of the hydroxy acid fraction, has the chromatographic properties of the saturated compound, 10-hydroxydecanoic acid. A small amount of this material was separated from the unsaturated acids by a modification of the method of Jantzen and Andreas[8]. The somewhat impure compound melted at 71·5–73·5° C., and a mixture of this material with the authentic compound melted at 72–75° C.

The third crude fraction yields on recrystallization a material that melts at 98–101° C. Analysis gives the formula $C_{10}H_{20}O_4$ and the neutral equivalent is 208 (calculated 204). The infra-red and ultra-violet spectra indicate a saturated carbon chain. Vapour-phase chromatography of the methyl ester indicates that this consists of three very similar and not completely separable components. The major compound constitutes about 85 per cent of the mixture. Although it has not been possible to separate the components, and only small amounts of material are available, preliminary work involving chromic acid oxidation, dehydration and acetylation indicates that the principal compound is a dihydroxydecanoic acid containing a hydroxyl group in the β-position to the carboxyl group. The other hydroxyl group does not appear to be terminal.

The complexity of the mixture of fatty acids in royal jelly indicates the need for caution in interpreting the results of experiments on the biological activity of crude samples presumed to consist of 10-hydroxy-2-decenoic acid. Many of the fatty acids have similar polarity and cannot be removed by repeated recrystallization. The presence in this mixture of a homologue of traumatic acid (duodecen-1,12-dioic acid), which is known to have a profound effect on cell growth, serves to emphasize the care that should be exercised in such experiments.

The fact that all fatty acids thus far identified in royal jelly contain ten carbon atoms and that the queen substance, recently characterized and synthesized[9], also is a decenoic acid (9-oxo-2-decenoic acid) probably indicates a common biogenetic origin of these compounds. It is tempting to speculate that some component of the diet fed to the queen by her workers is converted in her body to the queen substance. However, no evidence for this is now available.

Experiments have been performed using isotopically labelled compounds in an effort to demonstrate formation of hydroxy fatty acids in worker bees. Sodium acetate-1-^{14}C and sodium stearate-1-^{14}C have been fed to worker bees and included in an incubation medium with excised mandibular glands. In both cases considerable radioactivity was detected in lipid extracts of the mandibular glands, but the hydroxy acid fraction did not become labelled.

The details of these experiments will be reported elsewhere. This work was supported by research grants from the U.S. Public Health Service and the National Science Foundation.

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Malic Acid Synthesis in *Escherichia coli* and its Inhibition by Cocaine

IT has been shown that cocaine specifically inhibits the synthesis of citrate in yeast[1] and in animal tissues[2], and that other local anæsthetics possess a similar specificity of action in blocking cellular respiration[3]. An enzyme, malate synthetase, which catalyses the synthesis of malate from acetate and glyoxylate in a manner analogous to the formation of citrate from acetate and oxaloacetate, has since been discovered[4] and has been shown to participate in some micro-organisms in a modified citric acid cycle which has been described as the glyoxylate cycle[5].

In view of the analogous functions of malate synthetase and citrate synthetase, it occurred to us that cocaine might have a similar effect on both these condensing enzymes and would thus inhibit the synthesis of malate. Such inhibition has now been demonstrated in *Escherichia coli*, and it is of interest to compare the effects of cocaine on the two enzyme systems under similar conditions.

We find that, whereas citrate accumulates in an aerated suspension of washed baker's yeast in 0·2 *M*

magnesium acetate[6], malate accumulates in *E. coli* under these conditions. The bacterial cell suspensions, with and without cocaine, were aerated at *p*H 7 and 37° following the procedure previously described for the experiments with yeast[2]. Samples were withdrawn at intervals for the estimation of malic acid by the fluorimetric method of Hummel[7], or of citric acid by the colorimetric method of Natelson, Pincus and Lugovoy[8]. In a series of experiments in which malic acid synthesis occurred at the rate of 20–30 μgm./ml. cell suspension/hr., cocaine (0·001 *M*) inhibited by 79 ± 4 per cent. Citric acid synthesis in yeast under similar conditions was inhibited by about 70 per cent[1].

No citric acid synthesis occurred in the *E. coli* suspension, which suggests that a glyoxylate cycle in this organism may function independently of citric acid metabolism and would thus differ from the glyoxylate cycle of Kornberg and Krebs. We are investigating this possibility and extending the work with cocaine to a study of its action on the isolated enzymic systems.

We wish to thank Dr. N. F. T. Crowley of the Royal Free Hospital for supplying the pure strain of *E. coli* used in these experiments.

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β-Lactoglobulins in the Urine of the New-born Suckled Calf

IMMUNOLOGICAL, electrophoretic and ultracentrifuge data have been presented which show that certain proteins present in bovine colostrum contribute to a transient proteinuria which persists in the suckled calf for about 30–40 hr. *post partum*[1,2]. The work reported here supports previous findings, but emphasizes more specifically that it is the β-lactoglobulin in the colostrum which is absorbed from the gut along with the immune lactoglobulin, during the period of gut permeability immediately *post partum*, which is afterwards selectively cleared from the circulation probably by glomerular filtration by virtue of its low molecular weight and gives rise to a β-lactoglobulinuria. The immune lactoglobulin carrying the antibody activity is largely retained.

Aschaffenburg and Drewry[3,4] have shown that there are two lactoglobulins *A* and *B* which can be identified by their differing electrophoretic mobility and that the presence of either one or both is determined genetically. We have confirmed these observations using starch-gel electrophoresis and have used these characteristics to identify further and confirm the major contribution of β-lactoglobulin to the urine protein of the new-born suckled calf.

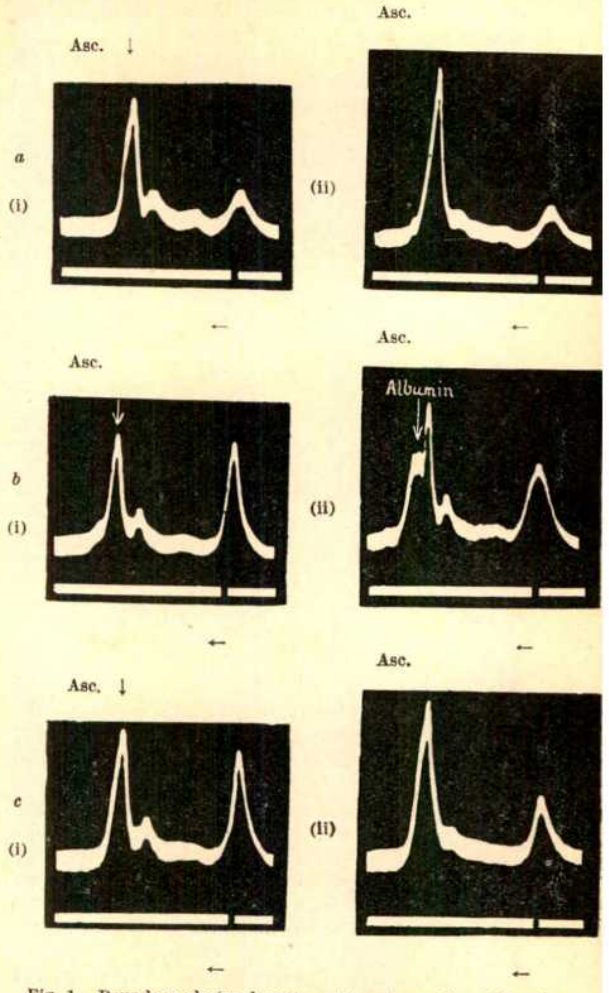

Fig. 1. Boundary electrophoretic patterns (ascending side only, phosphate buffer *p*H 8, $I = 0{\cdot}2$) for rennin milk-whey proteins showing β-lactoglobulins (↓) *A*, *B* and *AB* at *a*(i), *b*(i) and *c*(i), respectively, and at *a*(ii), *b*(ii) and *c*(ii) after the addition of a bovine serum albumin fraction to equal approximately the concentration of the β-lactoglobulin

In rennin-prepared milk-whey usually no separation of the mixed β-lactoglobulin *AB* was obtained by boundary electrophoresis, and bovine serum albumin could only be distinguished as a separate component from the slower β-lactoglobulin *B* (Fig. 1).

In starch-gel electrophoresis, on the other hand, the β-lactoglobulins *A* and *B* were easily separable and in addition both could be distinguished from serum albumin, which showed a slightly slower mobility (Fig. 2*a*). Therefore colostra were selected in which the β-lactoglobulin had been identified as either *A*, *B* or *AB* and were fed to new-born calves.

Calves 1, 2 and 3 were fed colostrum containing *AB*, *A* and *B* β-lactoglobulin respectively. Fig. 2*b*, *c* and *d* show an exact correlation between the electrophoretic mobility in starch-gel electrophoresis of the particular β-lactoglobulins fed and the major protein components in the associated urine during proteinuria. The heavily stained slow component (immune lactoglobulin) in the colostrum fed is almost entirely absent from the urine.

Although this method of electrophoresis does not give reliable quantitative data, it is evident that neither the immune lactoglobulin (mol. wt. 180,000)

present at high concentration in the colostrum and after suckling in the serum of the calf, nor, with the possible exception of calf 3, the serum albumin (mol. wt. 68,000) contributes significantly to the proteinuria.

The immune lactoglobulin has been shown to confer a passive antibody protection on the new-born calf, which prior to suckling is agammaglobulinæmic. Therefore its retention by the calf has a survival value, and since it is derived from the maternal serum[5-7] it is unlikely to be antigenic. However, the β-lactoglobulin is synthesized locally in the udder[8] and there is some evidence that proteins in this category may be antigenic in some circumstances when exposed to the general body tissues of the host[9]. The rapid elimination of this protein together with the relative unresponsiveness of the new-born to antigenic stimuli could help to avoid the development of sensitivity.

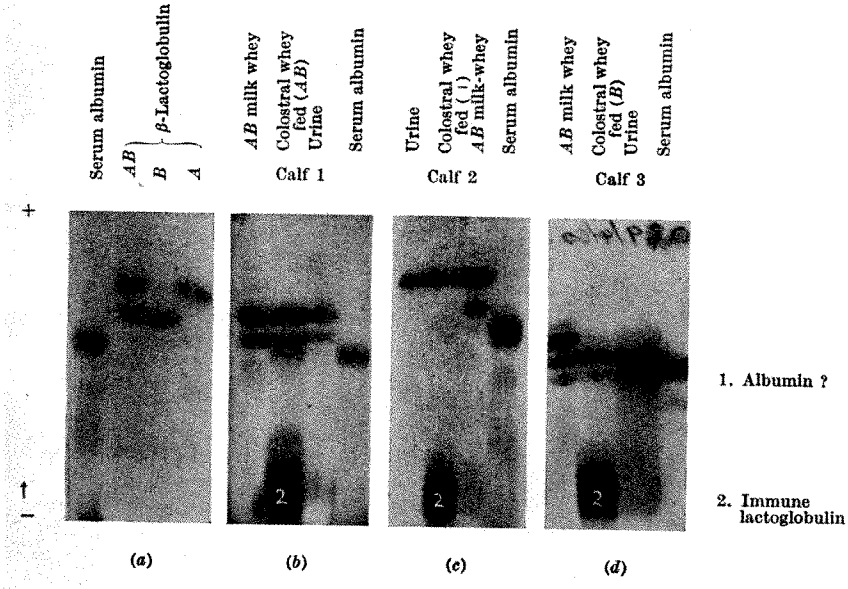

Fig. 2. Starch-gel electrophoretic patterns (phosphate buffer pH 7·6) showing at (a) serum albumin fraction and milk-whey β-lactoglobulins AB, B and A, at (b), (c) and (d) colostral whey fed and derived urine during proteinuria in calves 1, 2 and 3, together with control milk-whey β-lactoglobulin AB and crude serum albumin fraction

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Serotonin (5-Hydroxytryptamine) in the Male Reproductive Tract of the Spiny Dogfish

IN elasmobranch fishes, in which fertilization is internal, the caudal portion of the pelvic fin of the male is prolonged to form a stout rod-like copulatory organ or 'clasper'. The clasper is rolled up in a scroll-like fashion, enclosing on its medial side the so-called clasper groove or tube, along which at copulation the spermatozoa pass from the urogenital papilla of the male to the oviducts of the female. The clasper groove communicates with an accessory organ, located under the skin of the abdomen, which in the shark and dogfish usually takes the form of a muscular sac, the so-called clasper siphon, whereas in the skate it assumes the form of a solid glandular organ, the so-called clasper gland. Leigh-Sharpe[1], who studied in detail the comparative anatomy of secondary sexual characters of elasmobranch fishes, came to the conclusion that the clasper siphon of the Selachii acts as a "reservoir of sea-water" which is emptied at copulation by muscular contractions of the siphon wall, and in this way helps to pump the spermatozoa from the clasper groove into the oviducts. Gilbert and Heath[2], on the other hand, expressed the opinion that the siphons may actually have some secretory function, and contribute a part of the seminal plasma.

The total lack of data on the biochemical properties of the clasper siphon prompted me to study this organ in the spiny dogfish, *Squalus acanthias*, a viviparous aplacental elasmobranch, in which the abdominal siphons are particularly well developed and easily accessible. The siphon sacs of an adult male, caught early in July in the Gulf of Maine, were tapped by inserting through the apopyle the finely drawn-out end of a ball pipette, filled with water, and flushing the siphons with the water. Various chemical reactions were carried out with this fluid, including tests for ergothioneine, which is known to be secreted by male accessory organs of reproduction in certain mammals[3,4]. In the course of these analyses a strong diazo reaction was observed which, however, was not typical of ergothioneine but resembled other aromatic amines in its behaviour. This observation was followed up by a more extensive study of 25 ml. fluid which had been obtained by flushing the siphon sacs of five male spiny dogfishes. On deproteinization with zinc sulphate and barium hydroxide, and centrifugation, a water-clear extract was obtained, representing a dry weight of 175 mgm. or 7 mgm./ml. This extract, when used in 0·02–0·1 ml. quantities, yielded strongly positive colour reactions with sulphanilic acid and sodium nitrite; Ehrlich's dimethylaminobenzaldehyde reagent; 1-nitroso-2-naphthol; and ninhydrin. At this point, a

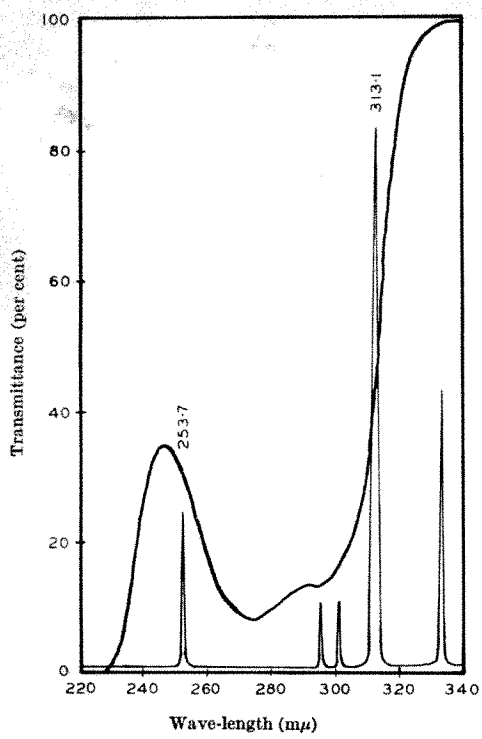

Fig. 1. Ultra-violet absorption curve of serotonin in the protein-free extract from the clasper siphon secretion; mercury lines are shown for reference

spectrophotometric analysis was carried out. The ultra-violet spectrum (Fig. 1) obtained with the 1 : 20 diluted extract in a Bausch–Lomb recording spectrophotometer exhibited all the characteristic features of the spectrum of the aromatic amine serotonin, known also as enteramine or 5-hydroxytryptamine. It possessed a maximum at 275 mμ and a subsidiary peak at 295 mμ ; on alkalinization with sodium hydroxide it exhibited two distinct maxima, at 275 and 325 mμ, respectively. From the optical density observed, and the molecular extinction coefficient $\varepsilon = 5 \cdot 3 \times 10^3$, the serotonin content of the protein-free extract was calculated as 437·5 μgm./ml., or 6·25 per cent of the dry material. A determination based on absorption measurement of the purple-coloured reaction product with 1-nitroso-2-naphthol[5] gave a closely similar result, 6·38 per cent. Further confirmation of the identity of serotonin was obtained by paper partition chromatography. The chromatograms were run at room temperature for 16 hr. on Whatman No. 1 filter paper, with butanol/acetic acid as the solvent (40 vol. *n*-butanol + 10 vol. acetic acid + 50 vol. water ; upper layer used) ; the spots were located with the following reagents : diazotized sulphanilic acid[3], Ehrlich's reagent[6], silver nitrate, ninhydrin. These reagents revealed spots the R_F value of which was identical with that of pure 5-hydroxytryptamine creatinine sulphate.

Six more male spiny dogfishes became available in August. Three were sexually mature (990–1,280 gm.) and contained numerous spermatozoa in the seminal ducts and the 'seminal vesicles' ; their clasper siphons were about 9 cm. long and 1·5 cm. wide. The siphons were opened longitudinally and the undiluted secretion was collected. Each pair of clasper siphons yielded about 250 mgm. of a highly viscous, yellowish fluid, the analysis of which revealed a remarkably high concentration of serotonin, namely, 5·7–7·7 per cent, which corresponds to a content of more than 16 mgm. serotonin per animal. After the removal of the secretion the siphons were washed with water, the tissue ground and analysed for serotonin. Pairs of siphons, weighing 2·8–3·6 gm., contained on the average 0·3 per cent serotonin, that is, about 9 mgm. per animal. Serotonin was absent, or present only in traces, in the sperm removed directly from the seminal ducts and the so-called seminal vesicles, in the contents of the cloaca, and in the liver and testes. The remaining three dogfishes were sexually immature males (275–440 gm.) which contained no spermatozoa in the reproductive tract, and had clasper siphons about 0·5 cm. long, and weighing about 100 mgm. The clasper siphons of these immature males contained 0·017–0·048 per cent serotonin, that is, some 200 times less than found in sexually mature fishes.

Serotonin is known to occur in certain organs, of vertebrates and invertebrates alike, usually in association with the so-called enterochromaffin cells ; it is implicated in various vital functions, including cardiac output, blood pressure, pulmonary and renal circulation, and the activity of the central nervous system and the gastrointestinal tract[7,8]. Serotonin exerts a powerful stimulating influence on the isolated rat uterus, in dilutions 1 : 100–200 millions[9] ; and when administered intravenously to dogs, 1–3 μgm./kgm., it elicits strong uterine contractions, followed by an inhibition[10]. The findings concerning the spiny dogfish show that the clasper siphon is a rich source of serotonin, the concentration of which exceeds by many times the values recorded for other animal organs : a fish weighing 1 kgm. contains in its clasper siphons some 20 mgm. of serotonin. The presence of so much serotonin in a secretion which represents an integral part of semen suggests that, in the spiny dogfish in any event, serotonin may play a part in the reproductive process, either by affecting the mechanism of copulation and ejaculation in the male, or by eliciting contractions of the female reproductive tract, thus influencing passage of sperm and fertilization.

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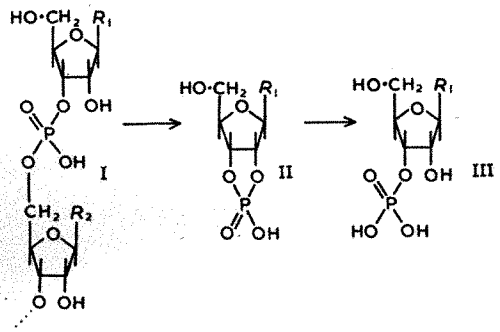
Function of Ribonuclease in Germinating Peas

ALTHOUGH ribonucleases have been found in a large variety of tissues of plant, animal and microbial origin, only the crystalline enzyme from bovine pancreas has been studied in detail. This enzyme is known to bring about the degradation of ribonuclease by transesterification. In this process, a 5′-phosphoester residue is split and a new 2′-phosphate ester linkage is formed, giving a 2′,3′-cyclic phosphate of a pyrimidine nucleoside as shown (I→II; R_1= cytosine or uracil; R_2=adenine, guanine, cytosine or uracil); subsequent hydrolysis of the cyclic phosphate by the enzyme then produces the 3′-hydrogen phosphate of the pyrimidine nucleoside (III)[1]. Synthesis of internucleotide linkages has been demonstrated with certain ribonucleases[2,3] by reversal of the above reaction (II→I), and it has been shown that the specificity of the pancreatic enzyme in the reverse reaction is such that only linkages of the type known to be present in ribonucleic acid are formed[4]. The involvement of ribonucleases in the synthesis of ribonucleic acid has frequently been suggested; but, although the capacity of the enzyme to effect synthesis is not in doubt, it is difficult to obtain direct evidence to support the hypothesis that ribonucleases fulfil a synthetic function in the cell.



Reddi[5] has found that infection of tobacco leaves with tobacco mosaic virus is accompanied by a substantial increase in the ribonuclease activity of the leaves, and since the virus possesses no independent enzyme systems, it was suggested that synthesis of viral ribonucleic acid occurs at the expense of leaf ribonucleic acid through the action of the leaf ribonuclease. In view of this suggestion, we wish to record our preliminary investigations on the activity of ribonuclease in the early stages of the development of the pea seedling.

We have measured the ribonuclease activity, the percentage of ribonucleic acid and of protein in the cotyledons and in the root and shoot in peas germinating in the absence of external nutrients. The results are shown in Fig. 1. It is seen that in the cotyledons, similar variations with time occur in protein and ribonucleic acid concentrations and in ribonuclease activity. In each case an abrupt change in the curve occurs around the fifth to the sixth day after sowing. Holden and Pirie[6] examined the ribonuclease of pea seedlings grown in compost and found that activity of the enzyme in the whole seedling increased from the second to the sixth day after sowing and remained constant thereafter until the tenth day when activity began to decrease. These results are not entirely comparable with ours, since in

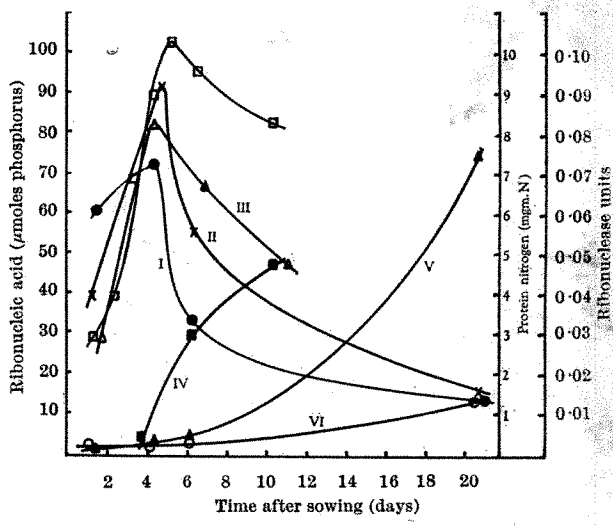


Fig. 1. Ribonuclease units per plant (1 unit ≡ 1 mgm. pancreatic ribonuclease). □, Total; △, cotyledons; ■, root and shoot. Ribonucleic acid per plant (μmoles P). ×, Cotyledons; ▲, root and shoot. Protein nitrogen per plant (mgm. N). ●, Cotyledons; ○, root and shoot

our experiments no external nutrient was supplied. However, it is significant that the time at which sharp maxima occur in curves I, II and III corresponds closely to the time at which Holden and Pirie observed maximum ribonuclease activity, and it appears that at about the sixth day after sowing a marked change occurs in certain reactions taking place in the cotyledons.

The situation in the growing parts of the plant is quite different from that in the cotyledons. The ribonucleic acid of the root and shoot remains at a very low level until after the acid of the cotyledons has reached its maximum value, after which a slow increase occurs. Whereas in the cotyledons the ribonucleic acid content and ribonuclease activity run approximately parallel, in the root and shoot the appearance of ribonuclease activity precedes the increase in ribonucleic acid content (curves IV and V). Furthermore, the increase in activity occurs at a time when total protein (curve VI) is not increasing in the growing parts.

It is felt that increase in ribonuclease activity at a time when synthesis of ribonucleic acid is taking place cannot be taken necessarily to imply involvement of the enzyme with synthesis, and no conclusions can be drawn regarding the function of the enzyme in the cotyledons from curves II and III, which run parallel both during increase and decrease of ribonucleic acid content. In the root and shoot, however, the appearance of active ribonuclease prior to the increase in ribonucleic acid strongly suggests a synthetic function for the enzyme, since activity increases at a time when there is apparently little or no substrate for the degradative reaction.

So far as is known, nucleoside cyclic phosphates of type II have not been recognized as normal cellular constituents, and it seems likely that, if internucleotide bonds are formed *in vivo* by a reaction of the type II→I, the process is involved not with net synthesis of ribonucleic acid but with the reversible breakdown and re-synthesis. During the early stages in the development of the pea seedling in the absence of external nutrient, the growing organs are dependent on the cotyledons for some cellular materials. We

suggest that in the germinating pea, ribonuclease is involved in the translocation of polynucleotide material by bringing about degradation of ribonucleic acid in the cotyledons and re-synthesis in the root and shoot. This mechanism, since it does not involve nucleoside 5′-polyphosphates as intermediates, could operate without interference with the synthesis of nucleotide coenzymes in the growing parts of the plant.

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Mechanism of the Action of Thymidylate Synthetase

IT has been postulated[1-4] that the enzymic synthesis of thymidylic acid from deoxyuridylic acid occurs according to the equations :

$$\text{Tetrahydrofolate} + \text{HCHO} \rightleftharpoons N^5,N^{10}\text{-methylene tetrahydrofolate} + H_2O \quad (1)$$

$$N^5,N^{10}\text{-Methylene tetrahydrofolate} + \text{deoxyuridylate} \rightarrow \text{dihydrofolate} + \text{thymidylate} \quad (2)$$

Previous evidence that dihydrofolate is a product has been indirect, since it rested on : (1) balance studies which indicated that tetrahydrofolate is a substrate, and that it assumes the role of catalyst only under conditions where it is regenerated[1,3,4] ; (2) isotope experiments in which it was shown that hydrogen isotope from tetrahydrofolate is incorporated into the methyl group of thymidylate[2].

We have now obtained direct evidence that dihydrofolate is a product of the reaction by experiments with thymidylate synthetase purified 100-fold from sonic extracts of *Streptococcus faecalis* R. Dihydrofolic reductase purified 300-fold from *S. faecalis* R. was used to generate L-tetrahydrofolate in the reaction mixture and the latter compound then reacted with formaldehyde to give methylene tetrahydrofolate, which produced a characteristic absorption spectrum. In the presence of the purified thymidylate synthetase (activity 10 μmoles of thymidylate synthesized/hr./mgm. protein), addition of deoxyuridylate caused a spectrum change, the rate of which has been used to determine enzyme activity. On completion of the reaction the spectrum was that of dihydrofolate. The product with this spectrum was hydrogenated by reduced triphosphopyridine nucleotide in the presence of the highly specific dihydrofolic reductase and the reduction was inhibited by aminopterin, which is a specific inhibitor of folic and dihydrofolic reductases.

Friedkin and Kornberg postulated[5] that in the thymidylate synthetase reaction deoxyuridylate and methylene tetrahydrofolate react to form an intermediate in which a methylene bridge links C^5 of uracil to N^5 (or N^{10}) of tetrahydrofolate. During the course of our work on the purification of thymidylate synthetase, none of the many fractionations has resulted in even partial separation of activity into the two different enzyme fractions which would be required to synthesize and cleave such an intermediate. When the reaction was followed spectrophotometrically there was no indication of a change in reaction-rate of the kind to be expected if an intermediate accumulated in the reaction mixture. Moreover, two well-defined isosbestic points were observed for the spectrum change, indicating that dihydrofolate was the only new species formed in significant amounts from methylene tetrahydrofolate.

In isotope experiments we have generally used labelled glucose-6-phosphate-^{3}H, glucose-6-phosphate dehydrogenase and triphosphopyridine nucleotide to hydrogenate dihydrofolate in the presence of dihydrofolic reductase to yield L-tetrahydrofolate-^{3}H. The hydrogen transfers proceeded to completion and the entire product was then allowed to react according to equations (1) and (2). The thymidylate formed was degraded to thymine, which was isolated by paper chromatography. The specific activity of the thymine did not differ significantly from that of the hydrogen attached to carbon-1 of the glucose-6-phosphate. The latter was estimated by forming glutamate-^{3}H from the glucose-6-phosphate-^{3}H in the presence of appropriate enzymes and substrates[6]. When tritiated water and unlabelled reduced triphosphopyridine nucleotide were used in a similar sequence of reactions the isolated thymine had only 2 per cent of the specific activity of the water. These results are similar to those obtained by Friedkin[2] with chemically synthesized dL-tetrahydrofolate, except that in our experiments the transfer of hydrogen occurred without significant dilution, and confirm that one hydrogen of the thymine methyl group is derived from tetrahydrofolate.

This evidence suggests that thymidylate synthetase is a single enzyme and that no intermediate of the type suggested by Friedkin and Kornberg[5] accumulates in significant amounts, although its transitory formation on the enzyme surface would be consistent with the isotope results and other data.

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PHYSIOLOGY

Derivation of an Equation for the Diffusion Potential

AN equation for the potential across a membrane arising from the steady-state diffusion of univalent ions was derived by D. Goldman[1] under the assumptions of a constant electric field and constant ionic mobilities across the membrane. His equation may be written as[2] :

$$V = \frac{RT}{F} \ln \frac{\sum_{i^+} P_{i^+} C_{i_l^+} + \sum_{i^-} P_{i^-} C_{i_r^-}}{\sum_{i^+} P_{i^+} C_{i_r^+} + \sum_{i^-} P_{i^-} C_{i_l^-}} \quad (1)$$

where V is the electric potential on the right side of the membrane relative to the left side, C_{i^+} is the concentration of the ith positive ion, C_{i^-} is the concentration of the ith negative ion, P is the permeability of the membrane to an ion, r and l denote the right and left side of the membrane respectively, and R, T, and F have their usual meanings. It is the purpose of this communication to derive, without the use of the above two assumptions, an equation similar to equation (1) in which the permeabilities are replaced by unidirectional rate constants.

H. H. Ussing[3] has shown under very general conditions without the use of the previous assumptions that if an ion diffuses across a membrane:

$$\frac{\vec{j_i}}{\overleftarrow{j_i}} = \frac{C_{i_l}}{C_{i_r}} \exp\left(-z_i \frac{FV}{RT}\right) \quad (2)$$

where $\vec{j_i}$ and $\overleftarrow{j_i}$ are the unidirectional diffusional fluxes from left to right and right to left respectively, and z_i is the valence of the univalent ith ion. For steady-state diffusion with no current:

$$\sum_{\text{all } i} z_i (\vec{j_i} - \overleftarrow{j_i}) = 0 \quad (3)$$

The unidirectional rate constants will be defined as:

$$k_i = \frac{\overleftarrow{j_i}}{C_{i_r}} \qquad k_i' = \frac{\vec{j_i}}{C_{i_l}} \quad (4)$$

The k's need not be constant, but may actually be functions of the concentrations and electric potential. Elementary algebraic manipulation of equations (2), (3), and (4) then yields the desired relationship:

$$V = \frac{RT}{F} \ln \frac{\sum_{i^+} k_{i^+} C_{i_l^+} + \sum_{i^-} k'_{i^-} C_{i_r^-}}{\sum_{i^+} k_{i^+} C_{i_r^+} + \sum_{i^-} k'_{i^-} C_{i_l^-}} = \frac{RT}{F} \ln \frac{\sum_{i^+} k'_{i^+} C_{i_l^+} + \sum_{i^-} k_{i^-} C_{i_r^-}}{\sum_{i^+} k'_{i^+} C_{i_r^+} + \sum_{i^-} k_{i^-} C_{i_l^-}} \quad (5)$$

When equation (1) is valid:

$$\frac{k_{m^+}}{k_{n^+}} = \frac{k'_{m^+}}{k'_{n^+}} = \frac{P_{m^+}}{P_{n^+}} \quad \text{(all } m \text{ and } n\text{)} \qquad \frac{k_{m^+}}{k'_{n^-}} = \frac{k'_{m^+}}{k_{n^-}} = \frac{P_{m^+}}{P_{n^-}} \quad (6)$$

Equation (6) yields an independent method in which the ratio of the permeabilities may be experimentally found. Thus, this ratio may be experimentally tested for constancy as the concentrations and electric potential are altered.

It should be noted that if equations (2) and (3) are satisfied for any sub-group of ions in the system, then equation (5), in which the summation is only over this sub-group, will apply. Thus, for example, for sheep erythrocytes there is a one-to-one exchange of sodium for potassium ions through the active transport system[4]. When there is no net movement of sodium or potassium ions across the membrane, equation (3) will be satisfied for these ions. Hence, letting $\alpha = k_{Na^+}/k_K$:

$$V = \frac{RT}{F} \ln \frac{\alpha\, Na_l^+ + K_l^+}{\alpha\, Na_r^+ + K_r^+} \quad (7)$$

where l and r now stand for the outside and inside regions. Equation (7) has been discussed by A. Hodgkin[5] under the assumption that the α equalled P_{Na^+}/P_{K^+} and was therefore a constant.

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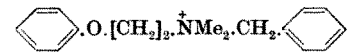
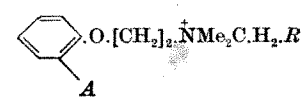
A New Anthelmintic for Canine Hookworm

AN earlier communication[1] reported the discovery of a new series of quaternary ammonium compounds possessing anthelmintic activity against a wide range of nematodes parasitic in the gastro-intestinal tract of mammals. The hydroxynaphthoate salt of one of these compounds (I; bephenium) has proved to be of considerable practical value in the treatment of hookworm and roundworm in man[2], and in the prevention and treatment of nematodiriasis and parasitic gastro-enteritis caused by other trichostrongylid nematodes of sheep[3,4] and cattle[5,6]. In addition, it has proved to be highly effective against hookworm in dogs[7], with less effect against canine ascarids, but its introduction into veterinary usage has been severely hampered by its emetic properties in the dog (Rawes, D. A., and McIntyre, A., private communications).



I

We now report a related series of compounds (II; R = 2-thienyl, A = H, Me, F, Cl, Br or NO_2) which were all effective against our two original screening organisms, *Nippostrongylus muris* and *Nematospiroides dubius*. The related compounds (II; R = 2-furyl) were also prepared and tested but were of much less interest.



II

One of these compounds (II; A = H, R = 2-thienyl), also known as 611C55, has since been tested extensively in larger animals (as its p-chlorobenzene-

sulphonate). It has been shown to be highly effective against both natural and experimental infections of *Ancylostoma caninum* and *Uncinaria stenocephala* in the dog. Compared with bephenium hydroxynaphthoate, 611*C*55 was marginally more effective against these two hookworms but at effective therapeutic dose-levels was only minimally emetic. Further experiments against natural infections suggested that 611*C*55 was also more effective against *Toxocara canis* and *Toxascaris leonina*. In contrast, 611*C*55 was substantially less effective than bephenium against some of the gastro-intestinal trichostrongyles in sheep. All these observations are of particular interest in the species/structure/activity complex, since salts of bephenium and 611*C*55 were of equal activity against *N. muris* and *N. dubius*; of the two, 611*C*55 was more effective against *Ascaris lumbricoides in vitro* (L. G. Goodwin, private communication) but they had similar and rather low activities against *Aspiculuris tetraptera* and *Syphacia obvelata*.

In those countries where hookworm infection in the dog is widespread and presents serious problems, tetrachloroethylene is the drug used in standard treatment. While effective, it possesses serious toxic properties. The development of 611*C*55 as an anti-hookworm drug for the dog is of considerable interest since it combines high efficiency with only mild emetic properties in this vomit-prone animal. Clinical trials with 611*C*55 against human hookworm infections are planned.

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Irreversible Elimination of Muscle Receptors

NERVOUS activity is closely related to, and dependent on, the afferent inflow from peripheral receptors. In order to study the effect of decreased afferent inflow on spinal synaptic functions many experimental models have been suggested and investigated, but all these are open to criticism. De-afferentation by section of the dorsal roots proximally to the ganglion leads to degeneration of the central stump and corresponding synaptic endings in the spinal cord, thus causing changes which are not directly associated with the elimination of afferent discharges from the periphery[1,2]. Section of the dorsal roots distally to the spinal ganglion[3] has a similar disadvantage since it causes changes of the retrograde degeneration type in the spinal ganglion cells. Besides this, both these methods lead to the elimination of all modalities of sensitivity, so that they are not suitable for investigations requiring the selective elimination of muscle afferent inflow. Bremer[1] attempted to eliminate muscle receptor discharges by novocain infiltration of the muscle; but this is not a reliable method, and besides it is not possible to maintain this for any period of time. Neither are experimental procedures, such as tenotomy[4], as yet sufficiently analysed to vouchsafe a solution in this direction.

During the study of the morphogenetic influence of the nervous system on the differentiation of muscle spindles in the rat, it was found that spindles begin to develop shortly before birth and cannot be considered as differentiated until 14 days after birth[5,6]. When the sciatic nerve is either sectioned or crushed at the beginning of their differentiation, at birth, for example, their development is arrested and spindles disintegrate within a few days. When re-innervation of the muscle occurs following crushing of the nerve, recovery of motor functions occurs within 14 days; but spindles which had disintegrated during the denervation period do not differentiate again. Even five months after crushing the nerve, the muscles studied contained on the average 0·5 spindles (Fig. 1); they were either completely devoid of spindles or contained an occasional single spindle small in size and atypical in structure (Fig. 2), whereas control muscles contained 32·3 spindles. The presence of atypical spindles can most probably

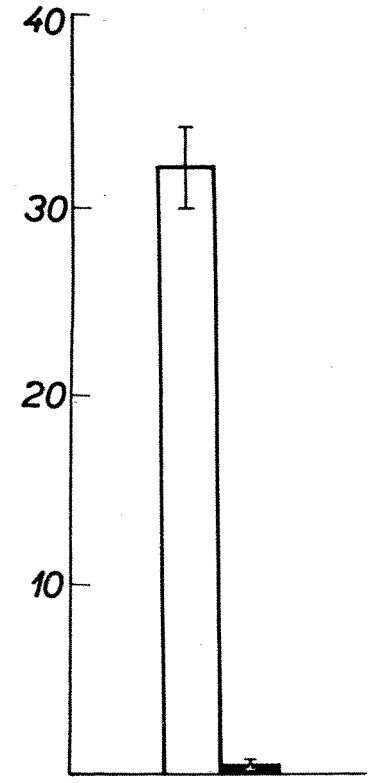

Fig. 1. Number of muscle spindles in normal (white column) and re-innervated (black column) extensor digitorum longus 5 months after crushing the sciatic nerve in new-born rats (arithmetical mean of six animals ± standard error)

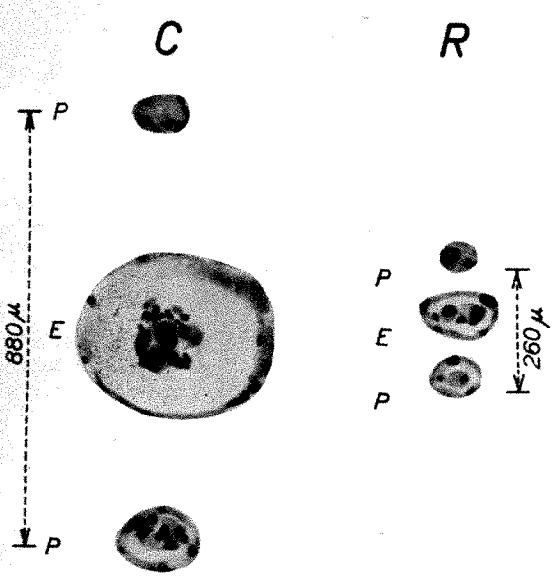

Fig. 2. Cross-sections of a normal muscle spindle from control extensor digitorum longus (*C*) and an atypical spindle from a re-innervated muscle (*R*) 5 months after crushing the sciatic nerve at birth. Hæmatoxylin-eosin, × *c.* 133. *E*, sections from the equatorial zone; *P*, sections from the polar zones of each spindle. The scales on each side indicate the length of spindles computed from serial sections

be explained by the assumption that they are spindles which had not disintegrated completely during the denervation period, and that the remnants were then re-innervated by the regenerating nerve fibres. As yet, only muscle spindles have been studied quantitatively, but tendon organs seem to behave in a similar way.

Since normal differentiation of spindles is governed by afferent nerve fibres[5,6], it was of obvious interest to find out whether in these animals afferent fibres have actually regenerated. For this reason muscle nerves were studied in rats after bilateral anterior rhizotomy. It was found that even though the nerve fibre diameters were somewhat smaller than on the control side, yet there were as many as 75 per cent regenerated afferent nerve fibres on the re-innervated side. They branched and formed free endings in the re-innervated muscles.

Pertinent data have also been obtained concerning the extrafusal muscle-fibres in re-innervated muscles, which were found to be even somewhat larger in diameter than those of the control muscle[7]. These re-innervated muscles, however, lagged considerably behind control muscles so far as their weight was concerned (38 per cent). It can thus be expected that the number of muscle fibres in the re-innervated muscles is reduced and probably also the number of motor neurons innervating these muscles[8]. Nevertheless, the remaining motor neurons, judging by the recovery of the muscle fibre diameter, seem to be functionally efficient.

Muscles without spindles may, after further analysis, represent a suitable model for studying the elimination of muscle proprioception when the afferent endings deprived of special terminal structures are functionally inactive. If free endings are still found to react to muscle stretch, then differences in discharges from endings with and without specialized end-organs could be investigated. Even the study of single atypical spindles might be of considerable interest since morphological and physiological properties of a single known receptor could be correlated using this approach.

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Lucerne Saponin Fractionation and Bloat

EVIDENCE has recently been presented that bloat on red clover is due primarily to the formation of stable foams due mainly to the clover cytoplasmic protein[1]. Even accepting this factor as an important one in the production of bloat on lucerne, variation in bloat potency of the herbage still cannot be accounted for in terms of protein differences[1]. Of course, extensive work in the United States on experimental bloat produced by lucerne saponins[2] still has to be taken into account when bloat factors are considered.

Following the work of Shaw and Jackson[3] at Purdue, we examined the response of rat diaphragm respiration to the isolated saponins of lucerne. So far we have not found qualitative differences between lucerne saponins isolated from bloat-producing and non-bloat-producing herbage on the basis of this test, but inhibition increases with the amount of saponin added. Since it is considered[3] that inhibition, as measured by this *in vitro* test, differentiates between bloat-producing and non-bloat-producing herbage, quantitative levels of saponins in lucerne may be a factor; however, little seems to be known about the seasonal variation in lucerne saponin-levels.

Previously, little chemical difference had been found between bloat-producing and non-bloat-producing herbage. Dried lucerne samples (kindly supplied by Dr. J. M. A. Tilley of the Grassland Research Station, Hurley) from bloat-producing and non-bloat-producing stands with no detectable difference in protein-levels or cytoplasmic/chloroplastic protein ratios (Tilley, J. M. A., private communication) had their saponins extracted and isolated by the cholesterol procedure of Thompson *et al.*[4,5]. The bulk triterpenoidal saponins were compared with those isolated from other lucerne, Aberystwyth[5] and Beltsville[4] (the latter kindly supplied by Dr. C. R. Thompson) by means of paper chromatography. One-dimensional ascending multiple development was used (ethyl acetate/acetic acid/water: 13/3/3 by 3; Whatman No. 3 *MM*; 15 hr.; 40 cm. run; 30° C.) and the saponins were detected by a modified Liebermann–Burchard reagent[6]. Ten (and possibly twelve) constituent saponins were revealed by the improved methods of saponin fractionation—six were previously thought to be present[5].

Differences have been found in the saponin constituents with high R_F values between bloat- and non-bloat-producing lucerne. The bloat-producing

lucerne contains an extra saponin (in low concentration) with the highest R_F. The constituent saponin with the next highest R_F is probably more abundant in bloat-producing lucerne than in non-bloat-producing samples. The other, 'random', lucerne saponin samples appear to correspond to those from the non-bloat-producing lucerne.

One would conclude from this evidence that certain constituent saponins may be involved in the production of the complex condition known as bloat. As one would expect, herbage samples chosen at random are allied to the non-bloat producing samples.

The saponin differences could possibly explain the transient nature of bloat potency of herbage. Certain saponin constituents acting in conjunction with foam-producing agents could provide the necessary conditions for bloat production.

The history of bloat research should have taught us to view with suspicion any theory of single-factor causation of pasture bloat and it should also underline the need for a chemical and biochemical study of bloat which seriously entertains the possibility of a multi-factor causation. The trend appears to be in this direction[1].

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Effect of Reserpine on Heart Mitochondria

RESERPINE has been shown to uncouple oxidative phosphorylation of brain and liver mitochondria *in vitro*[1,2]. In view of this, the effect of reserpine on heart mitochondria, *in vivo* and *in vitro*, and on the content of energy-rich phosphate compounds in heart muscle was studied.

Cats and guinea pigs were used. The experimental and control animals were injected intraperitoneally with 5 mgm./kgm. of reserpine in an average of 1·2 ml. of vehicle or with an equivalent volume of vehicle only, respectively. Twenty-four hours afterwards, the animals' chests were opened under artificial respiration. An 18-gauge hypodermic needle was inserted into the left ventricular cavity and coupled to a Sanborn Twin-Viso recorder through a Statham pressure transducer for recording intraventricular pressure. After the recording, a sample of tissue was excised from the left ventricle and quickly plunged into liquid nitrogen. These frozen tissue samples were saved for the analysis of catecholamine and energy-rich phosphate compounds. The right and left ventricles were then excised and homogenized for isolation of the mitochondria. The phosphorus : oxygen ratios and response to the addition of phosphate acceptor (hexokinase and glucose) of these mitochondria were studied by the methods utilized previously by Lee *et al.*[3].

Epinephrine and norepinephrine in ventricles of three control cats as determined by a spectrophotofluorometric method[4] averaged 0·18 and 1·48 μgm./gm. of tissue respectively. Following the reserpinization, the catecholamine content in three cats was decreased to 1–5 per cent of that found in control animals, confirming the previous work[5]. A similar degree of depletion of the catecholamine content was also observed following the reserpinization of guinea pigs. In addition, left ventricular systolic pressure and heart-rates of reserpinized cats and guinea pigs were 25–36 per cent lower than those found in control animals. In the examination of oxidative phosphorylation, it was found that the phosphorus : oxygen ratios of mitochondria of reserpinized cats and guinea pigs were significantly depressed compared to the controls (Table 1). It is noteworthy that the Qo_2 of reserpinized mitochondria is somewhat higher than the control values. Since the Qo_2 response of mitochondria to the addition of phosphate acceptor was found to be dependent on the extent of coupling of oxidative phosphorylation[3,6], experiments were performed in which the oxygen consumption of mitochondria was measured before and after the addition of phosphate acceptor. The results are also shown in Table 1. It is apparent in cats that the Qo_2 of control mitochondria is markedly increased by the addition of phosphate acceptor, whereas the Qo_2 of mitochondria from reserpinized cats show only a small increase following the similar addition of phosphate acceptor. Similar results were obtained with guinea pig mitochondria. These results suggest that oxidative phosphorylation is uncoupled in heart mitochondria of reserpinized animals. In view of these observations, the effect of reserpine, added *in vitro*, on the phosphorus : oxygen ratio of heart mitochondria from normal cats was studied. In these experiments, reserpine (final concentration of 50 μgm./ml.) or vehicle only was added to flasks containing normal mitochondria. It was found that phosphorus : oxygen ratios of normal mitochondria with and without reserpine were 2·40 ± 0·09 (*S.E.*) and 3·12 ± 0·08 (*S.E.*) respectively. These results suggest that reserpine uncouples oxidative phosphorylation in cat heart mitochondria both *in vitro* and *in vivo*. In two experiments, in which reserpine was administered subcutaneously to guinea pigs in a dose of 0·03 mgm./kgm. daily for 15 days,

Table 1. THE EFFECT OF PRE-TREATMENT OF ANIMALS WITH RESERPINE ON PHOSPHORUS : OXYGEN RATIO AND ACCEPTOR RESPONSE OF HEART MITOCHONDRIA

Type	No. of exp.	P : O ratio ± *S.E.*	Qo_2 ± *S.E.* μatom/mgm. protein/hr.
		Guinea pig experiments	
Control	17	3·11 ± 0·08	8·17 ± 1·08
Reserpine	10	2·39 ± 0·05	12·54 ± 0·71
		Cat experiments	
Type	No. of exp.	P : O ratio	Qo_2
Control	16	3·25 ± 0·08	9·43 ± 0·4
Reserpine	9	2·34 ± 0·20	11·89 ± 0·50
		Qo_2 without acceptor	Qo_2 with acceptor
Control	5	2·54 ± 0·5	8·16 ± 1·0
Reserpine	5	6·78 ± 2·1	8·80 ± 2·9

heart mitochondria from these animals showed a similar uncoupling of oxidative phosphorylation. However, due to a limited number of experiments no definite conclusion can be drawn at present.

In view of the above results, the contents of adenosine triphosphate, phosphocreatine and inorganic phosphate of heart muscle in control and reserpinized cats were studied according to the methods of Furchgott and deGubareff[7,8]. Although the uncoupling of oxidative phosphorylation in mitochondria might be expected to result in a lower level of energy-rich phosphate compounds, the results in Table 2 show that contents of these compounds in hearts of reserpinized animals are unchanged when compared to control values. No satisfactory explanation is at present available for this phenomenon. Two possibilities may be considered. First, the *in vivo* uncoupling effect of reserpine may not be pronounced enough to impair the synthesis of high-energy phosphate compounds. Secondly, if the synthesis of these compounds is assumed to be impaired, this impairment of synthesis may be compensated by the depressed utilization of them by heart muscle. It has been shown in the dog heart-lung preparation[9] that increasing the resistance against which the heart must work resulted in a decrease in the high-energy phosphate content of the left ventricle. Therefore, the lower ventricular pressure and lower heart-rate of reserpinized cats, resulting in less ventricular work compared to those of control, may compensate, at least partially, for the decreased synthesis of high-energy phosphate compounds in reserpinized animals, thus maintaining the control-level of these compounds.

Table 2. EFFECT OF RESERPINIZATION ON THE CONTENT OF ATP, PC AND IP IN HEART MUSCLE OF CATS

Type	No. of exp.	IP ± *S.E.*	PC ± *S.E.*	ATP ± *S.E.*
Control	4	2·52 ± 0·08	8·48 ± 0·27	5·47 ± 0·18
Reserpine	5	3·83 ± 0·57	9·61 ± 1·0	5·34 ± 0·25

All values are expressed in μmole/gm. wet weight tissue. ATP, Adenosine triphosphate; IP, inorganic phosphate; PC, phosphocreatine.

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HÆMATOLOGY

Identity of Hæmoglobin A_2

AT least two forms of adult hæmoglobin are present in the blood of the normal human adult, a main component hæmoglobin A_1 and a minor one hæmoglobin A_2 (ref. 1). In normal individuals the concentration of hæmoglobin A_2 is about 2·5 per cent of the total hæmoglobin. In persons heterozygous for the Cooley gene, this amount is increased to a level of about 5 per cent. The A_2 fraction can be isolated from the main component by starch-block electrophoresis and by chromatography on carboxymethyl cellulose[2]. The presence of two hæmoglobin A_2 fractions in some persons, belonging to different generations of one family, makes it likely that the synthesis of hæmoglobin A_2 is genetically determined[2]. This led us to investigate whether there exist chemical differences between the main component, hæmoglobin A_1 and hæmoglobin A_2, and to locate eventual differences.

We started with hæmoglobin A_2 prepared from erythrocytes of a person with thalassæmia minor, because of the higher hæmoglobin A_2 concentration in the blood of carriers of the Cooley gene. In a later stage of the investigation also the hæmoglobin A_2 of a normal person was investigated since the possibility of differences between these A_2 hæmoglobins could not be excluded.

The A_2 component was isolated and purified by chromatography on carboxymethyl cellulose using a *p*H gradient[2]. After tryptic digestion at *p*H 8·0 in a *p*H-stat of the heat-denatured protein, those peptides that are soluble at *p*H 6·5 were 'fingerprinted'[3]. The resulting pattern showed differences in peptides numbered 26, 12 and 16 from the pattern of normal adult hæmoglobin[3]. By specific staining reactions for arginine and tyrosine an additional difference in the unresolved part of the neutral band of the 'fingerprint' could be visualized. The remaining part of the 'fingerprint' was identical for hæmoglobin A_2 and hæmoglobin A_1.

The differences in spots 26 and 12 indicate that the differences are located in the β-chain; these peptides only being present in this chain. This, however, could not be said for peptide 16 and the difference in the neutral band, as it is known that these spots contain peptides which occur in both chains. In order to learn whether these differences are localized in the α- or β-chain, 100 mgm. of globin of hæmoglobin A_2 was prepared with the use of the method of Anson and Mirsky[4]. The globin was separated into two fractions, one consisting of the α-, the other of β-chains, by chromatography on 'Amberlite *IRC* 50', using a urea gradient[5]. 'Fingerprints' of the first fractions of hæmoglobin A_1 and hæmoglobin A_2 consisting of α-chains appeared to be identical when stained with ninhydrin as well as when stained with special reagents on arginine-, histidine-, tyrosine-, tryptophan- and sulphur-containing peptides.

All the differences mentioned above, however, could be visualized in the 'fingerprints' of the β-chains (Fig. 1). With the 'fingerprinting' method no differences could be detected between the hæmoglobin A_2 of a normal individual and the hæmoglobin A_2 of a carrier of the Cooley gene.

These results indicate that hæmoglobin A_2, like fœtal hæmoglobin, differs from adult hæmoglobin in the β-chains and can be denoted by $\alpha_2\delta_2$. The differ-

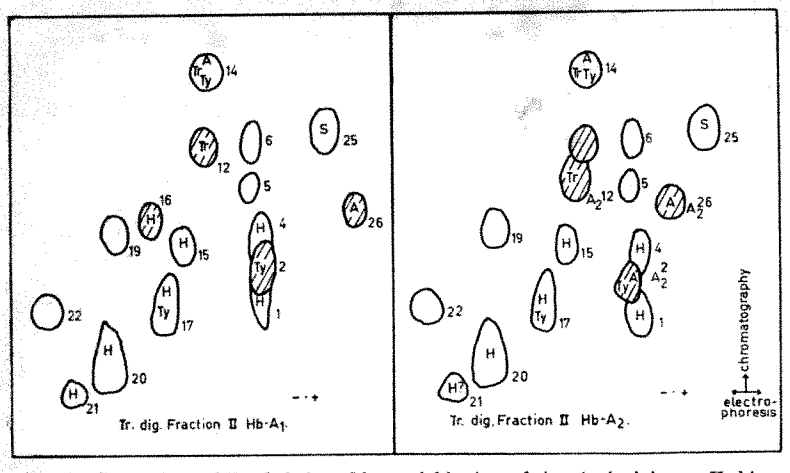

Fig. 1. Comparison of the β-chains of hæmoglobin A_1 and A_2. *A*, Arginine-; *H*, histidine-; *S*, sulphur-; *Tr*, tryptophan-; and *Ty*-, tyrosine-containing peptides

ences between the β-chain of hæmoglobin A_1 and hæmoglobin A_2 are, however, smaller than those between the β-chain of hæmoglobin A_1 and that of fœtal hæmoglobin.

We may conclude that in the human erythrocytes three hæmoglobins are present, all three with the same α-chains, but with β-chains that differ in several parts.

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The Half-life of Human Platelet Phosphatide

PLATELET life-span has been measured by incorporating into the platelet a tracer compound and following its disappearance. The labels used have included radioactive phosphorus, as ^{32}P-orthophosphate and as ^{32}P-di*iso*propyl fluorophosphonate, radioactive chromium, radioactive sulphur and radioactive carbon. Aas and Gardner[1] reported a life-span of 9–11 days using *in vitro* labelling with chromium-51. Leeksma and Cohen[2] calculated a life-span of 8–9 days using ^{32}P-di*iso*propyl fluorophosphonate *in vivo*. Both methods gave a calculated life-span that was longer than previous results had suggested and longer than the 1½–3 day half-life for transfused ^{32}P-platelets reported by Adelson *et al.*[3]. These authors pointed out the hazards of using *in vitro* techniques and attempted to reduce platelet handling to a minimum. A longer platelet life-span would explain more adequately the occurrence of a maximum depression of platelets at 25–30 days in human beings exposed to radiation[4].

Following the use of therapeutic doses of phosphorus-32 we have found radioactivity in isolated platelet phosphatides three and four weeks following injection. Platelets were obtained by differential centrifugation, using ethylenediamine tetraacetic acid as the anticoagulant. Smears revealed little or no contamination with white blood cells. The phosphatides were isolated using the Folch extraction procedure[5] and ascending chromatography on glass fibre impregnated with silicic acid[6]. The lipid spots were identified with rhodamine 6*G* and ultra-violet fluorescence; these spots were cut out, and their radioactivity was measured using a thin-window Geiger tube. Phosphorus was determined by the Gomori method[7]. Analyses were performed simultaneously on platelets and 'platelet poor' plasma samples (centrifuged at approximately 1,000*g*).

Table 1 presents the comparative results for platelets and plasma. It is evident that considerable radioactivity was present in platelets at the end of 21 days, and significant radioactivity was found at 28 days in patients Aregi and Whitehead (13 and 10 actual c./min. above background were found respectively, using 1,000 counts, with a background activity of 17 c./min.). Activities of similar magnitudes were found in the phosphatidyl choline of both platelets and plasma. However, platelets consistently yielded significant amounts of phosphatidyl ethanolamine whereas only small amounts were found in plasma and not in every patient. This was also demonstrated in radioautograms of the chromatograms.

The specific activities found are consistent with an exponential curve of disappearance, with a suggestive half-life of 10–13 days for platelet phosphatidyl choline. It should be emphasized that this is a figure for the phosphatide and not whole platelets. The data are not yet adequate to determine if there is a

Table 1. SPECIFIC ACTIVITIES OF PHOSPHORUS-32-LABELLED PHOSPHATIDE EXPRESSED AS COUNTS/MIN./μGM. PHOSPHORUS, CORRECTED FOR DECAY

	Days after phosphorus-32	Plasma	Platelets	
		Lecithin	Lecithin	Phosphatidyl ethanolamine
Butts, 2·5 mc. (62, F.), thrombocythæmia	4 11 18 21	48 62 46 41	51 59 36	53 52
Whitehead, 2·5 mc. (83, F.), chronic lymphocytic leukæmia	7 21 28	100 23 14	68 27* 12	40 10
Aregi, 2·5 mc. (67, M.), polycythæmia	7 14 21 28	35 29 22 19	31 45 24 20	25 47 15 19
Moore, 2·0 mc. (60, F.), lymphosarcoma	7 14 21	36 21 13	30 19 16	35 20 10

* Mixed platelets and white blood cells.

Analyses of platelet lecithin were 3 μgm. phosphorus or greater. Plasma yields were considerably higher. Some of the analyses of platelet phosphatidyl ethanolamine were of the order of 2 μgm. phosphorus.

levelling off to a relatively constant level of activity.

Our observations are compatible with the hypothesis that human platelet life-span is longer than present data in the literature suggest. It is likely that a combined megakaryocyte-platelet phosphatide half-life is being measured. The megakaryocyte probably incorporates the ^{32}P-orthophosphate into the phosphatides and on 'maturation' delivers the labelled platelets into the peripheral circulation. The time of this process is unknown in humans, although the fact that the peak of platelet radioactivity in humans is usually found one week after injection of ^{32}P-orthophosphate may suggest 7 days. Kinosita[8] has reported a 5-day period for the development of the mature megakaryocyte and release of the platelets by time-lapse photography of rabbit marrow.

The questions of adsorption of phosphatides from plasma, a more active process of exchange with plasma phosphatides, and that of possible phosphatide metabolism of platelets remain to be evaluated. The appearance of (2-^{14}C) acetate-labelled phosphatides in human red blood cells following *in vitro* incubation with labelled plasma was recently reported by Lovelock *et al.*[9].

The fact that labelled phosphatidyl ethanolamine is consistently found in platelets while little or no phosphatidyl ethanolamine is found in our plasma samples argues against simple adsorption from plasma. Indeed, the reverse has been postulated, namely, that plasma phosphatidyl ethanolamine may be derived in part from ruptured platelets[10]. Our results are compatible with this concept.

The half-life of plasma phosphatidyl choline varied from approximately 9 to 27 days, using a semi-logarithmic plot of the specific activities. This too is considerably longer than present turnover data in the literature indicates[11,12]. This will be discussed in more detail in a subsequent report.

Further work is in progress.

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RADIOBIOLOGY

Incorporation of Cæsium-137 from Nuclear Debris into the Biosphere

IT is generally assumed that cæsium deposited on plant leaves or stems can be taken up by the plant[1–5]. When such plants are ingested by a cow a considerable part of the ingested cæsium is excreted in the milk. The results of the experiments described here, however, seem to indicate that cæsium-137 can follow an alternative route from fall-out to man that under certain conditions could well be responsible for part of the cæsium-137 found in milk and meat.

In order to obtain data concerning the transport of cæsium in soil, experiments have been carried out with artificially contaminated soils. When cæsium is present at the top of a compact layer of clay it can scarcely be washed downwards by water free of electrolytes (Fig. 1). However, in a layer of crumbled clay or loosened sand a considerable transport of cæsium by water was observed. This transport is apparently caused by the downward movement of very small particles containing most of the cæsium. From sedimentation experiments, it became apparent that about 50 per cent of cæsium-137 present in a slightly alkaline clay (*p*H 7·5) was adsorbed on to particles smaller than 2μ, representing only 5 per cent of the total mass of the clay. In a sand free of humus (*p*H 7·2) more than 70 per cent of the cæsium-137 was found on only 2 per cent of the total mass. These small soil particles washed downwards with rain-water were retained by a compact layer of clay in a model experiment, causing a maximum activity at the top of the compact layer (Fig. 2). The relatively large activity at the bottom of a furrow described by Herbst[6] could be caused by a retention of small particles carrying a large fraction of the cæsium-137 by the compact layer of clay just under the ploughed layer.

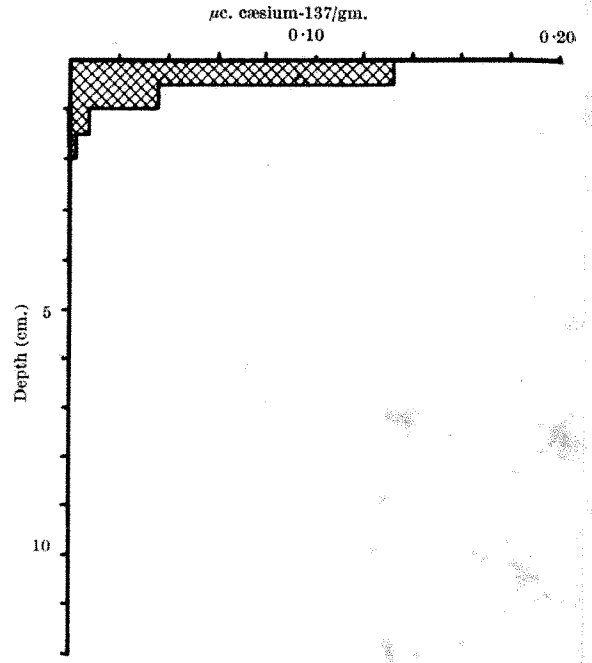

Fig. 1. Distribution of radiocæsium, after surface contamination with 0·10 μc./cm.², in compact clay after 700 mm. water precipitation (500 mm. with a drop-diameter of 0·2 mm. and 200 mm. with a drop-diameter of 6 mm.)

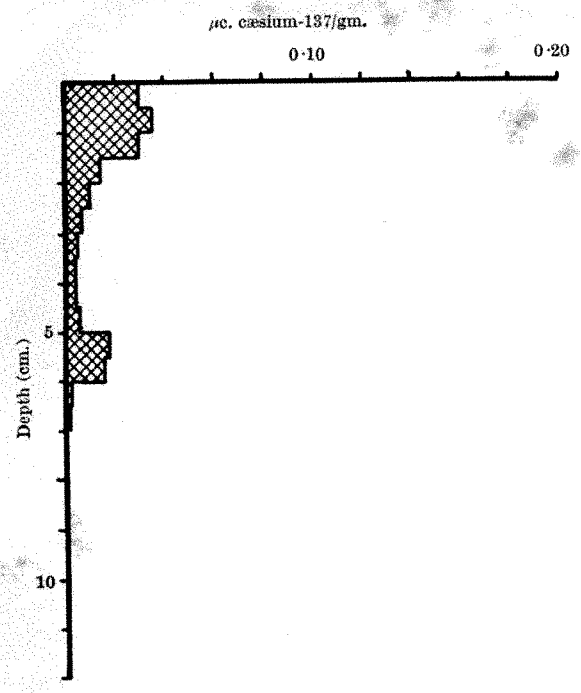

Fig. 2. The distribution of radiocæsium in clay after 1,000 mm. precipitation. The layer from 0–5 cm. depth is crumbled clay, from 5–12 cm. depth the clay is compact

When 1-gm. samples of a clay and a sand containing 0·1 μc. cæsium-137 per gm. soil were shaken for 4 hr. with 2·5 ml. acetate buffer (*p*H 4·8) only 2 and 5 per cent respectively of the cæsium-137 went in solution. This result might point to a small assimilation by the roots of plants. Indoor experiments on grass, growing on clay or sand containing 10 μc. cæsium-137/kgm., showed (in agreement with the results of Romney *et al.*[7] and Nishita *et al.*[8]) that only a few tenths of 1 per cent were actually assimilated in a period of several months. Probably only the exchangeable fraction of the cæsium-137 present in the near vicinity of the roots was assimilated.

The assumption that the main route of contamination of the biosphere is by foliar absorption was re-examined in experiments with cut grass. Thoroughly washed grass was held for 15 min. in solutions with cæsium-137 in different concentrations. The results of measurements of the amount of absorbed cæsium-137 indicate that from extremely

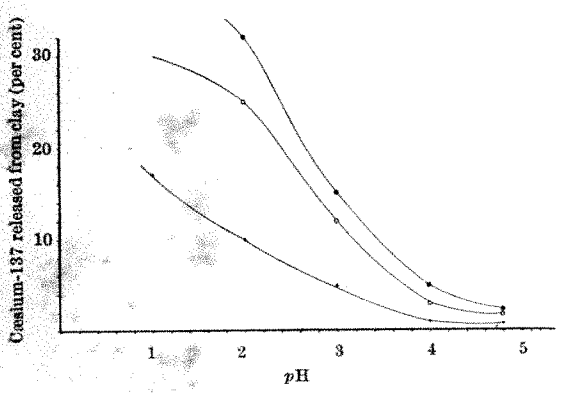

Fig. 3. The fraction of cæsium-137 coming off suspended clay after shaking for different lengths of time with solutions of varying *p*H. +, After 5 min.; ○, after 30 min.; ●, after 240 min.

diluted solutions of cæsium-137 in water about 30 per cent is fixed by the leaves in 15 min. Since even washed grass still contains about 0·1 per cent (weight) of adhering soil particles a considerable part of the absorbed cæsium-137 might actually be bound to these particles. Natural grass contains 0·2–2 per cent silica originating from adhering soil[9].

Cows may ingest together with grass several hundred grams of top soil a day (private communication by staff members of the University Veterinary X-ray Department). In Fig. 3 it is shown that with decreasing *p*H increasing amounts of cæsium-137 go in solution. In the omasum of the cow a *p*H of 2–3 prevails, and this is sufficient to dissolve in ½ hr. about 20 per cent of the cæsium-137. Under suitable conditions, for example, prolonged drought or low cæsium-137 activity of rain-water, soil could become of importance as a source of cæsium-137 to the cow and possibly also to pigs and goats. It might be worth while to re-investigate available data for an evaluation of the relative importance of soil in the transport of cæsium-137.

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In vitro Uptake of Iodine-131 by Salivary Glands, Stomach and Placenta

The ability of the thyroid gland to accumulate iodide against a concentration gradient and to maintain a high gland/plasma concentration is well known. Recently it has been shown that *in vitro* uptake of iodine-131 by the lactating mammary tissue of the rat was 10–15 times that of liver, muscle or boiled mammary tissue, and uptake of iodine-131 was increased to about twice the level observed in fresh mammary tissue by storage for 24 hr. in Ringer-phosphate at 7° C. and continued high for 25 days storage[1]. In the present experiments, *in vitro* uptake of iodine-131 by salivary glands, that is, submaxillary, parotid and sublingual; different regions of stomach, that is, fundic and pyloric; placentæ, that is, fœtal and maternal; duodenum and liver of rat were studied by incubating the tissue at 37° C. for 6 hr. in nutrient medium with *p*H 7·2 and the effects of thiouracil, potassium thiocyanate, sodium cyanide, iodide and thyroid-stimulating hormone on uptake of iodine-131 by these tissues were also investigated.

The T/M value (counts per minute per 100 mgm. tissue divided by counts per min. per 0·1 ml. medium) for uptake of iodine-131 by parotid gland was significantly higher when compared with that of submaxillary or sublingual glands. Slices from the fundic

region of the stomach showed significantly higher T/M value for uptake of iodine-131 when compared with slices from the pyloric region. The difference between the T/M values for uptake of iodine-131 by slices from fœtal and maternal placentæ was not significant. Slices of liver showed very low uptake of iodine-131 and the T/M values for the fresh and boiled tissues were practically the same. Addition of thiouracil (0·02 mgm./ml.) to the medium resulted in a decrease in uptake of iodine-131 by salivary glands and stomach slices, but it had no effect on uptake of iodine-131 by placenta or liver. Potassium thiocyanate and sodium cyanide also caused a decrease in uptake of iodine-131 by salivary glands and stomach, but not in the case of placenta or liver. Addition of thyroid-stimulating hormone (50–200 mgm./ml.) to the medium containing tissue slices did not show any effect on uptake of iodine-131 by these tissues.

Addition of large doses of penicillin (1,000 I.U./ml.) to the medium resulted in a decrease in T/M values for uptake of iodine-131 by salivary glands and stomach slices. The results for T/M values for uptake of iodine-131 by salivary glands and stomach of mouse, dog and cow were similar to that for rat except the difference between parotid and submaxillary glands was not so marked as in the case of rat. Uptake of iodine-131 by placenta of mouse was similar to that of rat. In general, the results indicate that iodide concentration mechanism in the salivary glands and stomach, but not in liver or placenta, appears to be similar to that of thyroid gland.

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Tumours of the Small Intestine in Rats after Intestinal X-Irradiation

CERTAIN effects of X-irradiation of the exteriorized or *in situ* intestine of Sprague–Dawley rats were previously reported from these Laboratories[1]. In view of the scarcity of information concerning the occurrence of tumours after exposure of the intestine to irradiation, survivors of that study, and their controls were kept for further observation. This communication reports the incidence of intestinal tumours among 51 rats that were irradiated at an age of 5 months and were killed between 9 and 30 months later. All but seven experimental and two control animals were killed because of the presence of tumours or other diseases. The nine rats were arbitrarily killed at an age of ten months at the conclusion of the period of experimentation.

In the exposures of the exteriorized intestine, the entire intestine except a portion of the duodenum and the rectum was delivered through an incision in the abdominal wall for irradiation while the remainder of the body was protected by a lead shield. The partial-body exposures were carried out through a window in a lead shield designed so that only the abdominal region was exposed. The $LD50$ was about 1,550 r. and the $LD90$ about 1,900 r. for both modes of exposure.

The incidence of intestinal tumours in irradiated and control groups is presented in Table 1. There the animals are grouped by exposure into doses below the $LD50$ and those at or above the $LD50$. The number of survivors at high levels was necessarily small. All intestinal tumours occurred in the small intestine, the region of principal histological damage. The earliest tumour was observed at 9·5 months.

Table 1. INCIDENCE OF INTESTINAL TUMOURS

Method of exposure	Dose range (r.)	Incidence	Type of tumour
Exteriorized	900–1,300	0 of 10	
,,	1,500–1,900	5 of 18	3 mucinous carcinomas 1 leiomyosarcoma 1 lymphosarcoma
Partial body	700–1,300	0 of 11	
	1,500–1,900	2 of 12	1 mucinous carcinoma 1 leiomyosarcoma
Control		0 of 25	

The incidence of malignant intestinal tumours is lower and the tumour development later than that reported by Osborne[2]. However, the radiation exposures cited here were predominantly in the mid-lethal range in contrast to the uniformly lethal dose-range employed by Osborne, who obtained survival by clamping the superior mesenteric artery and vein during exposure. Tumour development in this experiment was confined to the mid-lethal and higher dose-range, for which substantial acute intestinal damage was previously demonstrated histologically[1]. The results presented here are compatible with a dose-dependent carcinogenic effect of X-irradiation on the small intestine of the rat.

We gratefully acknowledge the technical assistance of Alma L. Crosby and Glenda S. Vogt.

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BIOLOGY

Fine Structure of the Neurosecretory System in Lepidoptera

THE following is a short account of an electron microscope study of neurosecretory cells found in three lepidopterous insects, *Bombyx mori*, *Philosamia cynthia ricini* and *Papilio xuthus*. I believe I may have succeeded in observing early stages in the formation of secretory granules in the perikarya of neurosecretory cells of the intercerebralis.

The brain-cardiaca-allata complexes were taken from mature larvæ and fixed in 1 per cent osmium tetroxide adjusted with phosphate buffer to pH 7·0–7·4. The tissue was then embedded in methyl methacrylate and n-butyl methacrylate in the proportions 1 : 3.

Mitochondria, Golgi apparatus and the endoplasmic reticulum are commonly present as in neurones in general. The most striking feature frequently encountered is the appearance of fine, elliptical, electron-dense granules (Fig. 1, g). These

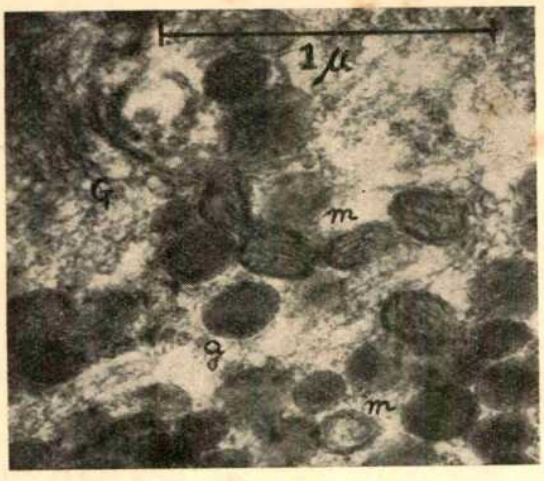

Fig. 1. Elemental granule (*g*), near Golgi apparatus (*G*) in the neurosecretory cells of intercerebralis (*Philosamia*). Note the mitochondria (*m*). Electron micrograph. (× 44,160)

granules are relatively uniform in size, each being 900–2800 Å. (1500 Å. on average) across their longest axis. These granules may be equivalent to the elemental granules[1-3] described in the neurosecretory system of vertebrates. They are either neurosecretory material or a substance intimately associated with it. They appear in crowds in the peripheral part of the cell and some are aggregated into giant granules. It is highly probable that the giant granules coincide with the secretory granules of high refractive index seen under the light microscope.

Those cells which possess few of these granules usually contain in their place many well-defined membranes of the endoplasmic reticulum. Since the secretory granules are frequently encountered within the Golgi zone, it seems possible that granule-formation occurs in close relation to the Golgi apparatus (*G*). Moreover, as shown in Fig. 1, the mitochondria which occur near the Golgi apparatus are constricted in such a way as to form strings of elliptical-shaped bodies (*m*). The cristæ in these bodies are more numerous than in the mitochondria seen in other parts of the cell. Some distance away from the Golgi apparatus the mitochondria appear to fragment and their parts (that is, the elliptical-shaped bodies) become scattered among the electron-dense granules already referred to. Gradations can be seen between the elliptical-shaped bodies and the more dense bodies which lack cristæ. These observations seem to favour the view that the elemental granules may originate from mitochondria which receive some material from the Golgi zone, as has been suggested for zymogen granules of the mouse pancreas[4]. The elemental granules in the perikarya of neurosecretory cells of the inter-cerebralis are transferred via axons into cardiaca and allata.

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Day-Length as a Factor affecting the Variation of *Chenopodium* spp. in Britain

CUMMING[1] has recently reported from the genus *Chenopodium* the existence of precociously reproductive individuals induced by short photoperiods. This communication is concerned with similar observations made during 1955 and 1956 on *Ch. album* L. and *Ch. polyspermum* L. These results were obtained during an experimental investigation into the variation pattern and cytotaxonomy of *Chenopodium* in Britain, further details of which are being published elsewhere.

Previously, Khlebnikova[2], Potapenko[3], Fuller[4] and Wahl[5] had shown that many species of the genus *Chenopodium* were photoperiodically short-day with or without a critical day-length. In addition, Wahl suggested that the day-length factor may be of significance in experimental taxonomy when he showed that the form of the mature phenotype in *Ch. bushianum* Aell. and *Ch. missouriense* Aell., in the United States, depended on the average day-length a plant received during maturation, and hence on its date of germination.

Independently, I had observed a similar, though more complex, situation in Britain. Both *Ch. album* and *Ch. polyspermum* are similar in possessing parallel intraspecific variation patterns. This intraspecific polymorphism involves a range of biotypes which form at one extreme of the continuum individuals which are predominantly vegetative with 'spicate' inflorescences, while at the other extreme plants are largely reproductive with 'cymose' inflorescences. The morphological extremes of this continuum have in the past been given taxonomic status of one form or another[5-10]. Some of these taxa are shown in Table 1.

Table 1

	Inflorescence largely spicate	Inflorescence largely cymose
Ch. album :	f. *spicatum* (Koch) Aellen	f. *cymigerum* (Koch) Aellen
	v. *candicans* (Lam.) Syme	v. *viride auct.* (*non* L.)
	v. *incanum* Moq.-Tand.	v. *concatenatum* Moq.-Tand.
Ch. polyspermum	v. *acutifolium* (Sm.) Gaud.	v. *obtusifolium* Gaud.

Both genetic and environmental variables (for example, temperature and day-length) are now known to be responsible for this polymorphism, and experiments under glass and in the field have elucidated some of the problems involved. It has been found, for example, that nearly all spicate biotypes of *Ch. album*, germinating in the field in southern England after the beginning of August (day-length about 15 hr. and decreasing), produce markedly cymose phenotypes which exactly phenocopy those biotypes which are less flexible and remain cymose under all conditions. Similarly, if seed from *Ch. polyspermum* v. *acutifolium*, which normally develops a vegetative, spicate phenotype when germinating in the spring, commences growth in the open after the third week in July (day-length about 15¾ hr. and decreasing) it will mature into the cymose type, which is usually described as v. *obtusifolium*.

Fig. 1 shows a plastocline of *Ch. polyspermum*. This plastocline was produced experimentally by planting this species in a heated greenhouse (*c.* 25° C.) at intervals of three weeks during the spring and early summer of 1956. Thus the various treatments comprised differing and increasing day-lengths. As illustrated, the form of the inflorescence and the leaf-shape progressively change as the length of day increases. Those plants receiving an average day-

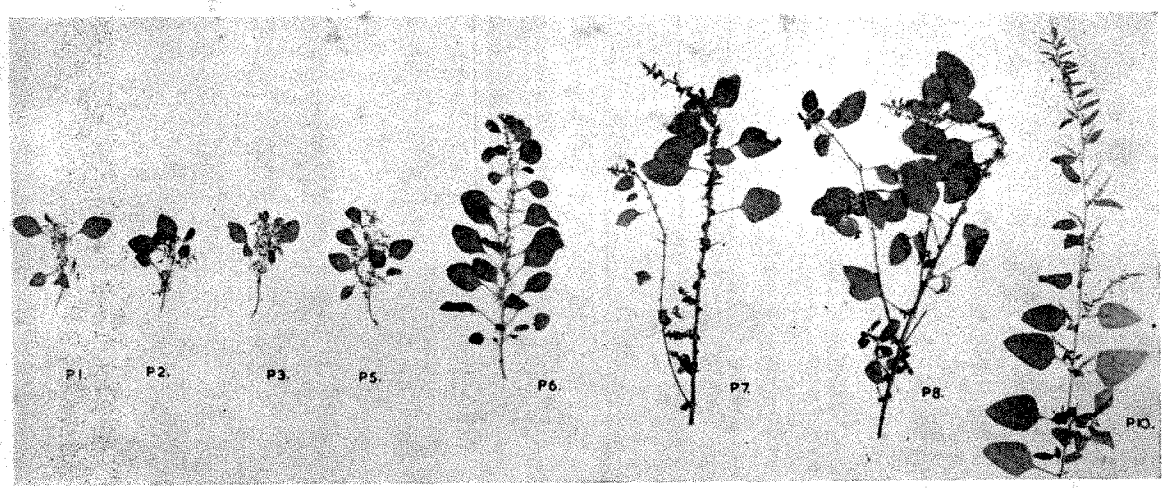

Fig. 1. A day-length plastocline of *Ch. polyspermum* L. (*P*1–*P*6 v. *obtusifolium* Gaud.; *P*7–*P*10 v. *acutifolium* (Sm.) Gaud. The day-lengths given below represent the average photoperiod (in hr.) received by each treatment: *P*1, 11·00; *P*2, 11·35; *P*3, 12·00; *P*5, 13·10; *P*6, 14·25; *P*7, 14·50; *P*8, 15·17; *P*9, 15·27; *P*10, 16·00

length (as calculated from germination to visible inflorescence initiation) of less than 13¼ hr. at 25° C. were more or less exact phenocopies of *Ch. polyspermum* v. *obtusifolium*. As the day-length increased so the plants became more vegetative, their leaves more acute, and the inflorescences less cymose until, in average day-lengths exceeding 15¼ hr., the treated plants became indistinguishable from v. *acutifolium*. A similar day-length plastocline of *Ch. album* was not obtained under the same conditions since the high temperature prevented normal growth in this species. However, a comparable plastocline was obtained by planting *Ch. album* in the open at monthly intervals from July until October.

While cymose individuals of *Ch. album*, which owe their predominantly reproductive habit to naturally occurring short-days (short-day plastodemes) and not to the inflexible expression of their genotypes (cymose genodemes), are reasonably widespread in Nature after the middle of August, at least in southern England, similarly naturally occurring populations of *Ch. polyspermum* have been observed in Britain only where this plant occurs as a greenhouse weed and never, as yet, in the open. This observed absence of short-day, cymose, plastodemes of *Ch. polyspermum* in the open is almost certainly due to the higher temperature requirements of this species, which occurs as a native only in southern England and finds its greatest development in warmer areas. Where short-day cymose phenocopies were produced experimentally, in the field in this species, full inflorescence elaboration was not completed owing to the prevailing low temperatures in October. In warmer climates, however, particularly in southern Europe and parts of the United States, the interaction of day-length and biotype and the resultant phenotypic distributions should prove worthy of further study.

In conclusion, attention is directed to the heterogeneous reaction of the spicate genodemes of *Ch. album* to autumnal short-days, in that not all the spicate biotypes do become cymose. In view of this, and in view of the phenocopying phenomena, it is conceivable that the origin of the inflexible cymose genodeme can be explained in terms of Waddington's "genetic assimilation"[11]. It is hoped that further experiments planned will add to our knowledge of this process in plants.

Most of the experimental results were obtained at the University of Southampton during the tenure of a Department of Scientific and Industrial Research maintenance award.

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Lepidoteuthis grimaldii—a Squid with Scales

IN August 1959, I collected the stomach contents of a sperm whale caught off Madeira and flensed at the whaling station at Canical in Madeira. These included three heads and four mantles of squids belonging to the genus *Lepidoteuthis*. The squids of the only known species in the genus are characterized by having a covering of 'scales' on the mantle. Joubin in 1895 first noted this unusual feature in his description of *Lepidoteuthis grimaldii* Joubin. The description was based on two mantles from a sperm whale's stomach and a fragment from the stomach of a Risso's dolphin (*Grampus griseus*). These animals were caught off the Azores. Lönnberg[1] regarded Joubin's description of scales with some scepticism, and considered that the structures referred to were the same as those he had described as papillæ in *Moroteuthis ingens* (E. A. Smith, 1891). Later, Joubin[2] gave a more detailed description of the material in his possession. No further records of this species were made until Rees and Maul[3] noted it in the fauna of Madeira. Mr. G. E. Maul, of Funchal Museum, saw two specimens of this species in the stomach contents of sperm whales caught off Madeira

Table 1. Measurements in cm.

	Present specimens				Joubin's specimens	
Dorsal mantle, length	88·6	69·0	75·3	62·0	86·0 (total length)	72·0
Ventral mantle, length	83·6	64·7	70·4	57·8		
Maximum mantle width	24·1	19·7	19·5	21·5	25·0	24·0
Fin, length	38·0	33·0	32·0	28·0	42·0	32·0
Fin, width	40·5	28·2	26·5	23·4	40·0	36·0
'Tail' behind fins	5·0	5·0	6·0	5·0		
End of pen projecting beyond body	1·8	3·0	4·2	3·3		
Maximum width of scales	1·0	0·9	0·8	0·8		

and one which was vomited by another whale killed in the same locality between 1952 and 1954[4]. He was also able to collect a complete specimen. Dr. R. Clarke[4] saw the mantle of a specimen, again in the stomach of a sperm whale caught off the Azores and processed at San Miguel.

Thus, the present record is the fourth published and only the second to include the head, which has not yet been described.

The 'scales' of these specimens are rather softer than those usually forming the external protection of fish, although, as suggested by Joubin in 1895, they resemble ganoid scales in general appearance. It is perhaps pertinent to mention that they seem to have become rather softer since being preserved in formalin, and my recollection of the fresh condition is of rather 'horny' structures. Those on the posterior of the mantle lie side by side but there is some overlapping in the anterior (oral) region of the mantle.

There is no reason for supposing that these newly found specimens belong to a different species from that described by Joubin.

With regard to the past controversy over the use of the word 'scales' when referring to the structures in *Lepidoteuthis*, I have examined the papillæ of *Moroteuthis ingens* (Smith, 1891) in several specimens collected from the stomachs of sperm whales and in their general appearance they are quite different from the 'scales' in these *Lepidoteuthis* specimens.

Fig. 1. Ventral view of mantle of *Lepidoteuthis grimaldii* Joubin 1895

According to the Concise Oxford Dictionary the term 'scale' includes "plate of thin outer piece with some resemblance to fish scale in organic or other object" as well as the narrower meaning of "one of the thin horny overlapping plates protecting the skin of many fishes and reptiles". Thus, the term covers the condition found in *Lepidoteuthis*, but seems inapplicable to that found in *Moroteuthis*.

d'Orbigny[5] described the mantle of *Onychoteuthis dussumieri* d'Orbigny 1839 as being "finement chagrinee". This was discussed by Adam[6] and sounds rather similar to the 'papillæ' described by him in *Pholidoteuthis boschmai* Adam, 1950, and to the "scale like plates" described by Voss[7] in *Pholidoteuthis adami* Voss, 1956.

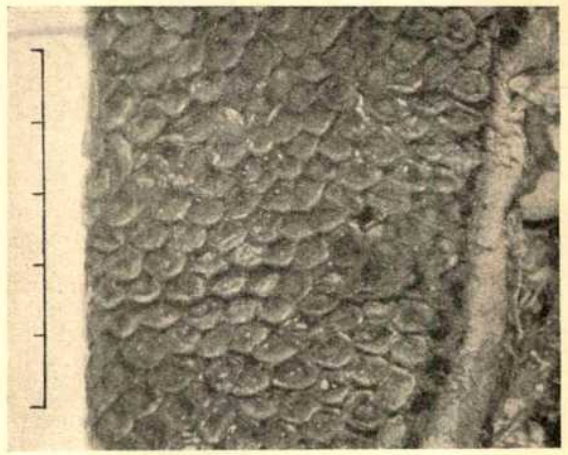

Fig. 2. Close up of 'scales' of *Lepidoteuthis grimaldii* Joubin 1895. Scale in cm.

These structures seem quite similar to those found in *Lepidoteuthis*, but are only about one-tenth of the size.

Voss[8] also described *Thysanoteuthis rhombus* as being 'scaled', but he adopted the term from previous literature (notably d'Orbigny[5]) which seems to be misleading. Specimens of this species in the *Discovery* Collections have no sign of structures which could be described as 'scales'.

A study of the relationships of *Lepidoteuthis* should prove of great interest, and a full description of the squid will shortly be published in conjunction with Mr. Maul.

I am indebted to Mr. A. Madgwick for the photographs.

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Origin of Angiosperms

PROF. T. M. HARRIS, in his recent presidential address to Section K (Botany) of the British Association[1], has directed attention to the successive failure of attempts to find fossils which appear to be ancestors of the Angiosperms. He makes a plea for more intensive study of Angiosperm-like fossils from rocks of the Triassic, Jurassic and Lower Cretaceous periods, in the confident hope that some will be found to be the early Angiosperms that have eluded search for so long. I suggest that this search for the forerunners of the Angiosperms might more profitably be directed towards gymnospermous plants occurring in the Middle Cretaceous period immediately before the first appearance of Angiosperms. In my opinion the origin of Angiosperms may have been so sudden and their early evolutionary change so rapid that there is little likelihood of early Angiosperms having been preserved as fossils.

Ten years ago I suggested[2] that the origin of the Angiosperms could be related to the occurrence of multiple-allele incompatibility between the pollen and diploid tissue surrounding the ovules. Recently, this hypothesis has received striking support from the work of Lewis and Crowe[3], who have made reciprocal crosses between self-compatible and self-incompatible species, and have shown, not only that the multiple-allele incompatibility in various Angiosperm families is of ancient origin within those families, but also that in the Solanaceae and Scrophulariaceae the incompatibility must have arisen before these families diverged from one another. In view of these findings, I believe that the abrupt origin of angiospermy, following on the evolution of this type of incompatibility, is a very real possibility. The sudden appearance of Angiosperms in the fossil record at a time when "no other stirring event occurred in the world", to quote Prof. Harris[1], would then be explained.

If this hypothesis is correct, it would follow that the Angiosperms originated immediately prior to their appearance in the fossil record, and that they arose from a single species in which this incompatibility had developed. Moreover, the change from gymnospermy to angiospermy would probably have been abrupt. Prior to the evolution of incompatibility, mutations which prevented direct access of the pollen to the ovules would be disadvantageous, owing to the greater likelihood of failure of the pollen to bring about fertilization, and the lack of any compensating advantages. However, once multiple-allele incompatibility had appeared, such mutations would be strongly favoured, since self-pollen would thereby be excluded from fertilization, while all but a minute fraction of cross-pollen would not. It is unlikely that fossils exist of this particular species in which it is presumed that the incompatibility evolved and the transition to angiospermy occurred. Hence, transitional forms may never be found. However, the family or order of Gymnosperms containing this hypothetical species might well be represented among fossils from just before the rise of the Angiosperms. This family would presumably be expected to show some of the characteristics of Angiosperms, such as the peculiarities of stamen construction, but nevertheless be gymnospermous in reproduction. Thus, in my opinion, the best hope of finding recognizable ancestors of the Angiosperms lies in a study of fossil Gymnosperms in the Middle Cretaceous period, just antecedent to the appearance of the Angiosperms.

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Nature of the Resistance of Oat Varieties to Races of Oat Stem Rust

WHETHER resistance of a given variety of plant to a given race of rust is based on a nutritional mechanism or on an inhibitory one seems still to be a debatable point. For example, is resistance due (*a*) to the inability of the rust fungus to obtain from the resistant host all the chemical precursors necessary for adequate nutrition, or is resistance due (*b*) to the presence of substances in and natural to the host or of substances arising from the interaction of the host and pathogen that directly or indirectly result in the inhibition of the pathogen? The observations recorded here contribute somewhat to the elucidation of the mechanism of resistance.

In the following experiments, the plant host comprises varieties of oats (*Avena sativa* L.) and the pathogen races of oat stem rust (*Puccinia graminis* Pers. f.sp. *avenae* Erikss. and Henn.). The 'leaf sandwich' technique designed and used in this work was a modification of a 'tissue transplant' technique described by Sharp and Emge[1].

The sandwiches were of three types: (*a*) a leaf from each of two susceptible (*S*) plants; (*b*) a leaf from a susceptible and from a resistant (*R*) plant; (*c*) a leaf from each of two resistant plants. To prepare a leaf sandwich, a strip of epidermis (2–3 cm. long) was removed from the under surface of each leaf. The exposed mesophyll tissue was bathed in 0·5 per cent water agar to prevent drying of the cells and to act as an adhesive when the two under-surfaces of the leaves were brought together. The margins of the two leaves were then cemented together with paraffin wax. One member of the leaf sandwich, the donor leaf, was inoculated with the uredospores of a given race of the rust. Once the rust mycelium was established in the donor leaf, it advanced in the region where the epidermis had been removed, through the thin layer of agar separating the two leaves, and entered the exposed mesophyll of the uninoculated (receiver) leaf.

The bridging of the rust mycelium from a donor *S*-leaf to a receiver *S*-leaf resulted in a susceptible type of infection on both leaves. Bridging from a donor *S*-leaf to a receiver *R*-leaf, or vice versa, gave rise, respectively, to a resistant or a susceptible type of infection on the receiver leaf. Bridging from a donor *R*-leaf to a receiver *R*-leaf resulted in a resistant type of infection on both leaves. The several results are illustrated in Fig. 1. In the scores of leaf sandwiches made by using the host variety combination Markton (*S*) and Rodney (*R*) and race 6 (Fig. 1), Markton (*S*) and Ajax (*R*) and race 7*A*, Markton (*S*) and Lanark (*R*) and race 8*A*, and Markton (*S*) and *C.I.* 4023 (*R*) and race 13*A*, the infection type was never found to differ from the standard reaction of the particular variety concerned.

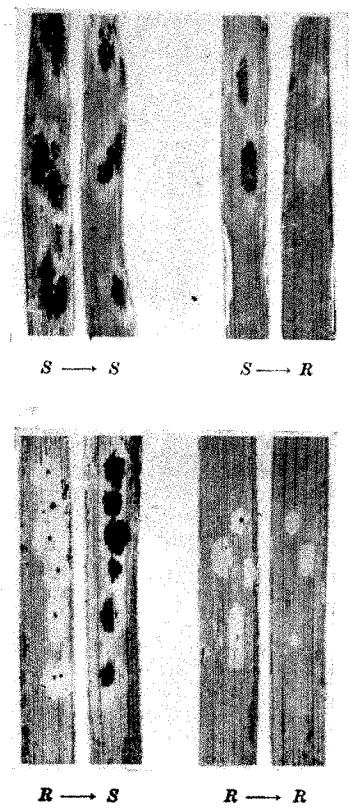

Fig. 1. Four different 'leaf sandwiches' showing the development of rust mycelium in donor leaves (left) inoculated with uredospores of race 6 and receiver leaves (right) invaded by the outgrowth of mycelium from the under surface of donor leaves. Susceptible leaf (*S*) = Markton; resistant leaf (*R*) = Rodney

The following evidence demonstrates that the failure of the *R*-leaf to show any trend toward a susceptible reaction is not due to the inability of the mycelium in the *S*-leaf to transport 'food materials' to its more remote hyphal extremities in the *R*-leaf. When the epidermis of a donor leaf was removed and the leaf merely maintained in an atmosphere of air saturated with water vapour, masses of aerial mycelium developed on the exposed under surface. This aerial mycelium received its nourishment from the mycelium living in association with the cells of the host leaf. Again, when a sandwich was made of a donor *S*-leaf carrying the radioactive tracer phosphorus-32 and a receiver *R*-leaf free from the tracer element, some of the phosphorus-32 passed through the mycelial bridge from the *S*-leaf to the *R*-leaf. The radioactivity in the *R*-leaf was concentrated at the site of the infection, though a low level of activity occurred in the immediate peripheral host tissue. In this experiment, the two leaf components were kept entirely separate from each other by means of a strip of plastic (0·5 mm. thick) except for a small opening (3 mm. diameter) in the plastic opposite the point inoculated on the donor *S*-leaf. In the absence of mycelium (uninoculated control), phosphorus-32 did not pass from the donor *S*-leaf to the receiver *R*-leaf. These results indicate that the mycelium in the *S*-leaf was able to support its mass extension beyond the confines of the leaf tissue itself and that, indeed, nutrient materials do pass over the mycelial bridge from the mycelium of the susceptible leaf to its more distant extension in the resistant leaf.

If resistance is due to a deficiency or an inadequate availability of the growth medium in the *R*-leaf, the mycelium in this leaf should be able, via the mycelium bridge, to supplement its local food supply from the mycelium in the *S*-leaf. Granted that the supplement received may not be entirely adequate to change the infection type from resistant to susceptible, yet it might reasonably be expected to shift the reaction somewhat in that direction. No such shift has been observed to occur, at least within the time interval of these experiments (14 days after inoculation). Resistance in the oat plant seems, therefore, not attributable to the failure of a resistant plant to supply the factors necessary for the growth of the rust pathogen, but rather to some specific type of inhibition, the nature of which has not been ascertained. The inhibitory mechanism seems not to be operative beyond the resistant tissue because the mycelium is capable of migrating from this tissue to a receiver *S*-leaf and of growing vigorously in it. This fact suggests that the inhibition arises from the interaction of the rust mycelium and the host cells. Details of this work will be published elsewhere.

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ENTOMOLOGY

Facultative Parthenogenesis in Collembola (Insecta)

PARTHENOGENESIS in insects is well known, and its occurrence in the class is fairly widespread. In the order Collembola (the springtails) its presence has been suggested on rather disputable grounds and then afterwards denied on more than one occasion[1]. Choudhuri gave the first real proof of the phenomenon within the order when he described[2] a new species of Collembola (*Onychiurus parthenogeneticus*). He was able to study this species not only by examination of museum material from Europe and Africa but also by observations on specimens maintained in culture for more than two years. No males of this species were ever seen by him. In all, some forty species of the genus were examined by Choudhuri, and this was the only species in which no males were found. This led to the assumption that the phenomenon may be rather rare in Collembola. Gisin[3] placed *O. parthenogeneticus* as a junior synonym of *O. hortensis* Gisin, 1949, and stated that "die Kolonien offenbar meist aus lauter Weibschen bestehen". This synonymy is not upheld by Choudhuri and Goto (in the press), but the two species are obviously very close. The suggestion that at least some males are present in Gisin's species indicates that facultative parthenogenesis might possibly occur in certain circumstances in Collembola.

A number of species of Collembola have been reared in this Department during the past ten years. Among these are two species of the isotomid genus *Folsomia* (*F. candida* Willem and *F. cavicola* Dela-

mare). In both these species, males and females have been found in wild populations in approximately equal numbers. They may easily be separated from each other by the form of the external genital aperture; the sexes are otherwise indistinguishable. Neither pairing of any kind nor the deposition of spermatophores has ever been noted in these species; but it was assumed that the males were functional since the testes were normally developed. Individuals raised from single eggs were kept in isolation and in the case of females produced eggs without ever having been in contact with a male. Great care was taken to ensure that the food and culture dishes were free from any possible contamination with spermatophores. The eggs produced under these conditions were viable and gave rise only to females. From these, completely parthenogenetic cultures were built up. Repetition of these experiments always gave the same results. There is no significant difference in the number of eggs viable nor is there any obvious structural or biological change in the parthenogenetic individuals.

Observations on other genera of Collembola are still in progress and all that can be said as yet is that facultative parthenogenesis is present, but by no means universal in the order.

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Antigenic Property of the Oral Secretion of Fleas

The development of hypersensitivity to bites of blood-sucking insects in man and animals requires an initial sensitization by the insect, or by antigens prepared from the insect. A latent period occurs between the time of the initial exposure and the time when challenge elicits skin reactions characterized by delayed and/or immediate types. Thus B. Hudson *et al.*[1] and Benjamini *et al.*[2] demonstrated that when guinea pigs were exposed to flea bites they developed an allergic state which required a latent period of 5–7 days for the appearance of delayed reactions, and an additional 2–5 days for the onset of immediate reactions. It was further shown by Benjamini *et al.* that guinea pigs could be sensitized to flea bites by intradermal injection of saline solution containing antigens prepared from fleas, or by the intramuscular injection of such antigens in combination with the complete Freund's adjuvant. When sensitization to flea bites with prepared flea antigens was achieved, the latent period required for the appearance of delayed skin reactions extended from 10 to 14 days, the immediate reaction still appearing within 2–5 days following first appearance of the delayed reaction.

Although most workers have assumed that the specific agent responsible for sensitization and for the allergic reaction is present in the oral secretion ('saliva') of hæmatophagous insects, this hypothesis lacks direct experimental evidence. By a series of delicate experiments it was recently shown by A. Hudson *et al.*[3] that severing the main salivary duct of mosquitoes prevented allergic reactions to their bites, thus suggesting that the source of the allergen lies in the salivary glands.

It is the purpose of this communication to present direct experimental evidence for the allergenic nature of the oral secretion of fleas. This was achieved by the experimental sensitization of guinea pigs to flea bites with oral secretion of these insects collected *in vitro*.

The oral secretion of laboratory-bred cat fleas, *Ctenocephalides felis felis* (Bouché), was collected *in vitro* in distilled water using the apparatus described by Kartman[4]. Approximately 1,000 fleas were confined in each feeding chamber. The insects were allowed to feed for 1 hr. on distilled water, maintained at 37° C., through a highly purified animal membrane[5]. At the end of the feeding period the substrate was collected and lyophilized. The lyophilized product was green-brown in colour and had a somewhat gummy consistency. The yield of the lyophilized product obtained from the feeding of about 100,000 fleas was approximately 100 μgm. The product was then taken up in 15 ml. of saline and filtered through an ultrafine glass filter to remove bacterial contamination. Controls consisted of identical distilled water collection and treatment, but with no fleas confined in the feeding chamber. On lyophilization, the control flask was colourless with no detectable yield.

The animals used were white or albino guinea pigs of mixed sexes weighing 200–300 gm. each. Each animal was injected intradermally twice, at weekly intervals, with 0·5 ml. of the oral secretion or the equivalent control in saline. The oral secretion consisted of 3 μgm. of the final lyophilized product, which is equivalent to the oral secretion collected from the feeding of about 3,000 fleas. With intraperitoneal injections, each animal was given 0·5 ml. of the oral secretion in saline, or in combination with Freund's complete adjuvant[6]. The oral secretion–adjuvant combination was prepared by mixing the oral secretion in saline with an equal volume of adjuvant (thus each intraperitoneal injection contained 1·5 μgm. of the final lyophilized oral secretion, which is equivalent to that collected from the feeding of about 1,500 fleas). The corresponding control was prepared in an identical manner. In addition, two other groups of guinea pigs were used. One consisted of animals each of which received two weekly intradermal injections of 0·5 ml. of 2 mgm./ml. whole flea extract in saline. In the other group, each guinea pig was exposed daily to bites of 20 fleas.

Two weeks following the initial injection, the animals were challenged daily with bites of 20 fleas each until delayed reactions appeared. The challenging procedure follows the method described by Benjamini *et al.*[2]. Results are shown in Table 1.

Results presented in Table 1 show that sensitization to flea bites was achieved when animals were injected intradermally with whole flea extract, and when animals were injected intraperitoneally with oral secretion in combination with the adjuvant. These results demonstrate the presence, in the oral secretion of cat fleas, of a substance or substances which are responsible for the development of hypersensitivity to flea bites in guinea pigs. The fact that the majority of animals injected with whole flea extract, or with oral secretion in combination with adjuvant, reacted to the challenging bite on first exposure demonstrates the ability of the oral secretion to induce

Table 1. INDUCTION OF SENSITIVITY TO FLEA BITES IN GUINEA PIGS BY INJECTIONS OF WHOLE FLEA EXTRACT, FLEA ORAL SECRETION, AND BY FLEA BITES

Method of sensitization	No. of animals used	Flea bite challenge two weeks after initial injection				
		Per cent animals showing delayed reactions on day of exposure				
		First day	Second day	Third day	Fourth day	Fifth day
Flea bites*	20	0·0	0 0	0 0	10·0	100·0
Whole flea extract (intradermal)	20	100 0	100 0	100 0	100 0	100 0
Oral secretion (intradermal)	20	0 0	0 0	0 0	10 0	100 0
Control for oral secretion (intradermal)	20	0 0	0 0	0 0	5 0	100·0
Oral secretion (intraperitoneal)	10	0 0	0 0	0 0	20 0	100 0
Oral secretion with Freund's adjuvant (intraperitoneal)	15	80 0	80 0	80 0	93·2	100 0
Control for oral secretion with Freund's adjuvant (intraperitoneal)	15	0 0	0 0	6 7	26 6	100 0

* Flea bite sensitization began on first day of challenge.

hypersensitivity. In comparison, the corresponding controls reacted only after five daily exposures, when sensitization finally was elicited by the challenging bites. The fact that sensitization was not induced when oral secretion was injected intradermally or intraperitoneally in saline alone suggests that oral secretion contains an incomplete antigen which by itself is incapable of inducing sensitivity. On the other hand, in combination with an adjuvant the oral secretion achieves its full antigenic properties. The observation that animals sensitized to flea bites by bites of fleas do react to skin challenges given with oral secretion is further support of the hypothesis that the substance in the oral secretion responsible for the induction of hypersensitivity shows characteristics of a hapten. It remains for future work to test this hypothesis.

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GENETICS

Natural Selection and the Sex Ratio

IN a recent article, Kalmus and Smith[1] have attempted to explain why a sex ratio of about one half is selectively advantageous. More recently, Bodmer and Edwards[2] have published a paper on the same subject. The two approaches differ in the emphasis placed on different forms of selection. Kalmus and Smith believe that there are two main selective forces: one which requires the chance of encounter of a male and a female at the reproductive age to be a maximum, and hence that the sex ratio at this age should be one half (as suggested by Crew[3]); and the other that the genetic variance of a population should be as large as possible for a given population size, which also requires a sex ratio of one half at sexual maturity. On the other hand, Bodmer and Edwards maintain that the most important selective force arises through the advantage of reproducing as efficiently as possible, that is, of making the maximum genetic contribution to future generations for a given amount of effort devoted to the bearing of young. As Fisher[4] pointed out, a sex ratio of about one half is the most efficient in this sense.

The fundamental difference between these two approaches lies in the mode of selection. The types of selection that Kalmus and Smith believe important can only operate *between* populations, whereas the latter, or Fisherian, type can only operate *within* a population. Thus Kalmus and Smith maintain that populations with sex ratios about one half are common because they have replaced populations with other sex ratios, while Fisher's argument supposes that even an isolated population will evolve towards a sex ratio of one half. It is thus clear that only in exceptional circumstances will a population be at a selective advantage over a competing population on account of its sex ratio since both will already have evolved a sex ratio of one half.

If interpopulation selection were of paramount importance in determining the sex ratio one would expect to have found that isolated populations, which are not subjected to it, frequently had sex ratios different from one half, which has not been observed. Furthermore, in polygamous species in which a single male, after defeating his competitors, fertilizes a large number of females, there is no longer any reason for it to be advantageous if the chance of encounter of a male and a female is at a maximum: prolific reproduction is ensured only if there is a plentiful supply of females and the sex ratio is very low. The fact that the genetic flexibility of the population is then somewhat restricted is unlikely to outweigh the advantages of such a sex ratio in interpopulation selection, where the ability to breed large numbers is of particular importance. Nevertheless, the sex ratio in such species seems to be about one half.

Kalmus and Smith concede the relevance of Fisher's theory when they state that "in the case of species which rear their young, a further reason for expecting equality of sex-ratio at the time of sexual maturity has been given by Fisher". But this is a misrepresentation of what Fisher actually wrote: his argument refers not only to species which *rear* their young, but also to species in which reproduction involves some expenditure of effort by the parents—

that is, to all sexually reproducing species. Furthermore, as Bodmer and Edwards have shown, it is not equal numbers of the sexes at maturity that is expected but equal numbers at the end of the period of parental dependence.

It thus seems that Kalmus and Smith have not fully appreciated the force of Fisher's argument. When the two points of view are compared in detail there is little doubt that it is Fisherian selection that is primarily responsible for the observed numerical equality of the sexes in many species.

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Chromosome Breakage induced by electrolytically produced Free Radicals

IN assessing the mode of action of radiations in biological systems, the free radicals have been recognized as playing an important part in producing the end effect[1]. It has also been shown that chemically produced free radicals (hydroxyl ions from hydrogen peroxide plus iron ions) are capable of inducing chromosome breakage in barley[2]. In the present work, attempts were made to study the biological effects of free radicals and secondary products produced electrolytically by the well-known Kolbes synthesis[3] in which the anode reaction can be described as follows:

$$(1)\ RCOO^- \text{——} RCOO^\cdot + e$$
$$(2)\ 2RCOO^\cdot \text{——} 2CO_2 + (2R\cdot)$$
$$R - R$$

Reaction 2 is accompanied by release of energy. Although the possibility that this energy may be emitted as light is certainly very low (about 1 in 10^{10}), it can be measured by means of a sensitive photon-counting detector system. The life of the light-emitting species can be measured by applying the pulses from the photomultiplier tube to a rate-meter circuit on an oscilloscope. The emission spectrum was recorded by means of six interference filters (350–700 mμ).

We have observed that when different plant oils react with alkaline buffers, there is a simultaneous emission of light during the reaction. The energy of the light emitted varies with different oils. At present it is not clear as to whether the light comes from the reacting radicals or from the decomposition of peroxides. However, the light-energy can be correlated with the mutagenic ability of the oils[4,5]; mutagenic oils emit light of higher energy than the non-mutagenic oils.

Similarly, it is possible by electrolysis of some simple amino-acid solutions to produce reactive species with different light 'emission energy' and different length of life; for example, tyrosine gives reactive species with high energy and long life, whereas cysteine, known as affording protection from radiation, gives light with low emission-energy and short life (high energy refers to quanta of 2·7–3·0 eV., low to about 2·4 eV.). Furthermore, when both tyrosine and cysteine are present during electrolysis, light emission and length of life were the same as in cysteine electrolysis[6].

In the present work we have used tyrosine and cysteine as a 'model system' and barley root meristems as the biological material, since the latter is known to be an extremely stable cytological material (ref. 7 and Ehrenberg, L., and Natarajan, A. T., unpublished work). Freshly germinated barley seeds (with roots about 5 mm. long) were placed with their root tips on a platinum anode and electrolysed (4·5 V.) for 1 hr. in the following solutions:

(1) Sodium acetate (0·06 *M*)
(2) ,, + tyrosine (saturated)
(3) ,, + cysteine (0·01 *M*)
(4) ,, + ,, + tyrosine (saturated)

After treatment, the seeds were washed and allowed to recover for 18 hr. The root tips were fixed in acetic alcohol (1 : 3) and slides were prepared as Feulgen squashes. The slides were scored for chromosomal aberrations at both metaphase and anaphase stages. The results are presented in Table 1. Two sets of controls were treated for 1 hr. without electrolysis in different solutions as well as in solutions which had been electrolysed for 1 hr. At least two hundred cells were scored for each treatment and no cytological abnormalities could be detected in this material. Material electrolysed in tyrosine exhibited at least a ten-fold increase in chromosome breakage over the rest of the treatments. It is of interest to note that by the addition of cysteine to the system, the effect of tyrosine could be nullified.

Table 1

Solution electrolysed	No. of cells studied	Aberrant cells (per cent)	Aberrations (per cell)
(1) Sodium acetate (0·06 *M*)	722	0·41	0·0041
(2) Sodium acetate (0·06 *M*) + tyrosine	172	5·80	0·0820
(3) Sodium acetate (0·06 *M*) + cysteine	414	0·23	0·0023
(4) Sodium acetate (0·06 *M*) + cysteine + tyrosine	215	0·47	0·0047

In the genetic material there are obviously chemically reactive groups susceptible to radiomimetic agents such as radicals, peroxides, epoxides, etc. To get a reaction, the radiomimetic agent and the reactive group in the nucleus must have more energy than the possible reaction products. If we assume the reactivity of the actual genetic material to be constant, then the energy content of the radiomimetic substance determines if a reaction will take place or not.

The results from the experiments mentioned above together with the emission spectroscopic measurements[6] on various substances make it reasonable to assume that the energy of the emitted light is an expression of reacting potential towards other molecules[8] (this is not valid in the case of molecules where the excited state is protected against external chemical reactions). Then it is possible, by means of emission spectroscopy, to screen reactive species from a radiobiological point of view.

In our experiments, the reactive species are produced outside the cell and must have a long life to reach critical sites inside the cell. Though the kind of reactive species involved is not clear at present, it is of interest that such types of species are certainly produced in irradiated biological systems also.

The occurrence of low energy-levels in the chromosome with high polarizability of electrons in these

levels makes it possible to assume that the reactivity of the genetic material is highly dependent on the chemical environment, for example, as determined by water content. Perhaps this polarizability can be increased by addition of particular substances and cause the reactive groups to be even more reactive towards radiomimetic agents. This problem is under investigation.

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ANTHROPOLOGY

The Olduvai Giant Hominid Tooth

THE giant molar tooth found by Dr. L. S. B. Leakey[1] in Bed II at Olduvai Gorge in Tanganyika was reported by him[1,2] to be a lower deciduous second molar of a hominid, possibly related to *Sinanthropus* and *Homo heidelbergensis*. This interpretation has been questioned by a number of workers including G. H. R. von Koenigswald[3] of Utrecht and John T. Robinson[4] of Pretoria, who conclude that the tooth is rather a permanent upper molar, probably Australopithecine.

I am in agreement with the views of the last two authors on all but one point, that is, the contention that it necessarily is a permanent tooth. Its size certainly places it in the range of the Australopithecine permanent molars (including those of *Zinjanthropus*), but several things make it difficult to rule out the deciduous grouping.

Beyond a doubt the root system is that of an upper molar. There are three roots, two obviously buccal and the large lingual one extending palatally in the typical fashion which required that it had the accommodations of the maxillary alveolus rather than the restrictions of the mandibular bony support. The cast of the tooth, available to me through the courtesy of Dr. K. P. Oakley of the British Museum (Natural History), suggests also that the roots may have been in the process of resorption from the influence of the developing permanent tooth which nestled above and between them. This may be questioned, though, by the fact that lack of wear suggests that the tooth is not old enough to be in the resorptive stage. The spreading disposition of the roots with the markedly constricted neck of the tooth strongly suggests a deciduous character.

The occlusal surface of the Olduvai tooth is long and narrow, as outlined by the tips of the cusps.

Table 1. LENGTH AND BREADTH OF UPPER MOLARS

	MD lg	*BL br*	M_1 *MD lg*	M_1 *BL br*	M_2 *MD lg*	M_2 *BL br*
Olduvai tooth	15	14				
Zinjanthropus			15 5	18 0	17 0	21 0
Australopithecus crassidens Swartkrans 89 (av.)			14 6	15·0		
Australopithecus crassidens Swartkrans 27 (av.)			14·0	13 2		

This is a feature seen mainly on deciduous teeth, although it does occur on the permanent ones but much less frequently. The strong development of the metacone also speaks in favour of this being a deciduous rather than a permanent tooth.

Robinson's points on the relative position of the buccal and lingual cusps, the intercuspal crest and the accessory cusps in the fovea, are valid. So is his argument against the heavily worn deciduous canine belonging to the same individual from which the molar came. Von Koenigswald used an index based on mesio-distal crown lengths to compare the tooth sizes in *Homo*, *Australopithecus* and the Olduvai specimen. He felt that the value of 214 for the latter placed it definitely within the range of *Australopithecus*, which had indexes of 148 and 187 as contrasted to 117 and 153 for *Homo*. The tooth dimensions of *Zinjanthropus boisei* (from Bed I in the same gorge)[5] were not available to him at the time. The difference in size between anterior and posterior teeth in *Zinjanthropus* is so considerable that applying von Koenigswald's index to the permanent first molar of the latter and the Olduvai deciduous canine[5] gives a value of $228 = \left(\frac{15 \cdot 5}{6 \cdot 8} \times 100\right)$. An Olduvai deciduous second molar would be expected to be smaller than this, and hence comes closer to the measurement of the giant Olduvai tooth being discussed. Thus, the argument of size and proportions favours rather than discounts the identification of the Olduvai molar as a deciduous tooth.

In my opinion, therefore, the Olduvai molar could very well be a left maxillary deciduous second molar.

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PSYCHOLOGY

Senile Dementia and Cerebral Oxygen Uptake measured on the Right and Left Sides

IN a recently concluded work[1] on cerebral oxygen uptake in the aged, an unexpected result was that uptake values based on blood drawn from the left internal jugular vein were more closely related to mental function than were values based on right jugular blood. Five normal aged men and nine male

patients with chronic brain syndrome were included in this part of the investigation. Bilateral cerebral oxygen uptake determinations were made with Lassen and Munck's modification[2] of the inert gas method of Kety and Schmidt[3]. This modification employs krypton-85 as the inert gas, and bilateral simultaneous sampling of internal jugular blood is carried out. Psychological functioning was assessed by the Wechsler adult intelligence scale and Raven's matrices[4]. The physiological and psychometric data were not compared until after completion of the investigation.

Table 1 lists the correlations obtained between the Wechsler adult intelligence scale sub-tests and matrices scores, and the cerebral oxygen-uptake values of the right and left sides. One patient was aphasic and unable to perform any psychological tests, and other patients did not complete all tests; the numbers for the several correlations therefore vary. It will be seen that the correlations are consistently higher on the left and that many are statistically significant. None of the correlations on the right achieves statistical significance. The values of cerebral oxygen-uptake for the two sides were negatively but not significantly correlated, $r = -0{\cdot}14$.

Table 1. CORRELATIONS OF CEREBRAL OXYGEN UPTAKE VALUES* MEASURED ON THE RIGHT AND LEFT SIDES WITH PSYCHOMETRIC TESTS

Wechsler adult intelligence scale sub-tests	Correlation with central oxygen uptake values		
	No.	Right	Left
Block design	12	0·22	0·63*
Similarities	13	0·15	0·60*
Digit span	13	0·04	0·32
Picture arrangement	10	−0·13	0·77†
Picture completion	10	0·00	0·62*
Digit symbol	9	0·38	0·57
Arithmetic	13	0·13	0·57*
Information	13	0·04	0·61*
Vocabulary	13	0·04	0·41
Progressive matrices	10	0·18	0·44

Uptake right versus uptake left, $r = -0{\cdot}14$.
$* P < 0{\cdot}05$; $\dagger P < 0{\cdot}01$.

* The uptake values with which the correlations of Tables 1 and 2 were computed are 'infinity' values, based on extrapolation of the venous curve (cf. discussion in ref. 1). Correlations based on 10-min. values, available in this work, showed an even more marked difference in favour of the left side.

In order to evaluate this finding further, correlations were computed on data available from previous work by Lassen *et al.*[5], which employed the same physiological techniques and similar psychometric methods on a population resembling our own. These correlations are listed in Table 2. It will be seen that the correlations are again consistently higher on the left, though the difference between sides is slight. However, in this work the cerebral oxygen uptake values on the right and left sides were themselves positively and significantly correlated ($r = +0{\cdot}58$). Therefore, partial correlations were computed; these indicate the relatively independent relationship to the psychometric data of the uptake values of each side. The results are listed in parentheses in Table 2. It will be seen that this procedure enhances the difference between sides: three of the four correlations on the left remain statistically significant, while none on the right does so.

These findings therefore suggest that cerebral uptake values based on right and left jugular blood have different significance for the aspects of mental function measured by the psychological tests. How may this difference be interpreted? One possibility is that uptake values based on jugular blood samples reflect predominantly the state of cerebral metabolism in the ipsilateral hemisphere. If this were so,

Table 2. CORRELATIONS OF CEREBRAL OXYGEN UPTAKE VALUES WITH PSYCHOMETRIC TESTS

Calculated from data available from a previous bilateral study. Partialled correlations in parentheses. $N = 18$

Psychometric test	Correlation with cerebral oxygen uptake values			
Wechsler adult intelligence scale sub-tests	Right		Left	
Block design	0·59†	(0·27)	0·72†	(0·58)†
Similarities	0·43*	(0·16)	0·57†	(0·44)*
Digit span	0·34	(0·12)	0·44*	(0·31)
Progressive matrices	0·59†	(0·27)	0·72†	(0·58)†

Uptake right versus uptake left, $r = 0{\cdot}58$†.
$* P < 0{\cdot}05$, $\dagger P < 0{\cdot}01$.

we might relate our findings to hemisphere dominance (12 of the 13 subjects were right-handed) and to the oft-noted special importance of the left side of the brain for intellectual function. (The relative importance of left and right hemisphere lesions as causes of cognitive impairment in man is not a settled issue. It has been well established that those intellectual functions closely related to or dependent on language are more severely impaired by lesions of the left hemisphere[6]. However, recent psychological work has yielded evidence that skill on certain 'non-verbal' or 'performance' tasks is reduced more by right than by left cerebral lesions[7]. It should be noted that, in our investigation, the 'performance' as well as the 'verbal' tasks of the Wechsler adult intelligence scale were more highly correlated with left cerebral oxygen uptake values.) However, the degree of intermixture of venous blood from the two hemispheres has not been definitely established. A study[8] of intra-carotid injection of T-1824, carried out in five normal subjects, found a mean ratio of dye recovery from the internal jugular veins (contralateral : ipsilateral) of 1 : 3. It can be shown mathematically that correlations of the magnitude we report here are not incompatible with this degree of intermixture. (We are indebted to Dr. S. Geisser, of the Biometrics Branch, National Institute of Mental Health, for this proof and for other statistical advice.) However, until the sources of blood draining into the jugular veins are more fully determined, it would be premature to interpret the difference in correlation with mental state as the result of a general metabolic difference of the respective hemispheres. It remains conceivable that it is the metabolic activity of a localized brain area, the drainage of which is strictly unilateral, which is the significant variable.

An alternative possibility is that the two sides have differing proportions of cortical/subcortical blood, and that it is some aspect of this ratio which is reflected in the differing correlations with mental state. However, while anatomical evidence suggests that frequently one side receives the larger proportion of cortical blood, neither side appears to be consistently favoured[9]. Further, bilateral cerebral oxygen uptake determinations in normals have failed to reveal significant differences between the right and left sides[2,3]; if one side consistently drained more cortical blood, one would expect its metabolic rate to be higher.

Whatever their underlying basis, our findings raise the possibility that cerebral oxygen uptake values on the right and left sides may not be of equal significance for mental function. If so, previous unilateral studies, which were performed predominantly on the right side and which failed to show any relationship to psychological variables[10], require re-evaluation. Reliable correlations between physiological and mental states have been notoriously

difficult to establish. It now appears possible that application of the bilateral method may considerably enhance the significance of cerebral oxygen uptake measurements and thus offer new opportunities for research in this area.

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[1] Lassen, N. A., Feinberg, I., and Lane, M. H., *J. Clin. Invest*, 39, 491 (1960).
[2] Lassen, N. A., and Munck, O., *Acta Physiol. Scand.*, 33, 30 (1955).
[3] Kety, S. S., and Schmidt, C. F., *J. Clin. Invest.*, 27, 476 (1948).
[4] Wechsler, D., "Manual for the Wechsler Adult Intelligence Scale" (The Psychological Corporation, New York, 1955). Raven, J. C., "Progressive Matrices; Coloured Progressive Matrices" (H. K. Lewis and Co., London, 1938 and 1956, respectively).
[5] Lassen, N. A., Munck, O., and Tottey, E. R., *Amer. Med. Assoc. Arch. Neurol. and Psychiat.*, 77, 126 (1957).
[6] Weinstein, S., and Teuber, H. L., *Science*, 125, 1036 (1957). Meyer, V., *Amer. Med. Assoc. Arch. Neurol. and Psychiat.*, 81, 299 (1959).
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[8] Shenkin, H. A., Harmel, M. H., and Kety, S. S., *Amer. Med. Assoc. Arch. Neurol. and Psychiat.*, 60, 240 (1948).
[9] Edwards, E. A., *Amer. Med. Assoc. Arch. Neurol. and Psychiat.*, 26, 801 (1931).
[10] Kety, S. S., Woodford, R. B., Harmel, M. H., Freyhan, F. A., Appel, K. E., and Schmidt, C. F., *Amer. J. Psychiat.*, 104, 765 (1948). Sokoloff, L., Mangold, R., Wechsler, R. L., Kennedy, C., and Kety, S. S., *J. Clin. Invest.*, 34, 1101 (1955).

The Relativity of Meaning

THE burden of Dr. Ross Ashby's communication[1] · "the meaning of a message also depends on the set that the message comes from" is known to every careful user of the English language who has learnt the meaning of the word 'context', but his example is incomplete. The messages that he instances may indeed change their meanings as the set is expanded, but "How we wish you were here" does not necessarily become ironic because "Do come and join us" is available as well. If the sender knows that such joining is impossible he may honestly choose the former message, which will then have the same meaning as if it were the only one of the two available. The set is of less importance in determining meaning than is the mutual knowledge that sender and recipient have of one another.

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[1] Ashby, W. Ross, *Nature*, 187, 532 (1960).

DR. ROSS ASHBY[1] advocates the "postulate that the meaning of a message [as well as its information content] . . . depends on the set of messages that the message comes from". It seems possible that Dr. Ashby was thinking primarily in terms of non-natural languages (such as those used as models in information theory). However, his example is drawn from natural language, and presumably his argument is meant to apply to all languages.

If this is so, I suggest that his point should be thought of as a special case of a quite general rule of language, when it is used to express empirical information. It is normally true that the meaning given to an empirical statement (a message) both by the deliverer and by the receiver will depend on a number of factors in addition to its 'intrinsic' properties; that is, the shapes and ordering of its signs.

The most influential of these factors is the 'purpose' of the statement, which in its turn determines what is its mode of justification or verification, what is the relevant 'set of messages' (context), how much the statement is to be taken as elliptical, and so on; all these are, of course, themselves part-determinants of meaning—of how a statement will be interpreted. Obvious examples are "That object has a low temperature" (in the kitchen or in the laboratory ?), "That hill is dangerous" (for motor-cars or aeroplanes ?) and "Water is H_2O" (definition or description ?).

In current linguistic theory, such cases are treated as exceptions. But in fact there are reasons[2] for thinking that a great deal of trouble could be saved, not only within the field of communication theory but also in controversy in general, if it were regarded as the rule that the way in which sentences (and sometimes individual words) are to be interpreted depends in part on the purpose for which they are used.

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[1] Ashby, W. Ross, *Nature*, 187, 532 (1960).
[2] Crawshay-Williams, R., "Methods and Criteria of Reasoning" (Routledge, London, 1957).

MATHEMATICS

Theory of Optimal Gammas

Ross[1] asks for a definition of the goodness of a game. A reasonable answer, though presumably incomplete, is that a game is good in so far as it involves skill. A measure, γ, for the degree to which a game is one of skill may also be of legalistic interest in those countries where gambling is somewhat against the law. Several years ago I suggested a definition for γ, and it may now be appropriate to publish it. The definition is relative to a population of learners and trainers and to the number of learners, and is relative to the training time and to the duration of play. If we assume all these parameters to be fixed we should find that the players would fall into γ grades, $C_1, C_2, \ldots, C_\gamma$, such that, on average, a player in grade C_g would have a probability of say 2/3 of beating a player in grade C_{g+1} ($g = 1, 2, \ldots, \gamma - 1$). The number, γ, of grades, is then the suggested measure of the degree to which the game is one of skill. It is not a good measure of difficulty, since some games, such as the child's game of 'boxes', are so difficult for human beings that training and ability do not count for much.

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[1] Ross, A. S. C., *Nature*, 187, 968 (1960).

FORTHCOMING EVENTS

*(Meeting marked with an asterisk * is open to the public)*

Monday, December 12

INSTITUTION OF ELECTRICAL ENGINEERS, ELECTRONICS AND COMMUNICATION SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Dr. P. R. Bryant: "Topology Concepts in Network Theory".

INSTITUTE OF METAL FINISHING (at the Northampton College of Technology, St. John Street, London, E.C.1), at 6.15 p.m.—Mr. J. M. Kape: "Unusual Anodizing Methods and Their Practical Significance".

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S.W.7), at 8.30 p.m.—Brig. Bernard Fergusson, D.S.O., O.B.E.: "A Return to Upper Burma".

Tuesday, December 13

ILLUMINATING ENGINEERING SOCIETY (at the Federation of British Industries, Tothill Street, London, S.W.1), at 6 p.m.—Mr. J. M. Waldram: "Visual Problems on Motorways".

INSTITUTION OF MECHANICAL ENGINEERS, AUTOMOBILE DIVISION (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Mr. J. P. Soltau: "Maximum Cylinder Pressure Fluctuations in a Petrol Engine".

BRITISH INSTITUTION OF RADIO ENGINEERS, ELECTRO-ACOUSTICS GROUP (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6.30 p.m.—Mr. G. D. Browne: "A Pulse Multiplex Stereophonic Broadcasting System".

INSTITUTION OF ELECTRICAL ENGINEERS, LONDON GRADUATE AND STUDENT SECTION (at Savoy Place, London, W.C.2), at 6.30 p.m.—Sir Hamish D. MacLaren, K.B.E., C.B.: "Electrical Engineering in the Naval Service".

INSTITUTION OF THE RUBBER INDUSTRY (at the Royal Overseas League, Park Place, St. James's, London, S.W.1), at 5.30 p.m.—Mr. E. E. Gunn: "Some Radiation Effects on Rubbers". 7 p.m.—Panel Discussion—"Competitive Polymers in Automobile Applications". Speakers: Mr. A. E. Bray, Mr. S. Mottran, Dr. L. Mullins, Mr. G. B. Oks, Mr. J. Walker, Dr. W. Stein and Mr. C. H. Gregory.

Wednesday, December 14

ROYAL METEOROLOGICAL SOCIETY (at 49 Cromwell Road, London, S.W.7), at 2.30 p.m.—Discussion Meeting on "Automatic Methods of Handling Meteorological Data". Principal Speakers: Mr. C. V. Else, Mr. J. M. Craddock and Mr. E. J. Sumner.

ROYAL STATISTICAL SOCIETY (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.15 p.m.—Mr. R. H. Daw: "The Comparison of Male and Female Mortality Rates".

EUGENICS SOCIETY (at the Royal Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Mr. A. C. Stevenson: "Modern Trends in the Population Genetics of Man".*

INSTITUTION OF ELECTRICAL ENGINEERS, SUPPLY SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. L. Gosland and Mr. R. G. Parr: "A Basis for Short-Circuit Ratings for Paper Insulated Cables up to 11 kV."; Mr. G. S. Buckingham: "Short-Circuit Ratings for Mains Cables".

INSTITUTION OF MECHANICAL ENGINEERS (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Dr. D. F. Galloway: "Machine Tool Research, Design and Utilization" (James Clayton Lecture).

SOCIETY FOR ANALYTICAL CHEMISTRY, MICROCHEMISTRY GROUP (in the Restaurant Room of "The Feathers", Tudor Street, London, E.C.4), at 6.30 p.m.—Discussion Meeting on "A Review of Topics in Organic Micro-analysis".

SOCIETY FOR PSYCHICAL RESEARCH (at Kensington Town Hall, Kensington High Street, London, W.8), at 7 p.m.—Mr. R. B. Warne: "Levels of Awareness—Their Relevance to Psychical Research".

WOMEN'S ENGINEERING SOCIETY (at "Hope House", 45 Great Peter Street, Westminster, London, S.W.1), at 7 p.m.—Capt. F. Potts: "Power Transmission by Submarine Cable".

Thursday, December 15

ASSOCIATION FOR THE STUDY OF ANIMAL BEHAVIOUR (at Birkbeck College, Malet Street, London, W.C.1), at 10.45 a.m.—Symposium on "The Effects of Chemicals and Drugs on Behaviour".

INSTITUTE OF PHYSICS and the PHYSICAL SOCIETY, OPTICAL GROUP (in the Physics Department, Imperial College, Prince Consort Road, London, S.W.7), at 2.30 p.m.—Dr. C. G. Wynne: "A Flat Field Microscope Objective"; Mr. R. W. Uffen: "The Field for Fibre Optics".

SOCIETY OF CHEMICAL INDUSTRY, ROAD AND BUILDING MATERIALS GROUP (at 14 Belgrave Square, London, S.W.1), at 2.30 p.m. and 5.30 p.m.—Scientific Papers.

INSTITUTION OF MINING AND METALLURGY (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Mr. H. Dalton-Brown: "Recovery of Cassiterite at the Sungai Besi Mines, Selangor, Malaya"; Mr. F. A. Williams. "Recovery of Fine Alluvial Cassiterite: Correlation of Bore Valuations with Plant-Scale Recovery".

LONDON MATHEMATICAL SOCIETY (at the Royal Astronomical Society, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Prof. R. C. Lyndon: "Projective Geometry and the Algebra of Relations".

INSTITUTION OF ELECTRICAL ENGINEERS, EDUCATION DISCUSSION CIRCLE (at Savoy Place, London, W.C.2), at 6 p.m.—Discussion on "How to Pass Examinations or the Psychology of Study" opened by Prof. C. A. Mace.

INSTITUTION OF MECHANICAL ENGINEERS, NUCLEAR ENERGY GROUP (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Discussion on "The Impact of Three-Fuel Economy".

Thursday, December 15—Friday, December 16

POWDER METALLURGY JOINT GROUP OF THE IRON AND STEEL INSTITUTE and the INSTITUTE OF METALS (at Church House, Great Smith Street, London, S.W.1), at 2.30 p.m on Thursday and 9.30 a.m on Friday—Winter Meeting.

Friday, December 16

ASSOCIATION FOR THE STUDY OF ANIMAL BEHAVIOUR (at Birkbeck College, Malet Street, London, W.C.1), at 10 a.m.—Symposia on "The Acquisition of New Behaviour Patterns" and "Releasing Stimuli in Animal Behaviour".

BIOCHEMICAL SOCIETY (in the Physiology Theatre, Guy's Hospital Medical School, London, S.E.1), at 10.10 a.m.—401st Meeting.

INSTITUTE OF NAVIGATION (at the Royal Geographical Society, 1 Kensington Gore, London, S.W.7), at 5.15 p.m.—"The Single-handed Trans-Atlantic Race".

Friday, December 16—Saturday, December 17

BRITISH PSYCHOLOGICAL SOCIETY (at University College, Gower Street, London, W.C.1)—Conference.

Saturday, December 17

NUTRITION SOCIETY (at the Middlesex Hospital Medical School, Mortimer Street, London, W.1), at 10.15 a.m.—Symposium on "Calorie Balance in Man".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

LECTURER (Grade II) IN PURE MATHEMATICS—The Registrar, The University, Bristol 8 (December 14).

BOOTS FELLOW (with a medical or honours degree in science), for research work under the Professor of Bacteriology—The Secretary, Wright-Fleming Institute of Microbiology, St. Mary's Hospital Medical School, London, W 2 (December 30).

ASSISTANT LECTURER IN ASTRONOMY—The Registrar, The University, Manchester 13 (December 31).

LECTURER (with a degree in bacteriology or equivalent qualification) IN BACTERIOLOGY—The Secretary, The West of Scotland Agricultural College, 6 Blythswood Square, Glasgow, C.2 (December 31).

LECTURER IN PHYSICS at the University of Cape Town, South Africa—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (South Africa and London, January 13).

CHAIR OF CIVIL ENGINEERING—The Registrar, University College, Singleton Park, Swansea (January 14).

ASSISTANT LECTURER (with special qualifications in experimental physics, aeronomy or astronomy) IN APPLIED MATHEMATICS (GEOPHYSICS)—The Secretary, The Queen's University, Belfast (January 15).

LECTURER IN ORGANIC CHEMISTRY at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, January 15).

SENIOR LECTURERS (2) (one an ANALYST); a LECTURER; and an ASSISTANT (teaching duties and research) IN THE DEPARTMENT OF MATHEMATICS—The Secretary, The University, Aberdeen (January 16).

SENIOR LECTURER or LECTURER IN PARASITOLOGY IN THE DEPARTMENT OF ZOOLOGY, University College Ibadan, Nigeria—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (January 20).

READER, and a LECTURER IN THE DEPARTMENT OF AGRICULTURAL CHEMISTRY at the Waite Agricultural Research Institute, University of Adelaide, Adelaide, South Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, January 30).

IMPERIAL CHEMICAL INDUSTRIES RESEARCH FELLOWS IN PHYSICS, CHEMISTRY, BIOCHEMISTRY, ENGINEERING, METALLURGY and PHARMACOLOGY or any related subjects—The Registrar, The University, Liverpool (February 11).

LECTURER IN MICROBIOLOGY IN THE FACULTY OF MEDICINE, University of Western Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, February 28).

ASSISTANT BIOCHEMIST (with a first- or second-class honours degree in chemistry or biochemistry, or A.R.I.C.) IN THE AREA PATHOLOGY LABORATORY, Stoke Mandeville Hospital—The Administrative Officer, Stoke Mandeville Hospital, Aylesbury, Bucks.

ASSISTANT PROFESSOR, and an ASSOCIATE PROFESSOR IN MATHEMATICS—J. W. Lawson, Head of the Department of Mathematics, University of Manitoba, Winnipeg, Manitoba, Canada.

LECTURERS and ASSISTANT LECTURERS IN BOTANY; LECTURERS IN PHYSICAL and IN INORGANIC CHEMISTRY, and ASSISTANT LECTURERS IN ORGANIC and IN PHYSICAL CHEMISTRY; a LECTURER (preferably with qualifications in algebra or topology) IN MATHEMATICS; and LECTURERS and ASSISTANT LECTURERS in both EXPERIMENTAL and THEORETICAL PHYSICS—The Secretary to the Council, Westfield College (University of London), Hampstead, London, N.W.3.

POSTDOCTORAL FELLOW IN THE DEPARTMENT OF CHEMICAL ENGINEERING, for research in flame spectroscopy or a related subject—Dr. A. G. Gaydon, F.R.S., Imperial College of Science and Technology, London, S.W.7.

SCIENCE GRADUATE (with experience in the bacteriological aspects of chemical disinfection) IN THE DISINFECTION REFERENCE LABORATORY—The Director, Central Public Health Laboratory, Colindale, London, N.W.9.

SENIOR RESEARCH FELLOW (with a degree in chemical or mechanical engineering, metallurgy or physics, and prepared to conduct research on the engineering principles which underline processes used for metal extraction, that is, on mass, heat or momentum transfer), IN PROCESS ENGINEERING—Prof. F. D. Richardson, Metallurgy Department, Imperial College of Science and Technology, London, S.W.7.

YOUNG LADY (with B.Sc. in chemistry or a biological science), to assist in a research programme on the Medical Professional Unit—The Secretary of the Medical College of St. Bartholomew's Hospital, West Smithfield, London, E.C.1.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences. No. 700, Vol. 243 (18 August, 1960): The Fine Structure of the Insect Ear. By R. G. Gray. Pp. 75–94+plates 4–15. (London: Royal Society, 1960.) 25*s*. [129

Tweed River Purification Board. Annual Report for the year ended 15th May, 1959. Pp. 24. (Newtown St. Boswells: Tweed River Purification Board, 1960.) [129

Frank Mason and Co., Ltd., Directors' Report and Statement of Accounts for the year ended 31st March, 1960. Pp. 8. (London: Frank Mason and Co., Ltd., 1960.) [129

International Journal of Heat and Mass Transfer, Vol. 1, No. 1 (June, 1960). Pp. 114. Subscription rates: (A) For Libraries, Government Establishments, Research Laboratories, etc. £7 (20 dollars) per volume. (B) For individuals who place their orders directly with the publisher and certify that the journal is for their personal use. £5 5*s*. (15 dollars) per annum. (London and New York: Pergamon Press, 1960.) [129

Symposia of the Zoological Society of London. No. 2: Cyclical Activity in Endocrine Systems. (Proceedings of a Symposium held at the Zoological Society of London, 8th December 1959.) Edited by E. J. W. Barrington. Pp. vi+120+2 plates. (London: Zoological Society of London, 1960.) 25*s*. [129

West African Timber Borer Research Unit. Technical Bulletin No. 3: *Trachystis ghanaensis* Schedl (Col., Platypodidae), an Ambrosia Beetle Attacking Wawa, *Triplochiton scleroxylon* K. Schum. By Dr. H. Roberts. Pp. 17+4 plates. (London: Crown Agents for Oversea Governments and Administrations, 1960. Published on behalf of the West African Timber Borer Research Unit, 1960.) 2*s*. [129

British Federation of University Women. Working Party on Women in Science and Technology, 1956–1960—Final Report. Pp. 8. (London: British Federation of University Women, 1960.) [129

Royal Institute of Chemistry. Lectures, Monographs and Reports, 1960. No. 1. Recent Studies in Boron Chemistry. By Dr. H. G. Heal. Pp. ii+39. 5*s*. net. No. 2: Use of Non-Aqueous Solvents in Inorganic Chemistry. By Dr. C. C. Addison. Pp. ii+25. 4*s*. 6*d*. net. (London: Royal Institute of Chemistry, 1960.) [129

The Eleventh Annual Report of the Wildfowl Trust, 1958–1959. By Hugh Boyd and Peter Scott. Pp. 167+32 plates. (Slimbridge, Gloucestershire: The Wildfowl Trust, 1960.) 10*s*. net. [129

British Association for Commercial and Industrial Education. Tips on Talking. Second edition. Pp. 12. (London: British Association for Commercial and Industrial Education, 1960.) 3*s*. [129

British Association for Commercial and Industrial Education. Education for Survival: Report of the Ninth Annual Conference of the BACIE East Midlands Group, Buxton, 25–27 March 1960. Pp. 30. 3*s*. net. The Implications of the Crowther Report: Report of the BACIE Spring Conference held at the Federation of British Industries, London, 27 April 1960. Pp. 28. 3*s*. 6*d*. (London: British Association for Commercial and Industrial Education, 1960.) [149

Soil Mechanics Limited. Geotechnical Pamphlets. No. 4: Corrosion Surveys, with particular reference to Foundation Engineering. Pp. 5. No. 5: Trial Pits and Shafts, with particular reference to Plate Bearing Tests. Pp. 7. (London: Soil Mechanics, Ltd., 65 Old Church Street, S.W.3, 1960.) [149

Annual Report for 1959 (No. 72) of the Marine Biological Station of the University of Liverpool at Port Erin, Isle of Man. Drawn up by J. S. Colman. Pp. 43. (Liverpool: Liverpool University Press, 1960.) 5*s*. [149

Government of Northern Ireland: Ministry of Agriculture. Leaflet No. 93: The Extermination of Rabbits. Pp. 6. (Belfast: Ministry of Agriculture, 1960.) [149

Friends of the Lake District. Report and News Letter, July, 1960. Pp. 17. (Ulverston: Friends of the Lake District, 1960.) [149

London and Home Counties Regional Advisory Council for Technological Education. Bulletin of Special Courses in Higher Technology, including Management Studies and Commerce, 1960–61. Part 1: Autumn Term. Pp. 127. (London: London and Home Counties Regional Advisory Council for Technological Education, 1960.)

Other Countries

United States Department of Commerce: National Bureau of Standards. Monograph No. 12: Stabilization of Free Radicals at Low Temperatures. Edited by Arnold M. Bass and H. P. Broida. (Summary of the NBS Program.) Pp. iv+110. (Washington, D.C.: Government Printing Office, 1960.) 1.50 dollars. [149

Institut Royal Météorologique de Belgique. Contributions. No. 57: Sur la Représentation des Séries Météorologiques au Moyen de Processus Aléatoires Stationnaires Persistants. Par Dr. R. Sneyers. Pp. 11. No. 58: Ion-Atom Interchange. By D. R. Bates and M. Nicolet. Pp. 6. Publications, Serie B. No. 28: Sur l'Impossibilité de Nucléation Homogène de Glace dans l'Air Humide. Par L. Dufour et Prof. R. Defay. Pp. 12. No. 29: Le Temps en 1959. Par Dr. R. Sneyers. Pp. 50. (Uccle-Bruxelles: Institut Royal Météorologique de Belgique, 1960.) [149

National Library, Calcutta. A Bibliography of Indology. Compiled by J. M. Kanitkar. Vol. 1: Indian Anthropology. Edited, revised and enlarged by D. L. Banerjee and A. K. Ohdedar. Pp. xl+290. (Calcutta: National Library, 1960.) Rs. 5.00.; 8*s*. [149

American Academy of Arts and Sciences, Boston. Records of the Academy 1959–1960 (including new members elected 11 May, 1960). Pp. 128. (Boston, Mass.: American Academy of Arts and Sciences, 1960.) [149

New York State Department of Health, Albany. Annual Report of the Division of Laboratories and Research for 1959. Pp. 135. (Albany, N.Y.: State Department of Health, 1960.) [149

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PROSPECTS FOR EDUCATION IN BRITAIN

THE debate in the House of Commons on H.M. the Queen's Address from the Throne was notable for the choice of education for a full-day debate on November 7, and in speaking in the debate the Minister of Education, Sir David Eccles, said that he thought this was unprecedented. Sir David covered many aspects in his speech, beginning with a reference to the public library service. He had hoped a Bill could have been introduced during the session, but further study had been found necessary; and there seemed to be agreement that a new Act could not come into operation until the reviews of the local authority boundaries had been completed. One difficulty was in determining the qualifications of a library authority. Sir David thought that the recommendations of the Roberts Committee would not do justice to some of the good work being done to-day, and that further examination from a technical point of view might help in reaching a larger measure of agreement among those with expert knowledge of the service. Sir David also said that the Government is considering its policy in relation to sport, which would take due account of recommendations coming from the committee under Sir John Wolfenden appointed by the Central Council of Physical Recreation. The Ministry of Education is spending about £8 million a year on playing fields, swimming baths, etc., for the schools and technical colleges being built under the regular education programme, and extra resources will be available for the youth service in 1962–63. He thought, however, that there is scope for more co-operation in the use of existing facilities. Sir David also mentioned that a handbook on Commonwealth studies, written by a group of H.M.'s inspectors of education, is being issued as a guide to a subject which he believed the House wished to see widely taught.

Sir David believes that everything possible is being done in Britain to get more teachers for schools. He does not think we could have increased earlier the number of places in the general teacher training colleges from 23,000 to 47,000; the present programme came on top of the building programme for schools and technical colleges, which was already stretching the resources of many local education authorities. Colleges of 500 places and more have already been authorized in London, Loughborough, Coventry, Leeds, Sheffield, Exeter, the Liverpool area and in North Wales, and entirely new colleges are to be built in Cardiff, Canterbury, Brighton and in the Nottingham, Oxford, West Midlands and other areas. Of the places so far approved, 60 per cent will be provided by local authorities and 40 per cent by the churches and voluntary bodies, and Sir David paid a tribute to the part played by the churches. He also welcomed the prospect of a greater number of graduate teachers, and, with the expansion of the universities, he hoped that more graduates, particularly women, would teach in the primary schools. He believes that our aim should be to establish a two-way link between the training colleges and the universities. Something should also be done about the wastage of women teachers, and a campaign on a national scale to learn more about the availability of the 50,000 or more qualified women teachers who had left the service but had not reached the age of retirement would reach its peak in the new year. The pattern of part-time teaching also requires study, and he hoped for some thorough research into this subject by one or two local authorities.

As regards the supply of graduates, the Government is giving much thought to the development of full-time higher education as a whole, and the Prime Minister is to make an announcement very shortly as to this inquiry. Neither Sir David Eccles nor Mr. John Maclay, Secretary of State for Scotland, replying on the debate, would commit the Government as to whether or not there would be a separate inquiry for Scotland. On university awards, Sir David repeated the earlier announcements regarding the eligibility of a student for an award if he got a place at a university and had two passes at Advanced Level in the General Certificate of Education, the abolition of State scholarships after the selection to be made in the summer of 1962, and the retention of up to £100 a year by winners of open scholarships and other university awards. As a result, he hoped to see the foundation of scholarships at provincial universities, and he would shortly announce a radical revision of the means test, which, he said, has proved to be a more complicated matter than anticipated.

Referring to technical education, Sir David said that students taking full-time and sandwich courses at the colleges of advanced technology have risen from 4,000 in 1955–56 to nearly 8,000 in 1959–60, and an increase to 14,000 in a few years is expected. He is also anxious that these colleges should vigorously develop applied research, and that all technical colleges should develop as centres of further education in the widest sense, serving the whole of the community in their area. Sir David noted that these colleges are drawing their students from all types of school, but he pointed out that the biggest problem is that of students between the ages of 15 and 18, and how many are not getting the education we wish to give them. Although nearly 500,000 students are benefiting from day release, the annual rate of increase has slowed down, and important decisions must be taken between possible lines of advance. It has been

decided to give priority to reducing the size of classes in schools, but discussions with the local education authorities and industry regarding day-release have commenced in a promising atmosphere. However, he pointed out that we may sooner or later have to choose between placing the primary responsibility for training young workers in industry and the French system under which about a third of their young people receive their further education and initial industrial training before entering employment.

In concluding, Sir David referred to the urgent need for more and better technicians. He said that the Ministry has during the past year been reviewing, reconstructing and bringing up to date the whole pattern of courses for some 500,000 technicians, craftsmen and operatives. He also referred to the wastage in further education and said that it should be possible to reduce this drastically, though not to eliminate it altogether. Sir David also mentioned that detailed proposals for technical education will be announced shortly.

Although there was some sharp criticism of the Government's educational programme in the debate, this was mainly on party political lines, and comparatively little that was constructive emerged. Mr. A. Neave suggested that Britain needs much better criteria as to the numbers of scientists and technologists required, and Mr. J. Boyden thought that the Chancellor of the Exchequer and the Minister of Education should have concerted lines of development and seen that the University Grants Committee is provided with adequate staff to work out plans for the expansion of university and technological education. He also commented on the importance of the universities themselves doing more to explain their policies and ensure public understanding and support.

Particular attention was given to the question of wastage; Miss H. Anderson, for example, pressed the point in relation to full-time education, on which she pointed out that very little research had yet been undertaken. A detailed analysis by Dr. D. MacIntosh of students in Fife holding bursaries had indicated a rate of failure of more than 16 per cent, compared with the agreed overall wastage of about 17 per cent indicated by investigations by Sir James Mountford at Liverpool, Dr. Malleson at University College, London, and by the University Grants Committee. Miss Anderson was also very disturbed at a rate of failure of 38 per cent in the science faculty as compared with 10 per cent in the arts faculty. Mr. W. Hannan was more concerned with the wastage in part-time education, and with the unsatisfactory position of day-release in Scotland, and Mr. John Maclay, in replying on the debate, agreed as to the need for more careful study of the causes of wastage. He also agreed that Scottish industry as a whole does not appear to recognize the contribution which day-release could make to the training of young employees; the number of day-release students in Scotland has risen from about 28,000 in 1955–56 only to 35,600 in 1959–60; but it is intended to provide 100,000 places in Scotland by 1965, and the opening of the new technical colleges should stimulate development.

Many of the points raised in the debate, particularly regarding university expansion, the functions of the technical colleges, etc., are clearly matters which will be referred to the inquiry into further education as a whole; and there was a welcome disposition in the debate to look at education in the broadest sense, though it would undoubtedly be to the advantage of all if there was less disposition to seek party political or even sectional advantage.

JET PROPULSION ENGINES

Jet Propulsion Engines
Edited by O. E. Lancaster. (High Speed Aerodynamics and Jet Propulsion, Vol. 12.) Pp. xvii+799. (London: Oxford University Press, 1959.) 140*s*. net.

THE teaching of up-to-date aerodynamics has always been hampered by a dearth of good text-books and reference works. The main reason for this has been the very high rate of progress in all branches of the field, due to the vast resources which the major countries have invested in the development of aeroplanes; the impetus being mainly from the military pressure of two World Wars. The output of data has consequently been immense, and while much of the information has been disseminated in the publications of various specialized bodies, such as the Aeronautical Research Council and the Royal Aeronautical Society in Britain and similar bodies in other countries, the sheer volume of printed reports has made it difficult for the young scientist or engineer to obtain a good grasp of the subject. To add to his difficulties, a large proportion of new aeronautical information has always had a military security value in the country of origin, and there has therefore been delay, sometimes serious, in its open publication.

It is therefore highly desirable to attempt to make periodically a review of the 'state of the art' in aeronautics, and the need for a really vigorous attack on the problem led to the formation in 1949 at Princeton University of an Aeronautics Publication programme which has culminated in the publication of twelve large volumes, treating in both a comprehensive and fundamental manner practically all aspects of aeronautics and jet propulsion and such allied sciences as thermodynamics, physics of matter, nucleonics and so on. That the editorial board consisted of Profs. Theodore von Kármán, Hugh Dryden and Sir Hugh Taylor guaranteed the high standard of the contributing authors, who were chosen on a truly international basis.

What has emerged is so huge that it cannot be referred to merely as a series of text-books. It is rather an encyclopædia of aeronautical knowledge and would be a valuable addition to most engineering libraries. Nevertheless, the very size of the work (each volume contains around 800 pages) and the large number of authors involved has meant that the publication has taken a very long time. It is noted, for example, that much of the material in the present volume was written almost ten years ago, and where it relates to performance data on actual engines is

therefore out of date. This would seem to be a failure of editorship. Either the book should have been brought up to date before publication or the obsolete material should have been omitted. It should be emphasized that this criticism may not apply with the same force to the previous volumes, which deal with the more fundamental and theoretical aspects of aeronautics.

Volume 12 is the last of the series, and deals with jet propulsion engines of all types, including rockets and reactor heat sources. It also includes some very valuable and useful information on the ground test facilities which are so necessary in the development of these types of engine. It is a very comprehensive and on the whole a well-written work.

In particular, the sections on solid- and liquid-fuelled rockets are small text-books in themselves, and will be excellent as introductions into a field which until recently has been almost entirely military and therefore to a large extent security classified.

The chapters on ram jets, ram-jet test facilities and on the use of atomic energy for jet propulsion are equally good and well presented, although suffering from the general criticism of being rather out of date in parts. Special mention must be made of the discussion on ram-jet control, which is excellent, presenting alternative methods and showing how difficult it is to sense truly representative internal pressures or velocities in closed loop systems.

The very width of the field covered has, however, meant a somewhat restricted treatment of many subjects. The volume sets out to be comprehensive, but it loses comprehension in a different sense by failing to take individual topics far enough. Many of the theoretical treatments have been so generalized as to necessitate over-simple assumptions and too perfect conditions. None the less, with this limitation, the treatments are well done, and, for example, would be useful to a flight vehicle engineer who wished to compare different methods of propulsion or to a propulsion engineer who wished to consider a different field of propulsion. The generalized treatment again could, with advantage, have been extended to cover adequately the overall performance of engine/flight vehicle combinations over complete flight patterns or trajectories.

A real weakness in the volume is the inadequacy of those parts dealing with the future of jet propulsion. Such subjects as flight in excess of Mach number 3, high-energy fuel combinations, vertical take-off engines are only touched on in the most superficial manner. Section *L*, which is entitled "Future Prospects of Jet Propulsion", consists of an interesting account of the morphological method of analysis which, however, fails to demonstrate how the most promising future lines of progress should be chosen. Indeed, some of the thinking in this section appears to be amorphous rather than morphological

In conclusion, Volume 12 of the series is a considerable effort by a large number of distinguished scientists and engineers. Whether, turning to the preface, it succeeds in meeting "the long-felt want in Research Institutions, Universities and private industry" would be a matter of some doubt if the decision had to be taken on this volume alone. My opinion is that a full set of these volumes would be invaluable to those libraries which have sufficient aeronautical readers to justify the high cost.

W. CAWOOD

APPLICATION OF LAPLACE TRANSFORMS

Laplace Transforms for Electronic Engineers

By James G. Holbrook. (International Series of Monographs on Electronics and Instrumentation, Vol. 10.) Pp. xiii+259. (London and New York: Pergamon Press, 1959.) 50*s*. net.

THE cult of manipulation without full understanding has achieved a degree of respectability since Oliver Heaviside made his remark about the necessity of eating even though the processes of digestion were not fully understood. He himself made full use of his own operational calculus without all the steps in it having been established with full mathematical rigour. It is indeed almost axiomatic that much progress in science and engineering is made by groping in the dark, and full understanding comes later, if at all. What is more controversial is whether it is desirable to teach the use of a technique, which is already fully and rigorously established, without, at the same time, explaining fully the steps on which the technique is based. The busy engineer, faced with the necessity of solving a particular problem quickly, may well feel justified in making use of the latest technique, without fully acquainting himself with the rigorous mathematics necessary to justify it. But should instruction of the student be based on the same principle of quick results? The mounting pressure of new subjects on an already crowded syllabus provides a great temptation to make the treatment of all subjects more superficial in order to introduce students to as many subjects as possible in the hope that a full understanding of the subjects of most use to him in later life will be acquired by detailed work after graduation.

Mr. Holbrook is in no doubt of the importance of a thorough study of the subject of Laplace transforms, and has the courage of his convictions to the extent of facing the possibility of this subject being excluded from the undergraduate course, rather than let it suffer from an unduly compressed course of instruction. He does not, however, insist on complete rigour, and there are places in his book where some additional rigour could be introduced with advantage, possibly by means of extended footnotes, which could be omitted during a first reading.

The first two chapters of the book deal with functions of a complex variable and the Fourier series and integral. These chapters might well prove difficult reading for a first study of Laplace transforms, but the advantage of this approach is very clearly seen in the third and following chapters, where the author establishes his transformations and transformation theorems with great ease.

The last half of the book is concerned with the application of Laplace transforms to circuit problems. Much of this is extremely interesting and valuable, but seems to lack the unity of presentation of the first half. Although the author deplores the reluctance of engineers to use nodal analysis and their fear of problems involving mutual inductance, mesh analysis is employed in most of the problems given in the book, and mutual inductance is not mentioned until the last quarter of the book where five pages are allowed for its treatment.

Apart from this lack of balance the book is most attractively written, and the arrangement of problems

in the text in preference to placing them at the end of each chapter, should encourage the student always to arm himself with pencil and paper when reading. The contrast between print and paper is restful to the eyes, but the diagrams are too small. Mistakes are few, and only on p. 140 would they be likely to mislead the student. The lay-out of the mathematics is good and there is a table of more than 200 transformations.

This book should be a useful addition to the library of many engineers and students.

A. H. M. Arnold

THE NUMBERS GAME

Electronic Computers

Principles and Applications. By T. E. Ivall. Second edition. Pp. viii+263 (32 plates). (London: Iliffe and Sons, Ltd.; New York: Philosophical Library, 1960.) 25*s*. net.

Computer Engineering

Edited by S. A. Lebedev. Translated from the Russian by Jane Stuart. Translation edited by J. P. Cleave and F. A. Sowan. Pp. vii+184. (London and New York: Pergamon Press, 1960.) 63*s*. net.

Analogue and Digital Computers

Consulting Editor: Dr. M. G. Say. Advisory Editors: A. C. D. Haley and W. E. Scott. Pp. viii+308+12 plates. (London: George Newnes, Ltd., 1960.) 50*s*. net.

Introduction to Electronic Analog Computers

By Prof. John N. Warfield. (London: Prentice-Hall Electrical Engineering Series.) Pp. ix+175. (London: Prentice-Hall International, Inc., 1959.) 30*s*.

COMPUTERS are assuming an ever-increasing importance in the modern world. Having started as the plaything of the mathematician in the cloistered bowers of universities, they have successively penetrated into industry, commerce and, finally, they are likely to find a place in the government of nations. A measure of this increase in computer popularity is the almost exponential increase in the number of books on computers which have been and are being published.

A decade or so ago most authors started their book with a preface in which they explained why they had written the book, quite often couched in apologetic tones and usually with some cogent argument to justify their labours. Such literary politeness seems, however, to be a thing of the past and authors nowadays tend to give no reason to justify their effusions. In fact, a book may be justified on several counts. In the first place, novelty. The pioneers in a subject, if they have the time, can often write the first book which is available. Such books are useful in that they make available material which may only otherwise be found in the more esoteric literature. After this phase of development, the most likely reason for writing a book is that of popular exposition, since the original works may either be difficult intrinsically or alternatively have been succeeded by pedagogically better expositions and so have become unsuitable for teaching. In the case of the volumes under review, these two classes of book are represented and also the rather less desirable class of book, which presumably is written for no other reason than the desire of the author or publisher to 'get on the waggon'.

To deal first with the book by Ivall, this is in fact a second edition of the original book which appeared in 1956. The original work consisted of an edited version of a number of articles which appeared in *Wireless World*. The book has now been brought completely up to date, and something like a hundred pages of new material have been added. It is a book intended more for the wireless 'ham' rather than for the pure scientist or for the man in the street. There is a limited amount of technical material, but not enough, however, to build a computer, and too much to be intelligible to anyone who is not familiar with modern electronics. To the class of reader who is interested in electronics without being a specialist in computers the book can be recommended; to others, however, there are better things available.

Lebedev's book is in a different category. It is a translation of a Russian book which appeared in 1956, and deals with a number of aspects of computer design on an advanced technical basis. There is no concession to popular exposition, and the papers contained in the book are in the nature of a research collection. There is an account of the power supply for the Russian machine *BESM*, an analysis of digital differential analysers, an account of dynamic flip-flops and their use in computers, papers on automatic checking and on word selection from a dictionary (the latter based on a paper by me, which appeared in *Nature* in 1955) and two papers on matrix storage. For those Western workers in the computer field who do not read Russian, this book will be essential. Unfortunately, the price is high, considering the production, which is in lithographed, unjustified typescript; but even so, the good things in it make it well worth the money.

The collection of papers edited by Haley and Scott is, like the curate's egg, good in parts. There is an introduction to computing machines which did not appear to me to be particularly well written, three chapters dealing with the operation, application and design of analogue computing machines: these are excellent, although it is perhaps unfortunate that they are written by two separate authors with consequent breaks in style and gross overlapping. These are followed by an account of the way in which digital computing machines are operated. Part at least of this is a repetition of the first chapter, but considered as an introduction it is considerably more readable. The book ends with chapters on circuit elements for computers, on storage, on input–output equipment and on programming. The chapter on storage is dated and follows well-trodden lines, repeating several things from earlier books which have now been shown to be incorrect. That on input–output equipment is a reasoned and up-to-date account of what is available in this field, but the final chapter on programming is too short to be really worth while. This book is quite expensive for what it contains and the dichotomy of styles makes it somewhat difficult to read. It does not appear to add anything which will be of interest to the specialist, and, at the same time, is too advanced for the man in the street.

The book by Warfield has a somewhat misleading title, since, apart from a very brief introduction, in which a verbal account is given of the nature of digital and analogue computing machines, it contains nowhere any indication of the engineering details of an analogue computing machine. It is, in fact, a book which is primarily concerned with the programming of differential analysers. Considered as

such an account of programming it is one of the best books available on the subject. The techniques proposed are clearly set out and justified by sophisticated mathematics of a type which is not usually given in books on analogue computation. Apart from statements as to the way in which analogue computers are used, there is a set of appendixes which give the bibliographies of analogue computer elements and analogue computer applications. These are reasonably up to date, but suffer from the usual defect of American books in that they ignore all the literature published outside the United States. Rather surprisingly, the book ends with some suggested laboratory experiments. These will be useful to the growing body of departments which have analogue computers and have to instruct students in their use. The book is well produced and reasonably inexpensive. It can be recommended to those interested in this art. A. D. BOOTH

INDIAN RESEARCH ON JUTE

Jute in India

A Monograph. By B. C. Kundu, K. C. Basak and P. B. Sarkar. Pp. xv+395 (47 plates). (Calcutta: Indian Central Jute Committee, 1959.) Rs. 30.

THIS book presents a most interesting and detailed account of the scientific and economic research work on jute carried out under the ægis of the Indian Central Jute Committee over the past twenty-five years. It is divided into three sections, the first being concerned with the botany, cultivation, and diseases and pests of jute, the second with the economic and marketing problems of jute growing, and the third describing the physical and chemical characteristics of the fibre, together with notes on the technology of jute manufacture.

The jute-manufacturing industries of the world consume nearly 2 million tons of fibre annually, virtually the whole of this being grown in the eastern States of India and in East Pakistan. Before partition of the sub-continent in 1947, jute was a monopoly crop for India; after partition, although India retained the jute mills, most of the fibre-growing regions went to Pakistan. In consequence, the jute-manufacturing countries outwith India now find themselves largely dependent on Pakistan for supplies of raw material, while India herself has striven to increase her acreage under jute sufficiently to maintain the volume of her production of jute manufactures independently. The book is solely concerned with the Indian aspect, but it is against this wider background that it will be read in Britain and Europe.

Commercial jute is a bast fibre obtained from the *capsularis* and *olitorius* varieties of *Corchorus*. It is an annual crop, commonly followed by a crop of transplanted paddy, and in the first section of the book Dr. Kundu brings out very well the main factors of importance in growing and cultivation. All concerned with the production of jute, or indeed any bast fibre, will find much of value here. It is perhaps notable that the agricultural methods described are entirely manual, no power-driven machinery being employed.

Most jute growers are small-holders, and a considerable number share-croppers who pay a share of the crop as rent of their plot of land. In section two Mr. Basak describes the economic studies which have been made into the circumstances of these small farmers, many of whom appear to live barely above subsistence-level. His comments and conclusions on the economic factors affecting the marketing of jute fibre must give food for thought to all concerned with the jute industry, and it is especially interesting to note the correlation between acreage under jute and the relative prices of jute and rice in the previous year.

The final section, by Dr. Sarkar, is somewhat condensed, and, although useful for reference, seems unrelated to the main theme of the preceding sections.

The book contains more than 400 references, the majority to Indian publications, and 75 photographs, one un-numbered and without legend. There are a few errors in the text, and throughout Indian weights and measures are used which may be unfamiliar to many readers. Unfortunately no index is provided, a serious omission in a work of this nature, which could serve as a useful reference book. These criticisms apart, however, the monograph is a welcome addition to the sparse literature relating to this fibre of world-wide usage.

H. P. STOUT

IN PURSUIT OF ANTIBIOTICS

Search for New Antibiotics

Problems and Perspectives. By Prof. G. F. Gause. (Trends in Science, Vol. 2.) Pp. x+97. (New Haven, Conn.: Yale University Press, 1960.) 4.75 dollars.

SINCE penicillin was developed as a commercial product there has been a feverish search for other antibiotics with similar or complementary properties. To-day, about a dozen antibiotics are in general use. Their discovery has been based on a purely empirical screening programme in which millions of potential antibiotic-producing organisms have been examined. Anything that could introduce a rational element into this search would be invaluable. Prof. Gause attempts to do this, and for this alone his book is worth study. His views are based on recent Russian research not too well known in Britain; it is useful to have an account of this work in English, and Prof. Gause is to be congratulated on the clarity of his exposition in a foreign language.

The author suggests that there are three principles by which the empirical search can be made more scientific. The first is concerned with the ecology of antibiotic-producers. He presents evidence that among fungi and spore-forming bacteria antibiotic-producers are more commonly found in warm soils than in cold northern soils. This could be a consequence of the richer microflora of tropical and sub-tropical soils. On the other hand, antagonistic Actinomycetes seem to be equally common in soils from all latitudes. My impression is that at present it would be premature to concentrate too much on soils from one climatic region in the search for new antibiotic-producers. But with Prof. Gause's general conclusion, that further study of the ecology of antibiotic-producers may make the search more rational, I wholeheartedly agree.

His second principle is that a given species, or other appropriate taxonomic unit, 'tends' to produce the same antibiotics whenever it is isolated, and that in consequence, rapid identification of organisms can accelerate screening procedures, preventing to some extent the continual rediscovery of a known antibiotic. If such a procedure were used too rigidly of course new antibiotics might be missed. This principle would be most useful where fungi and bacteria are being screened; in the case of Actinomycetes, identification of the antibiotic produced may frequently be more certain and more rapid than identification of the producing organisms.

His third principle is that test organisms used in screening procedures should include some chosen to detect selective inhibition of specific biochemical mechanisms. Prof. Gause illustrates this by his own work at the Institute of Antibiotics, Moscow, using mutant bacteria and protozoa with impaired respiratory pathways. He considers that these are in some ways analogous to tumour cells, basing this view on the work of Otto Warburg, and therefore proposes the use of such mutants in screening for antibiotics with anti-tumour properties. It seems to me somewhat naive to base a search for anti-tumour substances on so simple a biochemical lesion in the test organism. Nevertheless, the data presented on their specific sensitivity to known tumour inhibitors are suggestive. But, whatever one may think of this particular instance, the general principle, that test-organisms with known biochemical lesions may be valuable in the search for antibiotics with specific properties, is undoubtedly valid.

In conclusion, though there is much in this book that is controversial, and much that one feels inclined to treat with reserve until more evidence is available, it is stimulating reading, and should be read by everyone interested in antibiotics.

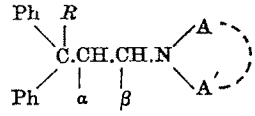
P. W. BRIAN

DIPHENYLPROPYLAMINES AS ANALGESICS

Synthetic Analgesics

By Paul A. J. Janssen. Part 1: Diphenylpropylamines. (International Series of Monographs on Organic Chemistry, Vol. 3.) Pp. vii+183. (London and New York: Pergamon Press, 1960.) 45*s*. net.

THIS book is the third volume of the International Series of Monographs on Organic Chemistry, edited by D. H. R. Barton and W. von Doering. The series is intended to cover a wide variety of aspects of organic chemistry in the form of concise summaries containing all relevant literature references. It is with this premise in mind that the book should be read, since it deals with a rather specialized topic, namely, the role of diphenylpropylamines of the type:



in the analgesic field.

It is an astonishing fact that although the analgesic methadone, which possesses the diphenylpropylamine structure, was discovered by the original German workers in this field during the Second World War, an apparently unabated stream of related compounds displaying not only analgesic but also a wide variety of other pharmacological activities has been appearing ever since. It is against this background of intensive and prolonged research by Paul A. J. Janssen and many other workers in various countries that this book has been written.

The first two chapters are concerned with some ideas on the nature of analgesic activity and the relative potencies of four of the best-known analgesics. The next sixteen chapters each deal with the synthesis and properties of compounds with one variant of the group *R* and are rounded off by a chapter on a few less-important variants. There follows a small chapter on dissociation constants, which have been regarded as being of possible significance in the activity of such compounds. The book is completed by a brief treatment of the work of A. H. Beckett and his collaborators, who postulate that the absolute configuration of all analgesically active optical isomers is identical and related to the configuration of D-(−)-alanine.

A valuable feature of the book is a tabulated survey of physical properties and analgesic potency ratios, measured against a few well-known analgesics, of all the diphenylpropylamines reported in the literature. That the main tables cover about 100 of the 183 pages of the book gives some idea of the tremendous amount of work done in this field. Despite this, the author is frequently able to suggest further areas of research.

The accuracy of a book so full of facts requires much time to check, but spot checks and my personal knowledge of the subject revealed no gross deficiencies, either in subject-matter or literature references. There are a few minor errors. For example, on p. 111, during a discussion on preparative methods, there is some confusion of nomenclature, formula 7.4 on p. 123 has a vital bond missing, the description of the reaction sequence on p. 120 is confused by an incorrect formula reference, "amine" instead of "amide" appears at the beginning of Chapter 11, ref. 87 on p. 132 should be 88, and '*J. Org. Chem.*' is omitted from ref. 317. However, in general, the errors are obvious and do not detract from the readability of the book. The correlation between the tabulated compounds and the structures discussed in individual chapters could possibly have been improved by the use of a common numbering system, but no great difficulty is involved on this score.

Dr. Janssen has written a thoughtful, analytical book which, although well confined to the subject-matter of the title, gives several glimpses of the many other pharmacological activities which modification of these propylamines produces. The reader may well detect a hint of the excitement which can be experienced during the investigation of structure-activity relationships in a successful line of research.

The book is recommended as being of value to the increasingly large number of those concerned with medicinal chemistry, as a concise method of following the work in this field. In addition, apart from its general interest, a number of chemically interesting points make it worth the attention of other chemists.

J. W. BILLINGHURST

The Great Barrier Reef and Adjacent Isles

By Keith Gillett and Frank McNeill. Pp. xiii+194 (161 plates). (Paddington, Sydney: Coral Press, Pty., Ltd., 1959.) 70*s*. (Australian).

TOURISTS with an interest in Nature will find all that they can desire in this book on the Great Barrier Reef of Australia by Keith Gillett and Frank McNeill. This is a first-class naturalist's guide book starting with a brief introductory account and taking the visitor first to the southerly Capricorn–Bunker group of islands. Then follow an account of the animals and plants to be found on land, an introduction to corals, and chapters devoted to molluscs, echinoderms, crustaceans, and other of the more striking reef inhabitants. This prepares the traveller for a journey farther north to the Cumberland group and other islands where a similar fauna will be found. An account is also given of Lord Howe Island and the Admiralty Islands.

There are other chapters on the resources of the reef, and the technique of underwater photography, together with practical hints for reef visitors. The book is well supplied with maps, and has good indexes to subjects and scientific names. It also includes mention of travel and tourists' facilities, including the underwater observatory at Green Island off Cairns. The interesting narrative is illustrated with superb photographs, many of which are in colour. The Great Barrier Reef is famous for the variety and splendour of its living organisms, and many of these are most beautifully portrayed. In fact, with this book the visitor can identify with certainty most of those animals which by their striking colour or form at once attract the naturalist's attention. The authors and publishers are to be congratulated on producing an authentic and beautiful handbook and guide, suitable for professional, as well as amateur, biologists, which will undoubtedly increase the enjoyment and value of a visit to the reef. It should also be in the library of those biologists not fortunate enough to go and see for themselves.

F. S. RUSSELL

Proceedings of the International Conference on Scientific Information, Washington, D.C.

November 16–21, 1958. Vol. 1: Pp. xxiv+1–812. Vol. 2: Pp. xii+813–1635. (Washington, D.C.: National Academy of Sciences—National Research Council, 1959.) 20 dollars the two volumes.

TEN years after the Royal Society Scientific Information Conference, the International Conference on Scientific Information, sponsored by the National Science Foundation, the National Research Council—National Academy of Sciences and the American Documentation Institute, was held in Washington in November 1958. All the Conference papers were issued as preprints to those who attended, but these are now re-published in two handsome volumes, together with additional material consisting of a memoriam to Dr. Alberto Thompson, who died before the Conference but who did so much towards its preparation, a preface by Dr. Wallace Atwood, jun., and the stimulating and scintillating opening address given by Sir Lindor Brown, one of the secretaries of the Royal Society. Moreover, the volumes contain the collected wisdom of the deliberations of the discussion panels and, in some instances, reports of the Conference discussions; there are also a list of those who attended and an index.

The papers cover the literature and reference needs of the scientist and their effectiveness, abstracting services, the organization of information services and storage and search systems, and the responsibilities of Governments and others in these fields. Some are verbose, some inconclusive, but there is much worth reading and pondering over. No rigid recommendations were made by the Conference, but, as Dr. Atwood remarked at the time, "'tis better to travel hopefully than to arrive". Scientific information bristles with complex problems, and while we travel hopefully towards their solution, the arrival of this important contribution to the literature is welcome.

C. A. RONAN

Lehrbuch der Physikalischen Chemie

Von Prof. John Eggert. Achte, neubearbeitete Auflage. Gemeinsam verfasst von Prof. John Eggert, Prof. Lothar Hock und Prof. Georg-Maria Schwab. Pp. xii+891. (Stuttgart: S. Hirzel Verlag, 1959.) 72 D.M.

THIS well-known book has been extensively revised and enlarged as compared with the English translation, and has to some extent lost its character as a readable elementary work and become a concise treatise on all branches of physical chemistry. Very recent work has been incorporated and there are abundant cross-references printed in the margins. References to literature are not given, apart from a list of books, mostly German and American, at the end, but the names of authors and the dates given will enable the publications to be traced in the abstract literature. The text is clearly and concisely written, and the mathematics is confined to elementary calculus. The sections on atomic physics and nuclear reactions are extensive, but the wave-mechanical theory of valency is only briefly treated. Experimental methods are dealt with concisely and there are many useful tables and graphs. As examples of modern topics the sections on low temperatures, semiconductors and reactions in solids may be mentioned. The chapters on photochemistry and colloids are good. The book covers all the branches of physical chemistry, and besides being a readable text-book it will be useful for reference purposes. The authors have evidently taken much trouble in the presentation of the material and the book will without doubt continue to be one of the best in its field.

J. R. PARTINGTON

Revision Notes on Biology for "O" Level of the G.C.E.

By G. T. Bolton. Pp. 17. (Oxford: Basil Blackwell, 1960.) 1*s*. 9*d*. net.

TO supplement existing text-books for the Ordinary Level examination in biology for the General Certificate of Education, G. T. Bolton, a biology master at Eton College, has prepared a set of notes which will be useful to all candidates in the twelve months before the examination. The notes include a number of lists and tables which the candidate can expand for himself into a full essay on the appropriate subject. The essential facts are briefly and boldly stated, but the notes can in no way be regarded as a substitute for a text-book. Some examination topics do not lend themselves to treatment in this way, and among the omissions are experiments which illustrate physiological processes in trees and plants throughout the year.

THE ROYAL SOCIETY

ANNIVERSARY ADDRESS*

By Sir CYRIL HINSHELWOOD, O.M., F.R.S.

AWARD OF MEDALS, 1960

Copley Medal: Sir Harold Jeffreys, F.R.S.

DURING the past forty-five years Sir Harold Jeffreys has carried out a long series of geophysical researches of fundamental importance. The problem of the internal constitution of the Earth involves many disciplines, and it was his outstanding achievement to take the existing scattered researches and weld them into the coherent subject now called the geophysics of the solid earth. His book, "The Earth", now in its fourth edition, is still the standard work in this field.

Jeffreys is best known as a theoretical seismologist. The Jeffreys travel-time tables, later revised in conjunction with K. E. Bullen, are not only the standard tables used in reductions of earthquake data but also are the basis of the best determinations of the elastic constants at all depths within the Earth.

He is the author of a number of papers on the radioactivity of rocks and the Earth's thermal history. Many years ago he emphasized the importance of making a deep boring through the ocean floor—a project which is now being undertaken by U.S. scientists. The interrelation of the phenomena of precession, nutation and the variation of latitude and the theory of the figure of the Earth led him to researches on these topics, and his analysis of gravity observations indicated a revision of the international formula for gravity, with a corresponding revised estimate of the Earth's ellipticity. The figures of the Earth and Moon formed the subject of his first paper in 1915, and in 1948 he gave a very important discussion of the general adjustment of the data relevant to the radius and ellipticity of the Earth, the lunar parallax and the moments of inertia of the Moon.

Jeffreys has carried out many researches in dynamical meteorology, and his classification of winds and his theory of monsoons are incorporated in the standard works on the subject. He extended the classical theory of the tides to atmospheric motions, and his work on the generation of water-waves by wind has led to many later developments.

His writings on the theory of probability and on scientific inference, his work on the asymptotic solution of differential equations and his systematic treatment of the Heaviside operational calculus have proved valuable. His continued interest in the problems of structural geology has helped markedly to close the gap that formerly existed between geology and geophysics.

Rumford Medal: Dr. A. G. Gaydon, F.R.S.

Dr. Gaydon is distinguished by his work in spectroscopy and particularly molecular spectroscopy. One of his main fields of research has been in the application of spectroscopic techniques to the study of flame phenomena. His studies of low-pressure flames, development of the nitric oxide test for atomic oxygen, measurements of rotational temperatures and discovery, with H. C. Wolfhard, of abnormal electronic excitation in the reaction zone, contributed much to knowledge of the processes occurring in combustion. Similar techniques have recently been applied to shock waves, and the shock tube has been developed into a tool for studying times of relaxation of molecular vibrations and dissociation.

Another main field of his interest has been the determination of the dissociation energies of diatomic molecules, and his book "Dissociation Energies and Spectra of Diatomic Molecules" is a standard monograph on the subject.

Gaydon has made many contributions in other branches of molecular spectroscopy as in the discovery of new band systems (for example, the ultra-violet $^1\Pi_u{}^1\Pi_g$ bands in N_2), the investigation of predissociation and laboratory observations of spectra similar to that of the night air glow.

Gaydon has also published "The Identification of Molecular Spectra" (with R. W. B. Pearse); "Spectroscopy and Combustion Theory"; "Flames, their Structure, Radiation and Temperatures" (with H. G. Wolfhard), and "The Spectroscopy of Flames". All these are distinguished works of much value and importance.

A Royal Medal: Prof. A. C. B. Lovell, O.B.E., F.R.S.

Much of our present knowledge of radio astronomy is due to Lovell's insight, initiative and originality. With his colleagues he has made contributions to our understanding of meteor astronomy and of 'discrete sources', and the conception and present achievements of the large radio telescope are largely due to his efforts. From visual observations it has long been known that meteors fall into two main classes. Shower meteors are clearly members of the solar system, but until the work of Lovell it was generally believed that the so-called sporadic meteors had velocities in excess of parabolic and were intruders from outer space. Lovell has been able to show conclusively that these objects too are members of the solar system, and further to show that the diurnal and seasonal variation in their numbers is consistent with such an origin. By his published works he has established the whole subject on a new and firm foundation.

Lovell and his colleagues have studied galactic radiation in the metre range. Fluctuations in this emission from certain constellations had suggested the occurrence of 'discrete sources'. Lovell was able to show that the fluctuations originate in disturbed regions of the ionosphere. It was found that the sources had diameters of a few minutes of arc, and thus

* Delivered at the Royal Society on November 30.

shown that the radiation did not originate in stars. Further work by Lovell's group showed that some of the discrete sources lie outside the galactic system, and that there is a roughly spherical halo well outside the visual system.

The conception and design of the large steerable paraboloid telescope are due to Lovell. Its construction represents the most significant advance in radio astronomy, and other larger instruments being built in different parts of the world are based upon it. It has proved invaluable for the tracking of stellar objects, but promises already to reveal much more about galactic radiation. Work on the 21-cm. hydrogen line is already providing much valuable information about the structure of the galactic system

A Royal Medal : Sir Roy Cameron, F.R.S.

Sir Roy Cameron's chief interest over many years has been the mechanism of cellular damage by various agents and the response of the damaged tissue towards restoration of normal structure and function. His early work analysed the pathology of liver disease by resolving it into simple components related to the vascular system and to the excretory apparatus of the organ. This led on to a series of researches into the actions of various poisons which selectively destroy liver cells. His elegant study of the prolonged action of the chlorinated hydrocarbons provided experimental proof of the 'reversibility principle' in chronic liver disease, an achievement which has changed our outlook on some of the degenerative diseases which were once regarded as hopeless.

Cameron's investigations of body fluid redistributions in disease have added much to our knowledge of the causes of shock and of the pathogenesis of œdema of the lungs. He was the first to produce a neurogenic lung œdema, a discovery which helped to explain certain clinical phenomena that had long baffled surgeons. His war-time studies of arsenical and other poisons revealed unexpected modes of disease production and supplied a key for effective prevention and treatment. He has made important contributions to our knowledge of the mechanisms by which under-water explosions produce pathological effects, the practical result of which has been improved methods of care and treatment of men injured during diving and exposure to depth charges.

Cameron has built up a lively school of cellular pathology which has undertaken the critical re-examination of many of the classical notions about cellular disturbances and thus reorientated the outlook on diseases to which such disturbances give rise. He is recognized throughout the world as one of the foremost of living pathologists and has contributed much to revitalize British pathology by ingenious applications of the experimental method in problems of human ailments.

Davy Medal : Prof. J. M. Robertson, F.R.S.

When X-ray diffraction by crystals was first discovered nearly fifty years ago, it was a problem in optics and as such was studied almost exclusively by physicists. W. H. Bragg realized that since the compounds to be investigated would become increasingly complex, it would be advisable to have an organic chemist in his team of research workers. He therefore invited John Monteath Robertson to work at the Royal Institution ; and the distinction of the research work he did fully justified that choice.

J. M. Robertson proved to have just the qualities needed for the field of crystal structure analysis by diffraction techniques. Using the two-crystal moving-film spectrometer, and numerical and mechanical methods of Fourier analysis that he himself devised, he was not only the first to make a systematic investigation of the structures of such simple organic molecules as anthracene, naphthalene, durene and *p*-benzoquinone but also was a pioneer in the study of polymorphic structures (α- and β-resorcinol), *cis*- and *trans*-isomers (azobenzene), series such as dibenzyl, stilbene, tolane, involving bonds of varying order, or such as oxalic acid dihydrate, acetylene- and diacetylene-dicarboxylic acid dihydrates, where the existence of structural isomorphism is disguised by changes of unit-cell shape. He developed the 'heavy-atom' and 'isomorphous-series' techniques and used them to obtain the formulæ, stereochemistry and structure of the phthalocyanines, and later of cupric tropolone, the polysulphides and sulphonyl sulphides. He used structural data for the determination of molecular weights and (with others) investigated the effect of isotopic substitution and of thermal expansion in structures containing hydrogen bonds. His later studies of large condensed aromatic molecules and of compounds where steric hindrance forces an aromatic molecule to lose its planarity have provided valuable data for theoretical consideration.

Darwin Medal : Mr. E. J. H. Corner, F.R.S.

E. J. H. Corner first showed himself to be outstanding by his work in collecting and identifying toadstools. At the same time he developed a strong conviction about the advantage of studying plants in the wet tropics. In pursuance of this idea, he went to Singapore, where he worked for a good many years (including the period of Japanese occupation), and later worked in Brazil. The climax of his interest in toadstools was marked by his monograph on the great and exceedingly difficult group Clavaria. He found that he could recognize different systems of basic architecture in the growing tissues, and with this in mind he was able to organize what had seemed chaos into orderly sections.

His work on the huge fig genus, its classification, distribution and probable evolution represents work, on orthodox lines, but his studies on the evolution of tropical plants in general culminated in his celebrated 'Durian theory', which is still developing and may be deemed a major contribution to botanical thought.

This theory deals with the probable course of plant evolution in tropical high forest from remote periods down to the present time. He assumes that the main stream of plant evolution flowed in this environment, and then considers how the special features of this environment would favour particular kinds of plant organization. He concludes that the durian tree of Indo-Malaya represents the archetype of tropical forest tree—with its thick stem, large leaf, large seed, edible aril and other characters.

The Durian theory met with opposition, but is now widely referred to with respect.

Hughes Medal : Dr. J. L. Pawsey, F.R.S.

Dr. Pawsey is acknowledged as one of the pioneers in the development of radio astronomy. Soon after the War the Commonwealth Scientific and Industrial

Research Organization established a division of the Radio Physics Laboratory at Sydney, Australia, to carry out research work in radio astronomy, and Pawsey became the head of this division. Apart from many major personal contributions Pawsey has inspired a great variety of other fruitful investigations.

The Radio Physics Laboratory has carried out extensive work in both solar and galactic radio astronomy. At an early stage the principle of the Lloyd mirror was used to devise a radio-interferometer, the surface of the sea being used as the mirror. With this new device, some of the earliest evidence of the existence of the direct radio sources, radio stars, was obtained, and extensive studies of solar radio emissions carried out. Later, much more elaborate new interferometers with greatly increased resolving power were developed. The results are important for the understanding of solar terrestrial relations and include evidence of ejection of matter from the Sun during a period of intense radio emission.

Pawsey and his colleagues also continued the study of the galactic radio sources. By improved resolution they were able to identify some of the 'discrete sources'. Soon after the initial discovery of the emission of the 21-cm. hydrogen line, the laboratory began a detailed survey of the distribution of neutral hydrogen throughout the Galaxy, so far as could be undertaken in the southern hemisphere. Together with the work of Oort in Holland, the results have established the spiral character of our Galaxy. It was also soon established that the hydrogen line was emitted from an extragalactic object—the clouds of Magellan.

In addition to playing the leading part in these investigations, Pawsey has always maintained an interest in ionospheric studies and made an important contribution to knowledge of the lower fringes of the *D* region by carrying out reflexion sounding from a site in New South Wales, where the background noise was exceptionally small.

Pawsey, in conjunction with Bracewell, has written a standard monograph on radio astronomy.

OBSERVATIONS ON CELL MECHANISMS

It is five years ago to-day that I assumed the office which within an hour I shall be handing over. The intervening years have proved eventful ones in the life of the Royal Society. The Antarctic Expedition sailed to Halley Bay, made its distinguished contribution to the International Geophysical Year and returned, having written one more chapter in the Society's proud record of scientific exploration. Yet another chapter has been added by a biological expedition to one of the most interesting regions of South America. Although the future in this field is uncertain, progress has been made in the planning of space research in Britain.

When infused with true vitality, tradition is indistinguishable from progress, a truth which is apparent in many of the affairs of the Royal Society, and in none more than in our relations with our colleagues abroad. The historic friendship with American men of science, unbroken since the days of Benjamin Franklin, was movingly demonstrated by the National Academy of Sciences when it devoted one of its most important annual occasions to the honouring of the Royal Society Tercentenary and in the most cordial way invited your President to take part. Regular exchanges of students and lecturers with the Soviet Union have been brought into operation by agreements with the U.S.S.R. Academy of Sciences. I am specially happy to record that relations with the Academia Sinica, initiated last year by my own visit to China at their invitation, are developing in an encouraging way.

The whole field of international relations has been extraordinarily active, and I want to pay just tribute to the retiring Foreign Secretary, Sir Gerard Thornton, who has throughout so admirably performed the ever-growing duties of his office.

A practical body like the Royal Society is always conscious of the problem of ways and means. The Tercentenary Appeal and the establishment of the Wolfson Research Professorship have increased the resources with which the Society can meet its many obligations. If to-day we face the future with very substantially improved prospects, it is due to the energy and the vision of Sir William Penney, who retires to-day from the office of Treasurer, leaving the Society lastingly indebted to him.

The Tercentenary Celebrations are fresh in the minds of us all and I shall not recapitulate the many thoughts about the past and the future which were then expressed. But there is one thing which must be said, and that is to record gratitude to all who toiled so hard to make the events of the summer a success, and above all to Dr. Martin and his staff; and as far as I am concerned I must express my indebtedness not only in respect of last summer but of my whole term of office.

We have now returned to the workaday world of the new century, when we do well to remember again that the great themes of science emerge only after the accumulation of the results of many patient labours. I shall revert to some of those details now, and devote the rest of this address to some recent work on the biophysics of living cells which I have been able to follow at close quarters.

It has sometimes seemed to me that many people speak too much as though little mattered in living cells beyond the code inscribed in their nucleic acids, the mechanism of expression of this code in the cell properties being a relatively trivial affair. A change in the code is a mutation, and a convenient simplification ascribes all adaptive responses to mutations, ignoring the latitude which may exist in the translation of the code. But the detailed study of cells shows that there is in fact very much latitude. To quote one example, my close colleague A. C. R. Dean has recently studied the proportions of RNA, DNA and bacterial protein in cells grown under varied conditions. They vary widely, as does the cell size. There are clear evidences of oscillatory or 'overshoot' phenomena, suggesting a subtle and adjustable balance of interacting systems in mutual dependence. With change of medium the proportions of various enzymes in bacteria change very considerably, and enzymes are of course necessary for the synthesis of nucleic acid components.

The code-pattern of the DNA determines the cytoplasmic make-up. But, unless a non-physical kind of influence is assumed, Newton's Third Law suggests that in principle the cytoplasmic constitution might influence the DNA pattern itself. In other words, mutations normally attributed to accident might be induced, though this back action might be quantitatively small. In the synthesis of DNA the code must be spelled out in some polycondensation reaction.

At any stage of this process the alternative addition of a monomeric unit X or Y is believed to depend on what are essentially steric conditions. Yet these define a probability, not a certainty, and the normal course of addition could be modified by mass action factors coming into play if the changed cytoplasmic organization changes the proportions in which the monomeric units are offered to the growing points of polymers.

Thus there are several ways for unicellular organisms to respond to changed environment: quantitative readjustments in the proportions of cell components, gradually induced changes in the DNA code, and, as commonly assumed, selection of mutants formed by chance errors in the code and ousting the original forms by growing faster or surviving longer.

It has been widely asserted that the simple selection of chance mutants is the only true mechanism of adaptation. This view may have been based on an exaggerated view of what natural selection can account for, on some misrepresentation of Lamarck and on the failure of experiments on the so-called inheritance of 'acquired characters'. Perhaps also the unmistakable evidence that natural selection has operated has masked the fact that the variations selected may have had many kinds of origin and that there is no exclusive virtue in chance.

Not all biologists indeed adopt this attitude. T. M. Sonneborn, for example, discussing cell differentiation, remarks: "There is thus in general a marvellous system of give and take among certain genes and the cytoplasm" and he refers to "successive cycles of differentiation of cytoplasm by nucleus and then of nucleus by cytoplasm".

Experiments with unicellular organisms continue to show how manifold, subtle and unexpected are the phenomena of growth and adaptation, and fail to countenance the view that mistakes in coding are the sole source of advantageous variation.

Some years ago Akiba and afterwards Szybalski reported that cells in bacterial suspensions exposed to streptomycin were found after a time to be all dead or all resistant. This result was later re-interpreted by the idea that sensitive cells underwent lysis and were replaced by pre-existent mutant types which multiply on the debris. Similar objections were raised against F. J. Ryan's experiments on cells of *Escherichia coli*, which originally required histidine for growth but which on storage in a medium deficient in histidine gradually acquired the property of histidine-independence. Ryan, however, demonstrated that lysis and re-synthesis did not in fact occur. The proof consisted in showing that, in a medium containing lactose, the predicted shifts in the proportions of (histidine)$^-$ (lactose)$^+$ and (histidine)$^-$ (lactose)$^-$ are not observed as they should be if cryptic growth is the explanation. Ryan thinks that the DNA pattern changes during the stationary phase by some process other than a mistake in replication during growth.

Further light on the course of an adaptive phenomenon is thrown by the experiments of Midgley on the utilization of D-arabinose, and of N. Richards on the utilization of lactose by *Bact. lactis aerogenes*. The bacterium when first offered D-arabinose as sole source of carbon begins to multiply only after a lag of some days, which represents, according to one view, the time needed for internal adjustments in all the cells, and, according to another view, time needed for the multiplication, to the threshold of detectability, of a very minute proportion of abnormally coded mutants. Arguments, counter arguments and rejoinders beset this apparently simple theme. The new evidence is as follows. At various stages of the adaptation, enzyme activity tests (relevant to the utilization of D-arabinose) are made on unit mass of the culture. The measured chemical activity can, as a purely arithmetical operation, be divided either by the total mass of bacteria, or by the actual increase in mass since the adaptation started. In the first case the resulting quantity rises gradually and naturally to a limit as the exposure to the sugar continues and growth sets in. In the second case, which is appropriate to show the properties of the hypothetical mutants, the specific activity shows a most improbable course. Soon after the onset of growth it rises sharply to a very pronounced maximum from which it then rapidly falls again. The maximum is very much higher than is ever again found, even with the most thoroughly adapted cells. The mutants apparently acquire, just at the moment when they happen to be outnumbering the original non-mutants, a momentary activity far greater than they ever show again in the whole course of their history. If the idea of special mutants is abandoned, this strange behaviour is explained away by the simple fact that the chemical activity has been divided by the wrong quantity, not, correctly, by the total mass, but, incorrectly, by the increase in mass.

The subsequent history of the adaptive enzyme changes during prolonged cultivation in D-arabinose, and during alternate periods in arabinose and glucose reveals an intricate pattern of successive reorganizations. At first the arabinose-utilizing enzymes prove unstable to growth in absence of arabinose, and decline. But with longer adaptation to arabinose they do this less and less, and in a way which shows the whole conception of 'stable heredity' in adaptive changes to be complex and relative. According to the precise conditions of growth, the special enzyme may either decline or continue to be synthesized in the absence of the original 'inducer'.

All these facts give a powerful impression of a machine with intricately geared parts, of equilibria and quantitative balances about which by no means the last thing can be said in terms of mistakes in coding.

Cannon has complained of the confusion caused by mistranslation of Lamarck's word 'besoin'. This should of course be translated 'need', and, without entering into more controversial fields, I should like to point out that in adaptive studies the development of functions in response to needs is very much in evidence. For example, N. Richards, in his studies of lactose utilization, finds that as a culture of *Bact. lactis aerogenes* becomes short of oxygen the galactosidase activity increases. In the absence of oxygen, utilization of carbohydrate is less efficient: more is needed, and more is made available by the increase in enzyme activity. This is clearly a response to a 'need'. It is not mysterious. When the enzyme is insufficient, processes dependent on it are retarded relatively to its own synthesis, with the result that its proportion increases until a proper balance is established.

It is a quite general law for the reproduction of living matter that the reaction system tends to be established which gives the greatest growth-rate. This, it is worth while pointing out once more, is itself a form of natural selection, automatically operating to

favour the predominance of the most efficient systems. In the long run the selection of the best reaction pattern gives the same result as the selection of a special type of individual.

The orthodox view, however, is that such phenomena are of little significance beyond the generation in which they occur. On this several things may be said. Cannon has objected that most of the negative experiments on acquired character transmission have been of a rather crude kind, in which failure proves little or nothing. There is no doubt that the persistence of adaptive enzyme formation through many cell generations in the absence of the inducing agent is a very variable and complex story. The persistence may be great even where the evidence suggests that the original adaptation was not a mutation.

There are perfectly natural physicochemical mechanisms by which a changed cell organization could survive for many divisions of a unicellular organism returned to a previous habitat after an adaptive interlude. But, in addition to this, Newton's Third Law, as I have already said, discourages belief in the absolute inability of genetic codes themselves to be modified by the workings of the very systems which are built to their instructions, and by which, be it said, they themselves have to be reproduced. The gradual stabilization of adaptations is a very striking phenomenon, upon which I think we should ponder deeply. In his book "Brain, Memory and Learning", W. Ritchie Russell says, "All living matter shows features that may be considered a form of memory. It all shows spontaneous activities that tend to form patterns which are at first relatively simple, but show a strong tendency to repeat".

An interesting variation on the theme of stabilization is reported by Ierusalimski. A spore-forming organism (*Clostridium acetobutylicum*) was adapted in continuous culture for 21 days to resist the toxic action of 0·6 per cent butanol. After sporulation, the strain was no more resistant than a control. When, however, the adaptive treatment had been further prolonged and the butanol concentration gradually increased, the resistance not only rose but also could now survive passage through the spore form.

I shall now turn briefly to some of our own results on the resistance of micro-organisms to drugs, and will begin by repeating my belief that not one but several mechanisms exist for this phenomenon, and, in particular, that accidents of code replication are not the sole or even necessarily the most important source of resistance.

To find the proportion of resistant mutants a common method is to spread a very large number, N_0, of organisms on an agar plate with nutrient and with the drug at concentration c and to count the number, N_∞, of colonies that eventually develop. $N_\infty/N_0 = \alpha_\infty$ is the required proportion. More detailed investigation alters the picture. The colonies take different times to reach a standard size, and the proportion, α_t, rises with time from zero to α_∞ according to a curve indicating an approximately Gaussian distribution of development times. J. B. Woof has studied the phenomenon with *Bact. lactis aerogenes* and chloramphenicol. As the drug concentration increases, L', the time at which $\alpha_t/\alpha_\infty = 0\ 5$, decreases, a rather paradoxical behaviour for mutants. With an adaptive hypothesis the paradox disappears. α_8 is small because there is a race between adaptive adjustments and lethal processes which, given time, stop the cells from forming colonies at all. Calculation shows that if the logarithmic death-rate is λ, L' will in fact decrease as λ increases, that is as the drug becomes more potent. If the cells die quickly only those that make haste to adapt ever have a chance to form colonies at all. The successful ones are those in the tail of the statistical distribution. The fiercer the drug action the more the colony formation is confined to the exceptional members of the distribution. Woof's studies show that this picture works out quantitatively.

The conception of adaptive and lethal processes in competition may be thought difficult. The reality of such superpositions of conflicting processes is illustrated by some of Midgley's experiments on the adaptation of *Bact. lactis aerogenes* to D-arabinose. At the initial transfer to the pentose the lag is x days and the subsequent growth-rate r_1, which is far below the optimum. If the lag in arabinose is interrupted by passages in glucose during which growth takes place, the total value of all the lags in arabinose before growth occurs in it still adds up nearly to x. But, as a result of the intermissions for growth in glucose, the growth-rate in the arabinose is now much greater than r_1. During the long adaptation to arabinose other cell mechanisms suffer from ageing unless they are kept mobilized by the opportunity for use in the glucose medium.

In the competition of adaptive and lethal processes the situation might perhaps be likened to that of a man dying of destitution while he is struggling to finish a job which will furnish the means for his physical salvation.

Another approach to the problem of chloramphenicol-resistant colonies has been followed by Dean. If the drug concentration on an agar plate is low enough, every cell plated can form a colony. An inoculum from one of these colonies is spread on a plate with a slightly higher concentration of drug, and again the proportion forming colonies approaches unity. Proceeding carefully in this way, and sometimes spreading for several successive tests at the same drug concentration, we can arrive at colonies growing on plates with ten or twenty times the concentration which would originally have been completely inhibitory. At every stage of the process the yield is so high as to rule out all possible talk of rare mutants. Errors of coding which can occur every time, or even once in two or three times, would seem to be misnamed.

The most powerful proof that resistant forms can sometimes arise fortuitously comes from Lederberg's elegant technique of 'replica plating'. The principle, briefly, is that, by means of a suitable pad, multiple prints can be made from a given bacterial plate on to several others, with and without drug. Resistant colonies can be detected on the drug plates, and their opposite numbers on the drug-free plates isolated. By successive enrichment resistant strains can be obtained without previous direct contact with drug.

Lederberg obtained in this way strains resistant to streptomycin and to bacteriophage. By a modified replication technique Cavalli, however, could obtain only a small increase in chloramphenicol resistance comparable with what can occur as a result of varied cultural history. It seems, nevertheless, to be tacitly assumed sometimes that the replica plating technique can be quoted to prove the existence of mutants in cases to which it has not been applied at all. This is particularly inadmissible because both phage resistance and streptomycin resistance can arise from

damage, for example, by ultra-violet light, depriving the cells of receptors for the agents in question.

It has also been pointed out that the organisms isolated by replica plating are never known to be resistant until they have been tested in the presence of a drug. What has been selected, therefore, may be not so much a resistant form as one specially endowed with the power of responding rapidly when exposed to the drug, that is of doing what in other examples a large proportion of the population succeed in doing more slowly. This reflexion suggests the possibility that the differences in behaviour are not necessarily more than quantitative. Valuable information may thus be forthcoming from a more detailed study of the response to drugs of organisms selected by indirect means.

Discrepancies in apparent results often arise from unsuspected differences in method. It is therefore of interest to note that W. T. Drabble, by the same methods which have provided evidence for direct adaptation to chloramphenicol and other agents, has obtained results with streptomycin pointing clearly to the presence of some initially resistant forms of *Bact. lactis aerogenes*. There are also indications, which he will report in due course, of a superposition of direct adaptation upon a selective process.

In this last address from the presidential chair I have, as it were, returned to the laboratory by a deliberate choice. It was not that large general themes, scientific or otherwise, were lacking. I had perhaps reflected a little on a remark I heard recently from a young colleague to the effect that scientists tended to deal with broader questions when they were getting past work in their own field, but I am, I think, on good enough terms with my younger colleagues not to be intimidated by them. It was rather that, after the Tercentenary, it seemed better to strike the workaday note once more. Some of the views I have expressed may seem to verge on the heretical. They are not, I think, irreconcilably so. In a recent study which Bartlett and I made on the crossing of resistant and non-resistant bacteria, we reached some conclusions which at any rate one colleague in genetics welcomed as support for an orthodox view. The truth, I believe, is that we need a re-synthesis of some of the widely accepted views with the kind of approach that appeals more to the chemist and the physicist.

Be that as it may, nobody would expect an occupant of this chair to subscribe against his beliefs to orthodoxy. May I quote once more the words of Horace with which you are familiar :

> "ac ne forte roges quo me duce quo lare tuter
> nullius addictus iurare in verba magistri"

I hope the President himself may be forgiven for following this example.

To have been President of the Royal Society is, it seems to me, the greatest honour which any man can have received, and one of which no man can feel he has been worthy. For myself I can only thank those who have done their best to see me through. I welcome my successor and wish him well. There are plenty of problems ahead. For example, our long and, though informal, immensely important relations with the Government are in process of adaptation to the vast scale and complexity of scientific activity to-day. The optimum solution of this problem is of the greatest importance both to the Society and to the country. Of equal importance is the establishment among the Fellows of the right balance between the pure and the applied sciences to enable the Royal Society to maintain its full influence in the modern world.

I regard the future of the Society with confidence not least because I see no sign that it is likely to depart from the principle declared in its motto that it will remain "nullius in verba".

TREND OF CÆSIUM-137 IN THE EFFLUENT OF A LARGE CITY*

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AND

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THE oceanographer is concerned with the mechanisms controlling the dispersion of materials in the ocean. For this reason, the progress of fall-out radioactivity in the ocean has been studied for several years at the Scripps Institution ; recently special consideration has been given to contributions coming from terrestrial run-off. Several radioactivities in sewage flowing from a large coastal city were monitored at the treatment plant for more than two years. Cæsium-137 was followed in detail ; this fission product has useful tagging properties ; it emits a penetrating, easily detectable γ-ray, and decays relatively slowly.

Detailed off-shore mapping has not yet been done ; however, the average and peak outputs from the city have been recorded over a period of 21 months, permitting estimates of the influence on coastal waters. The character and trend of the concentration, and comparisons with reported contamination of human food by fall-out, point to an unexpected source for the cæsium-137 observed in the sewage. Not a great deal is known about the chemical behaviour of this nuclide, at very low concentrations and in complex systems, so that the partition observed for cæsium in the plant should be of general interest.

* Substance of a paper read in part at the meeting of the International Association of Physical Oceanography, Helsinki, Finland, on August 5 1960.

We were fortunate in being permitted to make measurements throughout the Hyperion Treatment Plant of the City of Los Angeles. This modern installation is situated on the seashore 120 miles north of the Scripps Institution; it collects sanitary sewage from a large city centred about 30 miles inland; and disposes the treated material mainly through outfall pipes extending as far as 7 miles into the open sea where the depth is about 200 ft. Very little storm water enters this system.

For about ten years, until June 1, 1960, the treatment included primary settling, aeration with activated sludge, final settling, digestion of primary and activated sludge, followed by the filtering, washing and drying of part of the digested solids to produce a stable dry fertilizer that was sold as soil conditioner. After this date a change was made in the treatment scheme, so that routine drying of large amounts of fertilizer was stopped.

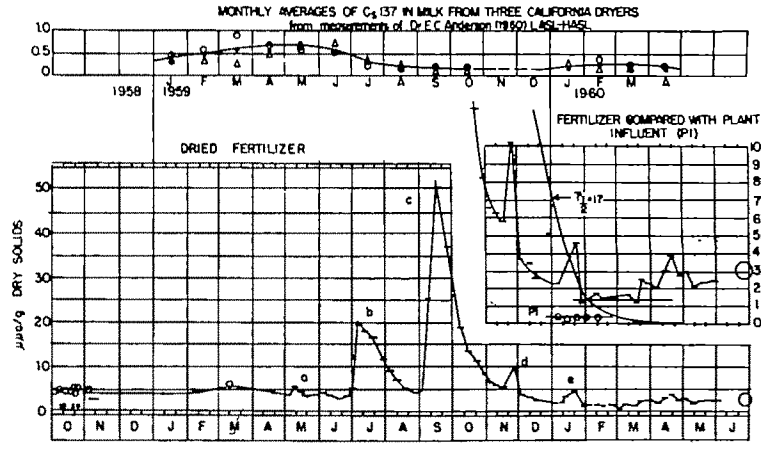

Fig. 1. Trend of cæsium-137 in the sewage treatment plant compared with the trend in milk. All ordinates are micromicrocuries per gm. of dried solids. Inset illustrates that batch inputs probably contributed little during comparisons early in 1960

Investigation at the plant consisted of: (1) sampling continuously and in detail at one point in the system; (2) sampling also at several points during a given short period, preferably when the input character was not changing rapidly. While it was available, the commercial fertilizer was used in the continuous monitoring; it was convenient, and because cæsium is greatly enriched by treatment up to this point, extremely small changes in input concentration could be deduced. These samples were assayed after being composited daily for periods of 3–5 days. Most of the other specimens used for establishing partition ratios were liquids, some of them very dilute. All were reduced to dryness at the plant in 40-gallon soup kettles heated with steam.

Assaying was done at the Scripps Institution by exposure of a sodium iodide scintillator crystal to the radiation from a relatively large specimen, one weighing about 200–400 grams. With a modern multichannel gamma-ray spectrometer a specimen may be analysed within a few minutes for one or more gamma-emitting nuclides, even when their concentrations are very low. Usually no wet preparation whatever was undertaken; however, specimens were assayed in plastic containers under uniform conditions, so that accurate comparisons with standard specimens could be made. The laboratory at Scripps had already developed a spectrometer accessory[1] permitting the rapid comparison of measurements with a library of background measurements and measurements of standard specimens all stored in digital form on magnetic tape loops.

In passing, it will be mentioned that the sewage had less radioactivity than was anticipated; no concentration was observed even approaching a recognized tolerance-level. Nevertheless, the natural background from the uranium and thorium families almost always was surpassed by one or more man-made activities. Iodine-131 appeared in nearly every input specimen as might be expected from its use in medicine; cobalt-60 repeatedly appeared in easily measurable amounts. Relative to the concentration of cæsium-137, the concentrations of both zirconium-95 and ruthenium-106 were extremely deficient when compared with the ratios observed in rainfall for this period. Details concerning these and other activities will be reported elsewhere.

Monitoring radiocæsium in digested material has several practical advantages; but because of the long dwell of material in digesters, the information is not contemporary, and some input detail is lost entirely. Fig. 1 shows the trend of cæsium-137 concentration over 21 months derived from 75 composited samples of digested fertilizer. The large peaks attenuate at a rate consistent with what is known about the purging-rate of these digesters. Actually a battery of digester units is used at Hyperion; nevertheless, their performance might be approximated roughly by a model having a single tank into which a daily input is suddenly injected and mixed thoroughly followed by the withdrawal of an equal amount, about one-thirtieth of the whole. It can be shown that this model would purge itself after a sudden excessive input to half-peak-concentration in about 21 days. The actual measured initial slopes of the two larger peaks correspond to a half-purging time T of about 17 days.

In spite of the large batch inputs, it appears from Fig. 1 that the input concentration varies only slowly much of the time and follows an easily measurable basic trend. It required roughly four months for attenuation of the largest batch, but ultimately this reached insignificance. An inset is shown in Fig. 1 magnifying the data for the first three months of 1960, and an exponential curve having half-value of 17 days has been added to it to illustrate that the largest peak and later smaller ones probably have become greatly attenuated during the period when input concentrations were compared with average concentrations in the digested material. These comparative measurements are plotted in the inset of Fig. 1 and listed in Table 1. From these roughly steady-state conditions we can derive ratios that should approximate fixed characteristics of the plant. Table 1 indicates that the incoming cæsium-137 is enriched after digestion by a factor of about 1·4/0·32 or 4·4 (on a dry basis).

It can be concluded from these measurements that the concentration of cæsium-137 in the sewage coming

Table 1. Comparison of Influent and Fertilizer Concentrations

Collection date of composite sample (5-day period ending)	Concentration of ^{137}Cs ($\mu\mu$c. per gm., dry)
Dry fertilizer (after long digestion)	
January 27, 1960	1·2
February 2	1·4
,, 10	1·8
,, 17	1·5
,, 24	1·6
March 2	0·7
,, 9	1·8
Fertilizer average	1·4
Influent (composited 5 days and dried)	
January 6, 1960	0·39
,, 15	0·22
,, 22	0·48
,, 29	0·19
February 12	0·32
Influent average	0·32

into the plant fell slowly over 21 months from about 1·1 to about 0·32 $\mu\mu$c. per dry gram; this corresponds to a change from 1·4 to 0·4 $\mu\mu$c. per litre.

Now it can be appreciated why direct monitoring was not carried out. No satisfactory chemical precipitation had been developed; boiling down all specimens in barrel-sized amounts would have been expensive; and the spectacular enrichment in the digested material was attractive. For example, raw sewage having 0·4 $\mu\mu$c. per litre of cæsium-137 produces dried fertilizer having 1,400 $\mu\mu$c. per dry kgm.

Obviously the large peaks in Fig. 1 arose from batch inputs. But no technical or medical practice has been discovered that would explain the slowly varying basic concentration-level. When measurements were made of representative samples from the city's major water supplies it was found that this source, too, was deficient. The average value measured for the fresh drinking water was only 0·025 $\mu\mu$c. per litre; this corresponds to only about 0·02 $\mu\mu$c. per gm. of sewage (having 1,250 p.p.m. total solids), so that fresh water could contribute only about 6 per cent of the cæsium-137 observed in the sewage.

Anderson[4] has considered in some detail the available reports concerning U.S. national dietary habits, and by introducing values of cæsium-137 found in foods, he has ventured a rough estimate of the amount of cæsium-137 that was daily ingested per person in 1956. There are several reasons for concluding that the value he derived, about 50 $\mu\mu$c. per day per person, would become no smaller if it could be corrected by deriving it from data pertaining to the spring of this year. If this value is tentatively accepted, and also if the estimates are taken that 2·8 million people contribute to a system carrying 250 million gallons per day and 1,250 p.p.m. total solids, then a possible daily input of cæsium is discovered that is much larger than could come through drinking water. In fact these, apparently conservative, values provide for roughly one-third of the average cæsium observed in sewage early this year. To this, of course, must be added a contribution from garbage now frequently disposed of through kitchen grinders in this community.

No attempt will be made to balance the budget precisely, but use here of a 1956 fall-out contamination value needs some justification. After 1956 world-wide fall-out increased in rate; later it decreased[5]. During the period of these investigations at Hyperion the concentration of cæsium-137 in dried milk from three nearby milk-sheds varied as shown at the top of Fig. 1. Milk is reported to be the largest contributor of cæsium-137 in diet, and the concentrations in dried milk reported for the spring of 1960 are not strikingly different from those reported for 1956. Between these dates there were higher levels in almost every food; and almost every food in practice experiences a lag before it is delivered and consumed. There is also a substantial lag that occurs between input and output of cæsium in the human system[4,6]. It would therefore appear necessary to correlate sewage concentrations not with contemporary food contaminations but with concentrations measured in foods produced several months earlier. Because of these circumstances, it appears quite possible that the basic trend of cæsium-137 in the Hyperion sewage could be controlled almost entirely by fall-out cæsium entering through human food.

In many circumstances cæsium behaves chemically and biologically like potassium, an essential tissue constituent; nevertheless there are several biological systems reported where a clear distinction is made between these two elements. In some cases, the discrimination has been observed to be against the intake of cæsium and in favour of potassium; for example, plants are reported to discriminate strongly against radiocæsium in taking the two elements up from the soil.

Concentration and digestion of sewage depends largely on metabolic processes, and much of the final solid material has been synthesized by micro-organisms. Therefore, it was not anticipated that cæsium would become strongly concentrated in the solid digested fraction relative to potassium. Table 2 indicates that cæsium-137 is enriched relative to potassium by forty-fold during the reduction of sewage to digested, dried fertilizer. This aspect is being studied further.

Although it appears that the sewage system studied can collect the minute traces of fall-out cæsium passing through in human food, the effect on the sea

Table 2. Cæsium-137 to Potassium Ratio in Raw Sewage and Fertilizer

Date of collection	Fertilizer			Date of collection	Raw sewage		
	^{137}Cs $\mu\mu$c./gm.	K(total) gm./gm.	Cs/K $\mu\mu$c/gm.		^{137}Cs $\mu\mu$c./gm.	K(total) gm./gm.	Cs/K $\mu\mu$c./gm.
January 27, 1960	1·2	0·003	400	January 6, 1960	0·39	0·024	16
February 2	1·4	0·003	470	,, 15	0·22	0·031	7
,, 10	1·8	0·002	900	,, 22	0·48	0·029	17
,, 17	1·5	0·003	500	,, 29	0·19	0·012	16
,, 24	1·6	0·002	800	February 12	0·32	0·020	16
March 2	0·7	0·001	700				
,, 9	1·8	0·003	600				
Average	1·4	0·002	620		0·32	0·023	14

cannot be great. This is because surface sea waters have caught and have failed to dissipate downward such large amounts of fall-out that the concentration of cæsium-137 persists at levels not far below what is seen in average sewage. Measurements[2] made of the cæsium-137 concentration in the local surface sea water early this year by us, gave an average of about 0·1 μμc. per litre. This should be compared with the value of 0·4 μμc. per litre representing the average concentration in the Hyperion sewage at the same period.

It is useful to compare average concentrations in this manner, but it should be pointed out that even in specimens taken from nearby points in the open sea the concentration may vary by more than 50 per cent. Smaller average concentrations were measured[2,3] in local coastal waters than in waters far off this coast; and Yamagata[7] has reported the average concentration for 1959 Japanese coastal water of 0·38 μμc. per litre, or essentially what has been observed in Hyperion sewage.

Even the peak concentrations observed at this plant should cause no alarm. From plant characteristics, it may be estimated that the largest peak in Fig. 1 corresponds to a batch input of about 0·4 curie. However, the sewage travels on the average 30 miles to the plant and is not likely to pass through in much less than one day, and the 250 million gallons of water put through in one day would dilute this to an average concentration of only $3 \cdot 7 \times 10^{-7}$ μc./ml. This falls far below the value of 2×10^{-5} μc./ml. now accepted as maximum permissible concentration for this particular isotope in water that is to be drunk continually by humans.

From these investigations something has been learned concerning the behaviour of radiocæsium in a large modern sewage disposal plant, and useful conclusions can be drawn concerning the probable influence on the downstream environment. It can be seen, for example, that the original objective of following the local dispersal of sewage by the ocean can be attained only if the most sensitive and refined methods are applied. It appears, too, that suitable monitoring of the gamma-ray activities in sewage systems might provide additional safeguards to the public against misuse of the radioactive materials that are becoming more and more common in research, medicine and in industry.

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OBITUARIES

Dr. J. M. Cowan, C.B.E.

With the sudden death of Dr. John Macqueen Cowan on the evening of October 26, after a very happy day with his friends on the Gardens Committee of the National Trust for Scotland, Scotland lost one of her most distinguished horticulturists.

A son of the manse, he was born in Banchory, Kincardineshire, in 1892, received his early education at Gordon's College, Aberdeen, attended the University of Edinburgh, taking the arts and science degrees with honours in botany, became an undergraduate at Oxford, reading honours in botany with Prof. Vines and Dr. Church and forestry with Sir William Schlich, before being appointed to the Indian Forest Service. At Oxford he met Adeline May Organe, who took an honours degree in botany, whom he married and who at all times was the source of the greatest possible encouragement to him; in fact, she was co-author of one of his earliest publications, "The Trees of Northern Bengal" (1929). In India he followed the example of some of his distinguished predecessors in the Forest Service, such as Brandis, Lace and Gamble, pursuing his botanical investigations as well as proving himself a forest officer of outstanding merit. It was not surprising, therefore, that from that Service he was chosen to officiate as superintendent of the Royal Botanic Gardens, Calcutta, the chief botanical post in the Indian Empire.

Retiring from India in 1928 and after undertaking, with Dr. C. D. Darlington, a botanical expedition to Iraq and Persia, on behalf of Kew and the John Innes Horticultural Institution, Cowan returned to Scotland in 1930 as assistant to Sir William Wright Smith, the regius keeper of the Royal Botanic Garden, Edinburgh. Soon he was deeply engrossed in the taxonomy of the genus *Rhododendron*, the genus which had fired the enthusiasm not only of his immediate chief but also of the professor who had lectured to him as an Edinburgh student, Sir Isaac Bayley Balfour. On the taxonomy of this complex genus he published widely, often in collaboration with his Edinburgh colleagues; he published, too, on the genera *Cyananthus*, *Roscoea*, *Wendlandia* and others, as well as on the history of the Royal Botanic Garden. At all times he took a keen interest in the welfare of the horticultural students in the Garden, and if at times the students were not altogether approving of some of his teaching methods, they were always appreciative of the generous hospitality of the Cowan household.

Late in the 1940's Cowan became deeply interested in the activities of the National Trust for Scotland,

and especially interested in the two great Scottish gardens the Trust took over—Crathes in Kincardineshire and Inverewe in Ross and Cromarty. He gave great prestige to the Trust when, under the Trust's auspices, he inaugurated the early 'Garden Cruises', a unique and previously unused method of transport which has enabled people from all parts of the world to visit famous, and sometimes somewhat inaccessible, gardens in great comfort.

Happy and industrious though he had been in India, and undoubtedly was in Edinburgh, he frankly admitted that not until he retired from Edinburgh in 1954 and accepted the post of gardens adviser to the National Trust for Scotland, with his headquarters at Inverewe House on the incredibly lovely and rocky peninsula at Poolewe, did complete contentment and satisfaction come to him; and naturally so, when through his great energy and drive he saw the number of visitors to the Garden steadily increase from a few hundreds in 1954 to 47,000 in 1960.

Cowan's services to horticulture were acknowledged by the Royal Horticultural Society by the award of the Veitch Memorial Medal in 1951 and by the Victoria Medal of Honour in 1955. He was made C.B.E. in 1952. Mrs. Cowan and a son and daughter survive him. H. R. FLETCHER

Prof. Yehuda Hirshberg

PROF. YEHUDA HIRSHBERG, head of the Laboratory of Photochemistry and Spectroscopy in the Weizmann Institute in Rehovoth, Israel, died on September 20. Prof. Hirshberg was born in 1903, went to Israel as a pioneer in 1923 and joined a Kibbuz. After a strenuous year he fell ill with malaria, and was compelled to move to Jerusalem. There he worked as a labourer and at the same time enrolled as one of the first students in the pre-faculty of sciences of the Hebrew University. He studied chemistry under Prof. A. Fodor, and graduated in 1928 (unofficially, since the Hebrew University was not yet recognized at the time). Being an outstanding student, he was given a study grant which enabled him to go to Brussels, where he continued his studies towards the degree of doctor of science under two distinguished teachers—Victor Henry and Jaques Errera. Despite the difficulties of a new language and environment, he completed his studies with great distinction, and was appointed an assistant. His first independent research paper was published in 1932. A year later he made the acquaintance of Chaim Weizmann, who soon recognized the high qualities of the young scientist and invited him to serve as the physical chemist of the Daniel Sieff Research Institute which was planned at the time. Thus began Hirshberg's life-long association with the Sieff and Weizmann Institutes. His scientific career can truly be called a fruitful one, as witnessed by nearly ninety research papers in various scientific journals. His well-known discovery of 'photochromism' in 1950 and the investigation of this phenomenon and of the 'photochemical memory' led by him since then, won him world-wide recognition and international acclaim.

Despite his success, he never ceased to be a 'man of the people', being on friendly terms with everybody, irrespective of grade or standing. His personality was marked by boundless devotion to his work, willingness to help, and eagerness to make a friend of whomever he met, a goal which he achieved almost always, thanks to his rich Jewish humour and his good-heartedness.

His last years were marred by great suffering because of his many maladies. Nevertheless, he put up a stubborn fight against his disease and refused to give in. He was active in the laboratory and full of plans to his last day, and succumbed to a heart attack while still wearing his white laboratory coat.

His colleagues and collaborators will always remember his high human qualities, his scientific ingenuity, and his infectious enthusiasm, and hope that the work being continued in his laboratory will serve as a living monument to him. E. FISCHER

Dr. Robert W. Lawson

ROBERT WILLIAM LAWSON, who died in hospital on November 14 in his seventy-first year, was a lecturer in the Physics Department of the University of Sheffield for thirty-six years. He went from his native town of Gateshead to Armstrong College (now King's College), Newcastle upon Tyne, in 1908 and obtained a first-class degree with honours in physics. This was followed by two years research work in the College on the production of those high-frequency oscillations which later developed into radio-waves, but the study of which was then in its infancy. This brought him an award which enabled him to go to the Radium Institute in Vienna in early 1914. He was interned on the outbreak of war but generously released on parole, so that he could continue his researches into radioactivity at the Institute. He worked long hours under difficult conditions, on an inadequate diet, and published a number of papers, particularly on the rate of emission of alpha-particles from radium. The result he obtained in this investigation was verified by later workers and is accepted as the standard value. These papers earned him the award of the degree of doctor of science of his own University of Durham. He also became one of the first Fellows of the Institute of Physics when it was founded.

On his return to Britain in 1919, Lawson was appointed a lecturer in physics at Sheffield and remained there for the rest of his life, being made a senior lecturer on the establishment of this grade. The privations he suffered in Vienna had an adverse effect on his health, and it was some time before this was sufficiently restored for him to resume experimental research. The work of teaching the influx of ex-Service students could not be deferred, however, and at once he entered on a life of service to the Physics Department. He was a lucid lecturer and it was his delight to give experimental demonstrations of his talks whenever possible. In the early nineteen-twenties he was placed in charge of the laboratories in which both the special and general degree students worked. Thus he had a large share in training the many Sheffield physicists who have attained distinction. He devised many ingenious experiments for them, some of which were shown at the open meetings of the Sheffield Physical Society which he organized between the two World Wars. He had a wide circle of friends among Continental physicists, and this, together with his proficiency in German, led to the publication of several translations of important books. Probably the most noteworthy of these was "Relativity", by Einstein, the first simple exposition of the theory which has affected science

so profoundly. His colleagues benefited from his wide reading, and in past years he was also a frequent contributor to the columns of *Nature*.

Lawson played a prominent part in the formation of the Non-Professorial Staff Association of the University and was one of its first representatives on the Senate when this recognition was accorded. He retired in 1955, but his interest in physics remained unabated. His unexpected death will be a shock to his old students, who had a high regard for him, and to his many friends. He married in 1922 and leaves a widow and daughter. J. R. CLARKE

NEWS and VIEWS

Inorganic and Structural Chemistry at Leeds: Prof. H. M. N. H. Irving

DR. H. M. N. H. IRVING has been appointed to the chair of inorganic and structural chemistry in the University of Leeds, in succession to Prof. E. G. Cox (see *Nature*, 185, 144; 1960). Dr. Irving was born in Oxford in 1905 and educated at St. Bees School and Queen's College, Oxford, where he was a pupil of F. D. Chattaway. He took a 'first' in chemistry in 1928, a D.Phil. in 1930 and was awarded the degree of D.Sc. in 1958. He became a demonstrator in Queen's College laboratory, but when this closed down Prof. Soddy appointed him as a demonstrator in the Inorganic Chemistry Laboratory of the University. Although his early training was in the field of organic chemistry, he rapidly acquired a mastery of inorganic chemistry, and skilfully used his knowledge of organic synthesis, and familiarity with a wide range of organic substances, in an attack on various analytical problems and particularly in the application of stereochemical principles to their solution. Later he exploited solvent extraction and radiochemical methods to good effect. In these fields he has built up an international reputation. During the War he was engaged on government research problems and took an active part in local Civil Defence. He was a lecturer at St. Edmund Hall during 1935–38, and has been an official Fellow from 1938 and vice-principal since 1951. He has played an active part in the Chemical Society, Royal Institute of Chemistry and the Society for Analytical Chemistry, and has served on numerous official committees. He is the author of nearly a hundred papers on scientific subjects, and in addition to many interests outside his ordinary work he holds the licentiate of the Royal Academy of Music.

Psychological Medicine in Edinburgh: Prof. G. M. Carstairs

DR. GEORGE MORRISON CARSTAIRS, director of the Medical Research Council Unit for Research on the Epidemiology of Psychiatric Illness, Tavistock Square, London, has been appointed to the chair of psychological medicine in the University of Edinburgh in succession to the late Prof. Alexander Kennedy. Dr. Carstairs was born in India and educated at George Watson's College and the University of Edinburgh. At the University he read arts as well as medicine and was a medallist in Fine Art He was also a well-known athlete. He served as a medical officer in the Royal Air Force in Europe and the Far East. During the War, Dr. Carstairs became interested in social anthropology, particularly in studies of the influence of different cultural environments in personality development. After the War, Dr. Carstairs held various senior appointments at mental hospitals in Edinburgh and Oxford, and also studied social anthropology as an external student of the Institute of Social Anthropology. For the next four years he held research fellowships which first took him to New York as a Commonwealth Fund Fellow, where he studied social anthropology under Dr. Margaret Mead during 1948 and 1949 in preparation for two years of field studies in Rajputana, where he carried out research while living in three primitive village communities. During part of this time he held a Rockefeller Grant and a fellowship from the Henderson Trust and worked as a graduate student of Cambridge under the direction of Prof. Meyer Fortes. His researches in Rajputana are published in his book, "The Twice Born". He has also published widely in psychiatry and in the psychiatric aspects of social anthropology.

Lister Medal of the Royal College of Surgeons: Prof. W. G. Penfield, O.M., C.M.G., F.R.S.

PROF. WILDER GRAVES PENFIELD, director of the Montreal Neurological Institute, has been awarded the Lister Medal of the Royal College of Surgeons of England, in recognition of his service to the advancement of medical and biological knowledge, especially in the fields of neurology, surgical neurology, and psychology; and equally as humane surgical healer and as scientific research worker. He will deliver the Lister Memorial Lecture in London on April 5, 1961, under the auspices of the Royal College of Surgeons of England. This is the thirteenth occasion of the award, which is made by a committee representative of the Royal Society, the Royal College of Surgeons of England, the Royal College of Surgeons in Ireland, the University of Edinburgh and the University of Glasgow.

Code of Practice against Radiation Hazards

A CODE of practice issued by the Imperial College of Science and Technology, University of London, describes the rules applicable to the use of equipment producing X-rays, to particle accelerators, and to the use of radioactive isotopes, either sealed or unsealed (Third edition, revised. Pp. v+35. London: Imperial College of Science and Technology, 1960). The code supersedes a previous one of December 1958, and deals, in the main, with administrative procedure and control; a second part consists of a number of appendixes giving detailed information and advice on practice. The purpose of the code is set out under the following headings: (1) the protection of the worker's health; the hazard includes direct radiation and the accumulation of traces of radioactive material in the body; (2) the avoidance of contamination of the laboratory; (3) to ensure the safe disposal of waste material and effluent. The code also describes the method of control, the names of referees and the health physicist, the kind of work to be registered and the procedure for registration. Conditions to be observed before work is begun are also described.

Parliamentary Secretary to the Minister for Science

In moving the second reading of the Ministers of the Crown (Parliamentary Secretaries) Bill in the House of Lords on December 8, the Minister for Science, Lord Hailsham, referred to the clause which permitted the appointment of a Parliamentary Secretary to the Minister for Science (see also *Nature*, December 3, p. 782). He said that the arrangement under which questions relating to responsibilities of the Minister for Science were answered by some six or seven different spokesmen in the House of Commons was neither popular in that House nor convenient to him. It frustrated what he thought was a main advantage in appointing a Minister for Science, namely, the production of an image of scientific policy as a consistent whole. A collection of spokesmen, however skilful, could not answer supplementary questions in the same way as someone in the Department who knew the mind of the Minister, and there was much background which could not be conveyed in the ordinary brief. He thought that the present practice prevented the building up and presentation as a whole of a coherent body of doctrine about the work of the Department. Lord Hailsham did not accept the view that the Minister for Science should necessarily be in the House of Commons. He thought there were advantages in the Minister being in the House of Lords, which might even be the ideal position; but he suggested that the Prime Minister is entitled to some latitude in this respect, and in this view Lord Alexander of Hillsborough, speaking for the Opposition, concurred.

Termites in the Humid Tropics

A symposium on "Termites in the Humid Tropics", organized jointly by Unesco and the Zoological Survey of India, was held in New Delhi during October 4–12 under the presidency of Dr. M. L. Roonwal, director of the Zoological Survey. Among the eighty-four registered participants were delegates from Burma, Ceylon, Indonesia, Pakistan and Thailand. In addition, Prof. A. E. Emerson (University of Chicago), Prof. M. S. Ghilarov (Academy of Sciences, Moscow), Prof. K. Gösswald (University of Würzburg) and W. V. Harris (Commonwealth Institute of Entomology, London) attended as guests of Unesco.

Some forty papers were submitted, the majority of which were read and discussed at one or other of the six sections—systematics and morphology, physiology and development, general biology, ecology, intestinal symbionts and termite control. Current research in India provided the basis for many of the communications. An interesting series of papers was contributed by workers at the Defence Research Laboratories, Kanpur, covering the laboratory culture of *Odontotermes* for testing purposes, the ecology of fungus gardens constructed by this genus, and the relative susceptibility of local timbers to termites. The development of the *Odontotermes redemanni* embryo was dealt with by D. Mukerji in a beautifully illustrated paper. Other communications dealt with regressive evolution among termites (A. E. Emerson), the termite fauna of the U.S.S.R. (M. S. Ghilarov), termites in relation to Indian agriculture (D. B. Reddy and T. Sankaran), a portable plant for termite-proofing timber, bamboo and thatch used for low-cost buildings (V. R. Sonti), to mention only a few. It is understood that the proceedings of the symposium will be published in due course by Unesco.

At the final plenary session a resolution was passed recommending to the consideration of Unesco the appointment of an International Termite Commission to undertake, among other things, the co-ordination of testing techniques for termite-proof materials, the study of the problem of accidental introduction of injurious termites, and the collection of information on termites as pests of growing crops and methods of control. A field excursion to the Forest Research Institute, Dehra Dun, provided a welcome break in a well-organized, but rather concentrated, programme of meetings, public lectures and broadcasts.

Trinidad and Tobago Coconut Research, Ltd.

The new Research Station situated at Champs Fleurs, Trinidad, West Indies, is an institution intended to foster research relative to coconuts. It is administered by the Directors of Trinidad and Tobago Coconut Research, Ltd., which is a non-profit making company financed jointly by West Indian Oil Industries, Ltd., Trinidad Manufacturing and Refining Co., Ltd., and the Coconut Growers' Association. The Station will be concerned with all problems pertinent to the cultivation of coconuts, with the ultimate object of increasing copra production at a decreased cost. The Station stands in the West Indian Oil Industries Compound and comprises a well-equipped laboratory, offices and stores. Relevant scientific periodicals and text-books will be collected to form the nucleus of a library to be located in the main building. The depredation of the destructive red ring disease of coconuts will compel the research team to devote most of its energies to this problem, but, as time permits, attention will be paid to other problems. It is hoped to study the insect pests of coconuts with special reference to their role as vectors of red ring disease: in this context particular attention will be paid to the coconut palm weevil (*Rhynchophorus palmarum*), and means of controlling this pest will be sought. The nutrition of palms will be investigated, again in relation to red ring, but it is hoped that the results of this work will also help in the framing of general recommendations for manuring programmes. Up-to-date summaries of literature on any coconut problems which appear to be causing concern in different parts of the territory will be circulated and it is thus hoped to keep the planting community informed of the results of research into this valuable crop.

Resistant Strains of Micro-organisms

It is to be expected, and accepted, that micro-organisms inhabiting the gut of animals in the presence of antibacterial substances, such as antibiotics, will be either naturally or developmentally resistant to those substances. It is neither to be expected nor accepted that this state of affairs is necessarily undesirable or such resistant strains necessarily of enhanced pathogenicity or virulence; indeed, the evidence of animal well-being on antibiotic-supplemented diets is overwhelmingly to the contrary. However, caution is justifiable, despite the continuing lack of adverse practical or experimental data in the veterinary field, being engendered to a considerable extent by experience in human medicine with resistant *Staphylococci*; here, though, both environment and dosage-levels are very different. A recent communication in *Nature* (187, 288; 1960) described the isolation by Williams Smith and Crabb

of resistant *Staphylococci* from pigs and chickens and from their attendants; most of these organisms were resistant to 'nutritional levels' of the antibiotics fed to the animals and would be expected still to be sensitive to therapeutic dosage-levels. More recently Williams Smith (*Res. Vet. Sci.*, 1, 182; 1960) has shown that the widespread use of antibiotics in pig feeding in Britain has had no pronounced effect in increasing the number of resistant *Salmonellae* in the general pig population. This is highly significant (or insignificant ?) epidemiologically, and is of particular interest in contrast with the observations of Garside, Gordon and Tucker (*Res. Vet. Sci.*, 1, 184; 1960) on experimental *Salmonella typhimurium* infection in chickens, concerning the possible effects of 'nutritionally induced' antibiotic resistance on the *Salmonella* carrier state. However, high levels of antibiotic feed supplementation were used for prolonged periods in some of their experiments, exaggerating the degree and persistence of the bacterial antibiotic resistance thus induced. Moreover, there was no evidence of any relationship between resistance, pathogenicity and virulence; it is thus important that, should problems exist, they would not relate to unduly malignant organisms of enhanced potency.

The High Polymer Research Group

The High Polymer Research Group has been founded under the chairmanship of Sir Harry Melville, for the purpose of organizing study conferences. The first conference, which will be held during April 17–20, 1961, will consider the relationship between chemical structure and physical properties of elastomers. The policy of the Group is to encourage the free exchange of ideas between active workers from all countries in the chosen field, and for that reason participation will be by invitation only. The proceedings of the Group will not be recorded, nor will papers which are read before the Group be available for publication. The offices of the Group are at 14 Belgrave Square, London, S.W.1.

Historic Books on Mining and Kindred Subjects

Recently the Science Museum, South Kensington, has staged No. 4 of its occasional exhibits of historic books on scientific and technological subjects. This new exhibition is of works on metalliferous mining, metallurgy, mining machinery, mining laws and customs, mineralogy, precious stones and related subjects (see *Nature*, 188, 538; 1960). The books themselves have been generously lent to the Museum by Mr. Robert Annan, a mining engineer, from his private collection. Many are illustrated, and nearly all are of considerable rarity. Mining is perhaps the oldest of human industries, extending back into prehistoric times, when flints were mined to make implements. Records of early mining activities before the commencement of printing are naturally very scarce, but the exhibit contains a reproduction of the illustrated title page of a fifteenth century manuscript, the "Kuttenberger Kanzionale". This is primarily a treasury of old mining songs, but contains illustrations that form a valuable record of the life and activities of a mining community of the period. The printed books cover the period from the late fifteenth to the early nineteenth century. Opportunities for the public to examine such a comprehensive collection of classic mining works occur very seldom indeed, and this exhibit should not be missed by those interested. The exhibition will remain open until December 31. An annotated catalogue has been issued, which can be obtained from the Museum, or from H.M. Stationery Office (Book Exhibitions, No. 4: Historic Books on Mining and Kindred Subjects. Pp. 32. 1*s*. 6*d*.).

Theoretical Atomic Physics in Norway

During the period covered by its second annual report (1958–59), the Nordisk Organization for Teoretisk Atomfysik was still operating on an interim basis, since the adoption of the convention on which its activities are to be based formally has had to be postponed (Pp. 46. Copenhagen: Nordisk Organization for Teoretisk Atomfysik, 1960). The temporary board, consisting of four members each from Denmark and Norway, three from Finland and Sweden, and one from Iceland, with Prof. Niels Bohr as chairman, held two meetings during the year. The staff on June 30, 1959, consisted of Prof. C. Møller as director and three scientific and three administrative staff. There were eleven Research Fellows. As in the previous year, courses of lectures and colloquia were held regularly, and detailed lists of these together with the papers published by members of Nordita are given in the report. Offprints of the papers appear as numbers in a series entitled "Nordita Publications", and are sent on request without charge to institutions and scientists interested in them. Notes of some of the lecture courses have also been issued and are similarly available.

Ergonomics and Automation

The Department of Scientific and Industrial Research has sponsored a study of the human implications of automation. This was carried out under the direction of A. T. Welford and included a critical appraisal by Miss H. M. Clay and Mr. Welford of recent research, as well as a survey of existing practice in industry by E. R. F. W. Crossman. Two publications have now been issued in the series "Problems of Progress in Industry", describing these investigations. The first, "Ergonomics of Automation", describes research relevant to the problems of the human operator in an automatic plant, with special emphasis on the design of equipment (Problems of Progress in Industry, No. 8. Pp. 60. London: H.M. Stationery Office, 1960. 3*s*. 6*d*.). The second, "Automation and Skill", gives an account of the industrial survey, and discusses the skills required of human operators in highly mechanized and automatic plants, as well as problems of selection and training (No. 9. By E. R. F. W. Crossman. Pp. 59. London: H.M. Stationery Office, 1960. 3*s*. 6*d*.).

The National Museum, Bloemfontein

The annual report of this Museum for the year ended March 31, 1960, forms encouraging reading as it records the near-completion of two new wings (Pp. 22. Bloemfontein: National Museum, 1960). This increased accommodation will give four exhibition halls and twelve extra workrooms for the staff. The latter provision will give much better facilities for research. A cafeteria has also been included. The building programme interfered with the normal activities of the Museum, and research and field work almost ceased. It has also entailed the withdrawal of the usual facilities to senior university students in anthropology and history. In spite of these additions to the buildings, exhibits illustrating the proto-bushman and fossil reptile-tracks have been prepared.

Thomas Anderson (1743/4–1812)

THE proceedings of the Scottish Society of the History of Medicine for 1959–60 is particularly interesting for the report of an address by Dr. Noel L. Poynter on the life of Thomas Anderson, the pioneer of vaccination in Scotland (Pp. 30+2 plates. Edinburgh: Scottish Society of the History of Medicine, 1960). In 1799, soon after an outbreak of cowpox in London, Anderson, "who had doubtless read the account of Jenner's *Inquiry* in Duncan's *Annals of Medicine* (12), wrote to Jenner in April asking for material to introduce vaccination in his own practice; he was able to accede immediately to his request". The excerpt from Duncan's *Annals* in the autumn of 1799 is attributed to Andrew Duncan, senior, and reads as follows: "In the village of Newhaven, in the neighbourhood of Edinburgh, many children have lately been inoculated with vaccinous matter, and they have from thence obtained complete protection against the natural disease, which then prevailed, and which still does prevail with great severity. And, indeed, from upwards of an hundred trials in Edinburgh and its environs, it has now appeared that inoculation with vaccinous matter affords equal protection against future small-pox, as inoculation with variolous matter. For these trials we are chiefly indebted to that very ingenious and able practitioner, Dr. Anderson of Leith, who was, we believe, the first to introduce vaccinous inoculation at this place, with matter which was sent him from London".

The Matjes River Rock Shelter

SOME time ago the Matjes River rock shelter was in part studied by the late Dr. Dreyer; now the excavation has been concluded by Dr. Louw as research leading to a Ph.D. degree (Researches of the National Museum, Bloemfontein. Memoir No. 1. The Museum, Bloemfontein, 1960). The result is a very competent work, and the finds have been examined in great detail. The rock shelter is in the extreme south of the African continent, roughly in the region of Plettenberg Bay. The finds include stone and bone implements, as well as skeletons. Five layers can be determined, labelled *A* to *E*. It would seem that everything found belongs to the Recent period and no trace of any true Middle Stone Age habitations occurs. The most interesting finds come from layer *C*: they recall those unearthed from the well-known Oakhurst shelter by the late Prof. Goodwin. At this time Wilton influences were penetrating into the region and mixing with the then existing folk, who would seem apparently to have been more of a Smithfield type. There are plenty of illustrations, but unfortunately they are not too good, especially those figuring the stone tools. Drawing stone implements is a specialized art, and the draughtsman must know a lot about stone knapping if a really useful illustration is to be produced. But it is excellent to gather that the study of this rock-shelter is now completed and Dreyer's beginnings brought to a conclusion. Most of the skeletons seem to be of a bushman or proto-bushman type.

Chromium in Water Supplies

THE need for research on the toxicity of chromium is emphasized in *Water Research News*, No. 9, July 1960—a periodical publication of the Water Research Association, Redhill, Surrey. In an article on "The Problem of Chromium in Water Supplies" it is pointed out that there are possibilities of chromium reaching water supplies from industrial effluents. It is generally considered that this element, particularly in its hexavalent form, is toxic, and that only very small amounts should be permitted in water supplies—less than 0·05 p.p.m. hexavalent chromium is laid down in the Drinking Water Standards of the United States Public Health Service. Methods available for removing chromium from water are costly, and the Research Association suggests that more information on the effects of chromium on living creatures is required. The available data on the concentrations toxic to various organisms are conflicting, and there appears to be no information on the mechanism of its toxic action; research on this subject would appear to be an important step in determining permissible concentrations in water supplies. Another item in this issue gives a warning that polythene joints may fail if they are brought into contact with certain active compounds, which include various oils and detergents, and are then subjected to stress. It is recommended that jointing materials should be kept away from compression fittings used for polythene, and that if possible stresses in polythene fittings should be relieved by immersion in hot water.

BIO-RAD Laboratories: Supply of Deuterium Oxide

BIO-RAD Laboratories, 32nd and Griffin Avenue, Richmond, California, have announced that deuterium oxide, a component of nuclear reactors and a key material in basic studies involving biological systems and moderation of nuclear-particle paths, will be leased for periods ranging from three months to two years at a fraction of the cost of purchasing or producing the material. The heavy water (99·8 per cent) will be on a lease/purchase basis, and can be used as the customer desires. The water is returned to BIO-RAD Laboratories when and if the customer wishes, and he will receive a credit based on the length of time water has been kept and the amount of dilution it has undergone. Plans are now being considered for similar forms of lease covering other stable isotopes including nitrogen-15 and carbon-13.

American Academy of Arts and Sciences: Grants-in-Aid

GRANTS-IN-AID, usually ranging between 500 dollars and 1,500 dollars, are available from funds administered by the American Academy of Arts and Sciences for research in any recognized scientific field, including mathematics, physical, biological and the social sciences. Applications must be received before February 1 for grants to be made in March, and before September 1 for grants to be made in October. In general, applications from individual scientists rather than from institutions are favoured, although this is not an inflexible policy. Projects dealing with explorations of the frontiers of scientific knowledge, whether interdisciplinary or within a single discipline, are preferred. Support is not usually given for work aimed primarily at fulfilling the requirements of an academic degree, or for the purchase of non-expendable laboratory equipment. Further information and requests for application forms should be addressed to: Committees on Research Funds, American Academy of Arts and Sciences, 280 Newton Street, Brookline Station, Boston 46, Massachusetts.

David Anderson-Berry Prize (1961)

A DAVID ANDERSON-BERRY Medal, together with a sum of money amounting to not less than £100, will be awarded in 1961 by the Council of the Royal Society of Edinburgh. The Prize will be awarded for recent work on the effects of X-rays and other forms of radiation on living tissues. Published work will be taken into consideration if submitted to the Society with the application. In addition to direct application for the Prize, proposals may be made on behalf of others. Applications and proposals should be sent to the General Secretary, Royal Society of Edinburgh, 22/24 George Street, Edinburgh 2, not later than March 31, 1961.

University News: Edinburgh

THE title of Research Fellow in the Department of Animal Genetics has been conferred on Dr. J. L. Sirlin; Mr. D. M. Weir has been appointed lecturer in the Department of Bacteriology, and Dr. R. G. S. Leask has been appointed lecturer in the Department of Clinical Chemistry.

Glasgow

DR. J. H. RENWICK has been appointed senior lecturer in human genetics. The following have been appointed lecturers: R. W. P. Drever, W. Jack and E. W. Laing (experimental and theoretical physics); I. M. Hoodless and W. Parker (chemistry); J. S. Keates (geography); and D. J. Simms (mathematics). G. L. le Bouvier has been appointed to a research fellowship in genetics, and I. Hughes and D. A. R. Wallace in mathematics. A. L. Porte has been appointed an Imperial Chemical Industries Fellow in chemistry.

The second Fleck Lecture is to be given on February 22, 1961, by Dr. John Paul (biochemistry).

For the present session, 396 new students (286 men and 110 women) have been admitted to the Science Departments, compared with 392 in 1959. The total of matriculated students in the University as a whole now stands at 6,600, compared with 6,566 in 1959.

London

DR. D. G. EVANS, director of the Department of Biological Standards in the National Institute for Medical Research, has been appointed to the University chair of bacteriology and immunology tenable at the London School of Hygiene and Tropical Medicine. Dr. J. D. N. Hill, senior lecturer in the Institute of Psychiatry and lecturer in psychological medicine at King's College Hospital Medical School, has been appointed to the University chair of psychiatry tenable at Middlesex Hospital Medical School.

Announcements

DR. S. M. PARTRIDGE has been appointed head of the Eggs and Poultry Department of the Low Temperature Research Station, Cambridge, following the death of Dr. J. Brooks (see *Nature*, 188, 451; 1960). Dr. Partridge will also continue to be in charge of the Protein and Ion-Exchange Department.

DR. H. E. DADSWELL has been appointed chief of the Division of Forest Products of the Commonwealth Scientific and Industrial Research Organization, Australia. He succeeds Mr. S. A. Clarke, who retired in August. Dr. Dadswell, who has been with the Division since its inception, was previously assistant chief and officer-in-charge of the Division's Wood and Fibre Structure Section.

DR. J. R. FURLONG, scientific adviser since 1953 to the Pyrethrum Board of Kenya, has retired and will take charge of the London office of the African Pyrethrum Technical Information Centre in succession to Dr. T. F. West, who has been appointed editor of *Chemistry and Industry*, the journal of the Society of Chemical Industry. Dr. Furlong was chairman of the Consultative Committee on Insecticides of Vegetable Origin at the Imperial Institute, and in 1946 he took a leading part in the survey of methods for the analysis of pyrethrum, which resulted in the world-wide collaborative scheme carried out in 1948–49.

D. VAN NOSTRAND CO., LTD, regret to state that there are mistakes in titles of authors mentioned in their advertisement of the "International Dictionary of Applied Mathematics", published in *Nature* of December 10 (p. i of Supplement); thus Prof. B. H. Flowers, author of the section on "Nuclear Science", is now professor of theoretical physics in the University of Manchester; the section on "Aerodynamics and Hydrodynamics" is by Prof. W. A. Mair and Dr. R. S. Scorer, and that on "Probability and Statistics" by Prof. M. G. Kendall.

THE Faraday Society is holding an informal discussion on "Mechanisms of the Gas-phase Reactions of the Halogens and their Compounds" in the Chemistry Department, University College, Cardiff, on March 28, 1961. Further information can be obtained from Dr. J. H. Thomas, Chemistry Department, University College, Cathays Park, Cardiff.

A SYMPOSIUM on "Molecular Structure and Spectroscopy" is to be held in the Department of Physics and Astronomy, Ohio State University, during June 12–16, 1961. Further information can be obtained from Prof. R. A. Oetjen, Department of Physics and Astronomy, Ohio State University, Columbus 10, Ohio.

THE first international congress on "Metallic Corrosion" is to be held at the Imperial College of Science and Technology, South Kensington, London, S.W.7, during April 10–15, 1961. Further information can be obtained from the Honorary Secretary, First International Congress on Metallic Corrosion, 14 Belgrave Square, London, S.W.1.

THE Mather Lecture for 1961 will be given in conjunction with the annual general meeting of the Textile Institute to be held on April 20. The Lecture will be given by Dr. A. Clow, senior producer of the Science Unit of the British Broadcasting Corporation, and his subject will be "Chemistry in Scotland and its Pioneer Contributions to Textile Technology". Further information can be obtained from the Secretary, Textile Institute, 10 Blackfriars Street, Manchester 3.

ASKED for a statement on the Low Temperature Research Station, Cambridge, Mr. C. Soames, the Minister of Agriculture, Fisheries and Food, as representing the Minister for Science, in a written answer on November 24 stated that the building occupied by the Station was held on a 10-year lease from the University. The lease expired in 1966 and the University had given notice that it could not renew the lease as the space is required for other purposes. The Agricultural Research Council was considering the future of the work being carried on at the Station.

THE IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

NEW PHYSICS DEPARTMENT

IN 1953 the Government decided that, within a period of less than ten years, the size of the Imperial College of Science and Technology should be doubled. Plans were eventually prepared by the College for a massive expansion programme, involving the redevelopment of a large site in South Kensington, which culminated in the Jubilee scheme, announced by the College in 1957.

A significant stage in this expansion was reached on October 20, with the formal opening of the new physics building by Sir John Cockcroft. The Departments of Aeronautics and Chemical Engineering and part of the Department of Mechanical Engineering have already moved into new buildings during the past few years, but the Department of Physics is the first to be completely rehoused as part of the Jubilee scheme.

The new building has twelve floors (levels 0–11) in which the complete activities of the Department, both teaching and research, are carried out. Levels 0 and 1 are below ground-level, and levels 2–7, T-shaped in plan, rise 80 ft. above ground. Four more floors of smaller area (levels 8–11) extend the spine of the T some 50 ft. higher. The given area of 183,000 sq. ft. doubles the space provided by the old physics building, and it is interesting to note that this is provided on a site only half the size.

Teaching facilities are provided for 350–400 undergraduate students, and are confined to levels 1–4, where large corridors and several staircases make for the easy movement of large numbers of students between lecture theatres and practical laboratories. There are three lecture theatres, the largest seating 250 and the others 150 each. The former is well equipped with ciné and still projectors, and with sound equipment. In addition to its use for undergraduate courses, it has been designed in conjunction with the entrance halls and the library reading room, with a view to the holding of scientific conferences.

The main practical instruction is given in three large teaching laboratories, each of which is provided with ancillary photographic dark rooms, preparation rooms and storage space. Library facilities have been considerably extended; the book capacity is 12,000 volumes, and tables and seating for 100 persons are available day and night.

The teaching of undergraduates, concentrated on the lower floors of the building, has been further co-ordinated by the appointment of Prof. W. D. Wright, who continues also to hold the chair of technical optics, to the new post of director of undergraduate studies. He, assisted by several other members of the academic staff, will arrange the undergraduate courses and generally supervise the facilities for students in the teaching areas of the building.

Below ground-level are some very large rooms, used as research laboratories for acoustics, high-temperature physics and spectroscopy. Here, too,

Fig. 1. New Physics Department of the Imperial College of Science and Technology, London

are the students' and main workshops, used largely for the construction of research apparatus.

The main research activity, however, takes place on the upper floors of the building—levels 5–11. Although laboratories individually designed for various types of work offer advantages in the first few years to the first occupants of a new building, these are usually far outweighed by the difficulties of adapting them later for use for new people and different research. Consequently, every effort has been made to avoid the specialized design of particular rooms. Throughout the research areas an attempt has been made to provide in rooms of all sizes a uniform high standard of background amenities.

Fig. 2. Main entrance

Large, double-glazed windows provide good natural lighting, give acoustic and thermal insulation and can be blacked out completely or fitted with venetian blinds to avoid excessive glare or heating from the Sun. The building is completely ventilated with filtered air to minimize harm caused by dust on delicate apparatus and to reduce the inconvenience and cost of cleaning. Ceilings are faced with demountable acoustic tiles for quietness. These are also the source of heating, conceal some piped services and support recessed lights, so that clear plane interior surfaces are provided without restriction on the placing of apparatus. To further this flexibility in the use of rooms, recessed wall racks and concealed attachment points in the ceiling are provided for the erection of apparatus.

Electrical supplies are contained in surface-mounted aluminium wall ducts, water and gas on narrow wooden service rails. These are provided in nearly all rooms, so that even the smaller ones, which may be used as academic staff rooms or administrative offices, can equally well be used for experimental work. Practically no laboratory furniture is built-in, but is composed of standardized units which can be grouped together and, if necessary, bolted to the wall racks, according to particular needs.

The large ducts above the corridor ceilings and vertical ducts in the thickness of the corridor walls interconnect all rooms in the building. Initially these carry only those minimal supplies of electricity, water and gas for the work at present envisaged, but as new projects arise and require new supplies, readily accessible space in the ducts is available for them.

During the past five years a considerable expansion of the Department has already taken place, under great difficulties, in the old building, in preparation for the move into the new one. Physics undergraduates have increased by some 50 per cent to 315, and postgraduates by a similar proportion to about 90. Approximately 100 undergraduates from other departments also attend courses. A particular feature of the Department's development is the number of independent research groups which have been formed, each headed by its own professor. In addition to the long-standing Technical Optics Section, three more have been established in recent years: Instrument Technology, Theoretical Physics and Cloud Physics. At the same time three other professors have been appointed to assist the head of the Department, Prof. P. M. S. Blackett, in the direction of its other research activities, which now include high-energy nuclear physics, cosmic rays, electron diffraction, high-temperature physics, spectroscopy, acoustics, rock magnetism, electron physics and metal physics.

That such an active and flourishing expansion in the Department's activities should be matched with the environment and facilities of what must be one of the finest physics buildings in the world, gives promise of a great future for physics at the Imperial College.

N. C. Barford

THE NATIONAL CHEMICAL LABORATORY

The National Chemical Laboratory held open days for visitors from industry, the universities and Government departments during October 19–21. The Laboratory's work was last on view in October 1958, shortly after the re-organization of the former Chemical Research Laboratory, so that this year's exhibition gave the first opportunity to inspect the changes and the progress made in implementing the revised research programme. Especially noteworthy, perhaps, were the increasing scope and facilities for hydrometallurgical research, and the decision to develop the earlier work on the purification and physical properties of organic compounds into a full programme of chemical thermodynamics. Although the open days showed also the progress in the Laboratory's continuing lines of research, emphasis was on newer developments.

The Extraction of Metals Group, concerned with hydrometallurgical processes and their underlying chemistry, showed its new laboratory wing, occupied

Natural and Synthetic Bradykinin

SINCE the isolation of natural bradykinin by Elliott, Lewis and Horton[1], a nonapeptide has been synthesized[2,3] and its structure agrees with that proposed[4] for the natural product. The structure is as follows: Arg.Pro.Pro.Gly.Phe.Ser.Pro.Phe.Arg.

The reported pharmacological properties of the synthetic bradykinin[5,6] appeared to be similar to those found with the natural product[7]. However, in order to establish the fact that the synthetic and the natural substances are the same, it was necessary to make a direct quantitative comparison of their pharmacological actions.

Table 1. RATIO OF ACTIVITY OF NATURAL TO SYNTHETIC BRADYKININ

Biological activity and preparation	Natural/synthetic
Smooth muscle contracting activity	
Guinea pig ileum	1·0, 0·8, 1·0, **1·1**
Rabbit duodenum	0·6, 0·8, **1·0**
Rat uterus	1·4, 0·6, 1·0, **1·0**
Smooth muscle relaxing activity	
Rat duodenum	0·8, 1·4, 1·1, **0·9**
Rat colon	1·4, 0·7, 0·8, **0·8**
Vasodilator activity	
Human forearm*	0·7, 1·0
Cat hind limb	1·0, 1·0, 0·9, **1·0**
Depressor activity	
Cat blood pressure	1·0, 0·8, **0·9**
Increased capillary permeability	
Guinea pig skin	1·0, 1·0, 0·9, 1·0, **1·0**, **0·9**
Rabbit skin	1·1, 1·0, 0·9, 1·0, **0·9**, **0·8**
Pain production	
Human blister base†	1·0, 1·0, 1·0, **1·0**

Each numeral represents the result of one experiment. The numerals in bold type are the result of comparison with synthetic bradykinin made by Parke, Davis (which was 80 per cent pure), the remainder with that made by Sandoz (which contained 35 μgm./ml.).
* From Fox, Goldsmith, Kidd and Lewis (ref. 8).
† This test was sufficiently accurate only to establish that the threshold dose of each sample was of the same order, that is, 10^{-7} gm./l.

The pure natural bradykinin of Elliott *et al.* was compared with two samples of synthetic bradykinin—one made by Sandoz, Ltd., and the other by Parke, Davis and Co.—on eleven different biological preparations. In Table 1, the ratio of natural bradykinin to synthetic bradykinin is given for the activity on these eleven preparations, and in Fig. 1 the method of obtaining these ratios is illustrated for the vasodilator activity by comparing the responses to a range of doses varying between 0·5 μgm. and 0·02 μgm.

Within the limits of experimental error the sensitivity of all eleven preparations to both natural and synthetic bradykinin was the same, proving that the natural and the synthetic bradykinin are identical.

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Direct Comparisons of the Synthetic Nonapeptide with Trypsin Bradykinin

IN April 1960, Elliott, Lewis and Horton[1] proposed an octapeptide structure for bradykinin. This was synthesized and found inactive by three independent groups of workers[2-4]. After discussion between Boissonnas and Elliott[5], Boissonnas, Guttmann, Jaquenoud, Konzett and Stürmer[3] described the nonapeptide L-arginyl-L-prolyl-L-prolyl-glycyl-L-phenylalanyl-L-seryl-L-prolyl-L-phenylalanyl-L-arginine, with properties resembling those of bradykinin. Elliott, Lewis and Horton[5] have concluded on chemical grounds that trypsin bradykinin has the structure of this nonapeptide, and Konzett and Boissonnas[6] have recently published biological evidence supporting the view that this peptide is identical with bradykinin.

The present work aimed at comparing directly on several biological preparations the synthetic nonapeptide with bradykinin to provide further evidence bearing on the question whether the two substances are identical. We used a specimen of the nonapeptide synthesized by Nicolaides and De Wald[7] and specimens of highly purified trypsin bradykinin (85 and 30 per cent pure) prepared by Elliott, Lewis and Horton[8]. In comparisons on the guinea pig ileum we also used a crude isolate of bradykinin (0·05 per cent pure) prepared by Lockhart and Jones[9] by

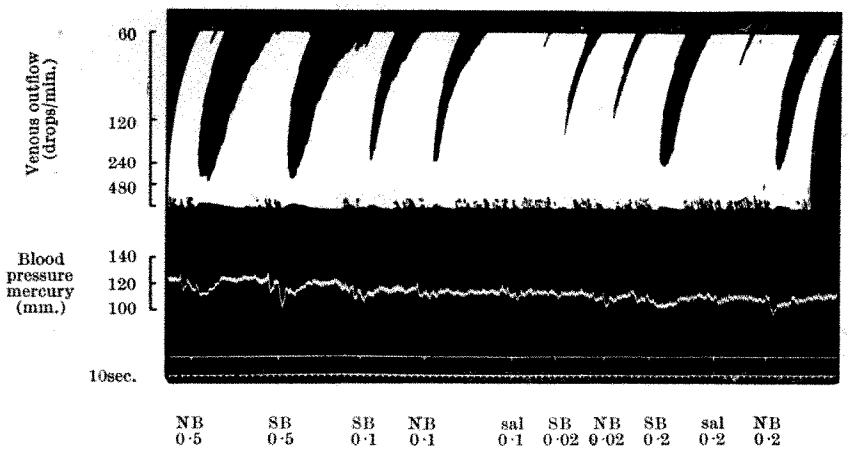

Fig. 1. Cat, 2·5 kgm. anæsthetized with chloralose 60 mgm./kgm. Upper tracing record of venous outflow from the hind limb. Lower tracing arterial blood pressure. Close arterial injections of natural bradykinin (NB) and synthetic bradykinin (SB), 0·5, 0·1, 0·02 and 0·2 μgm., and of saline (sal) 0·1 ml. and 0·2 ml. Comparison of the dose-response curves in this experiment gave a ratio of 1·0

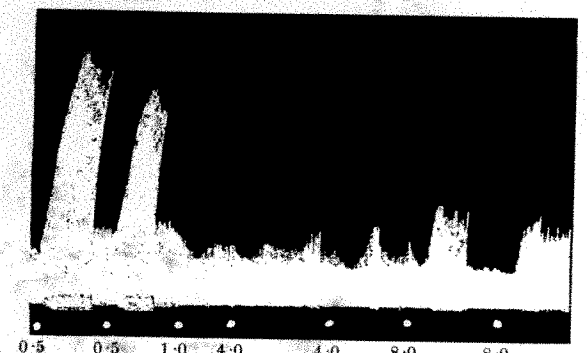

Fig. 1. Guinea pig lungs *in vivo*. Bronchoconstrictor responses to nonapeptide (N) and 85 per cent pure bradykinin (B) and their suppression by calcium acetylsalicylate (CaA). Substances administered intravenously. The guinea pig weighed 580 gm.

the action of crystalline trypsin on heated bovine serum globulin and previously standardized against pure bradykinin. The results (Table 1) show no significant difference between relative potencies of nonapeptide and trypsin bradykinin on the three preparations. This specimen of nonapeptide appeared to contain roughly 70–90 per cent active substance.

On the guinea pig lungs *in vivo*, both nonapeptide and bradykinin caused bronchoconstriction (Fig. 1), which was suppressed by calcium acetylsalicylate[10] (2 mgm./kgm., intravenous). Larger doses of nonapeptide or of bradykinin overcame this suppression.

The foregoing evidence supports the view that L-arginyl-L-prolyl-L-prolyl-glycyl-L-phenylalanyl-L-seryl-L-prolyl-L-phenylalanyl-L-arginine is identical with bradykinin prepared by the action of trypsin on bovine serum.

Table 1. COMPARATIVE POTENCIES OF NONAPEPTIDE AND TRYPSIN BRADYKININ ON THREE BIOLOGICAL PREPARATIONS

Biological preparation	Reference specimen of bradykinin (percentage purity)	Potency of nonapeptide in terms of pure bradykinin	95 per cent fiducial limits
Guinea pig ileum	85	0·75	0·58–0·94
		0·67	0·54–0·78
	30	0·68	0·64–0·72
	0·05	0·86	0·79–0·94
		0·85	0·79–0·92
		0·90	0·82–1·02
Rabbit blood pressure	85	0·71	0·49–0·94
	30	0·56	0·39–0·78
Rat uterus	85	0·86	0·76–0·99

We thank Dr. Warner for statistical analyses.

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MEMBRANOUS CYTOPLASMIC GRANULES IN INFANTILE AMAUROTIC IDIOCY

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INFANTILE amaurotic idiocy is characterized chemically by an accumulation of gangliosides in the nervous system. It has been suggested that the gangliosides occur naturally in polymeric form and in association with polypeptides or proteins[1]. The appearance of the involved neurons and results of histochemical investigations of this disease suggest that the ganglioside increase takes place within neurons and in some of their processes[2]. In two chemically confirmed cases of infantile amaurotic idiocy, examination of neural tissue by the electron microscope revealed structures unique to this lipidosis and of theoretical importance. We are presenting the morphology of case 1 as illustrative and the analytical findings of both cases as supporting the clinical and histological diagnosis of infantile amaurotic idiocy as well as for their bearing on the morphological findings.

In case 1 the neurons within the central nervous system were everywhere distended and rounded. The few remaining Nissl granules were grouped about the nucleus, which was usually peripherally located. In paraffin-embedded material the neuronal cytoplasm contained fine granules loosely packed in the largest cells and densely arranged in the smaller cells. This material in the most distended cells was very faintly positive in preparations stained with periodic acid–Schiff but more strongly positive in the dense neurons. The neuronal contents stained very pale yellow with sudan IV. They were strongly positive when stained by the iron hæmatoxylin method of Spielmeyer and Kultschitsky. Macrophages in the molecular layer, the white matter, and necrotic zones contained large amounts of fat stained brick red with sudan IV. Large reactive astrocytes were very prominent throughout. Severe neuronal loss was seen in the cerebellar granular layer. Myelin was best preserved in the corpus callosum, around the dentate nucleus and in the striate bundles of the basal ganglia. There was no particular sparing of subcortical association fibres.

The tissue fixed with formalin was treated with Palade's solution of veronal acetate buffered osmium tetroxide, embedded in methacrylate, sectioned on the Porter–Blum microtome and examined in a Siemens Elmiskop 1. The tissue was poorly preserved

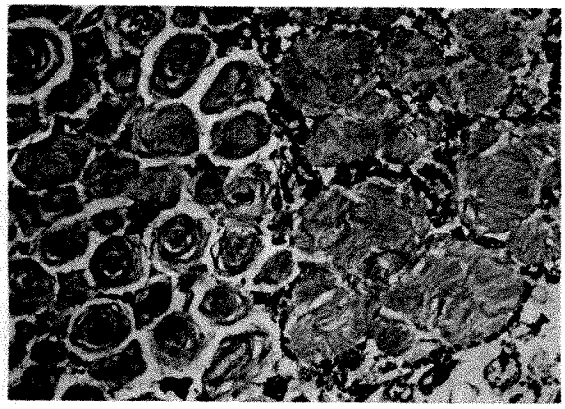

Fig. 1. Close-packed cytoplasmic granules of both types (× c. 9,700)

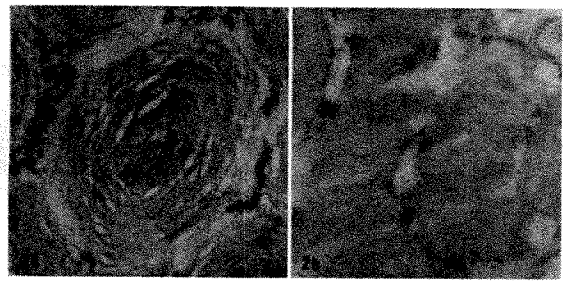

Fig. 2. *a*, concentric or spiral types of intraneuronal granule (× c. 12,000). *b*, cytoplasmic granule of type with flat lamellæ (× c. 27,000)

because it was a post-mortem specimen and had been previously fixed in acidic formalin. However, there were membranous granules measuring 0·5–2·0μ in diameter very strikingly prominent in the neuronal cytoplasm (Fig. 1). These were of two general types. The more common was a sphere made up of spiral or concentrically layered membranes which were arranged in pairs of osmophilic lines separated by a clear zone (Fig. 2). The lines and the clear zone each measured about 25 Å. The membrane pairs were irregularly arranged and separated from each other. The second type of granule was ovoid and bounded by a paired membrane which enclosed close-packed, flat, paired lamellæ. The membrane spacings were similar to those of the first type. Compound type granules with a concentric periphery and central flat lamellæ were seen occasionally.

Membranous granules with similar characteristics were found in the second chemically confirmed case where the tissue was frozen immediately subsequent to autopsy. In a third case of infantile amaurotic idiocy cortical tissue fractions obtained by gradient centrifugation also contained these granules in a good state of preservation.

For determination of lipid constituents brain tissue of both cases was treated by the procedure of Folch[3]. This resulted in a chloroform lipid-rich phase, an aqueous phase containing gangliosides and water-soluble small molecules, and an insoluble residue, largely denatured protein, which was removed by filtration. The aqueous phase was dialysed extensively. In addition to the usual determinations for lipids in the chloroform phase, the phospholipids were identified chromatographically[4]. The gangliosides were estimated in the aqueous phase by sialic acid-dependent methods[5,6]. Amino sugars in the aqueous and lipid phases were determined following hydrolysis[7] and separation on a 'Dowex' column[8]. The neutral sugars of the aqueous hydrolysate likewise were estimated following this separation and all the sugar fractions were chromatographed for identification. Cerebrosides were measured according to Svennerholm[9] and Radin[10].

Analysis of formalin-fixed and pathological material has several difficulties. With fraction and storage significant modifications of tissue constituents occur. In the presence of abnormal lipids or/and unusual proportions of normal lipid components, the distribution of these tissue components between the several phases may be affected.

In case 1 (Table 1) the amounts of insoluble residue and total lipid were not altered. The decrease in the phosphatide content may be the result of formalin fixation. The percentage of cholesterol esters in the white matter was slightly elevated and the cerebroside content depressed. Both changes can be related to demyelination. Hexosamine was increased in grey and white matter. The ganglioside content of grey matter was slightly increased and that of white matter markedly increased. During fixation in unbuffered solutions and storage the sialic acid moiety may be split from the remainder of the ganglioside molecule, and methods which depend on the measurement of sialic acid for estimation of gangliosides tend to lower results. This consideration is especially applicable to grey matter where changes consequent to fixation and storage occur most intensively. For this reason the hexosamine value in case 1 may be of greater significance (Edgar, G. W. F., personal communication). In this case as well as in case 2 the only sugars obtained following hydrolysis of the ganglioside fractions were galactosamine, galactose and glucose. The relative amounts of these sugars in the gangliosides obtained from pathological material may vary. This observation is now being investigated.

Case 2 (Table 1), which consisted of unfixed frozen tissue obtained several hours *post mortem*, demonstrated an elevation of lipid weight in grey matter. There was a great excess in the amount of lipid nitrogen found in the chloroform phase of the cortical tissue. The lipid nitrogen may be derived in part from gangliosides or their fragments which were distributed in the non-aqueous phase. This observation was supported by the increased amount of hexosamine found in the lipid phase. Also an adaptation of the Warren method[6] applied to the chloroform lipid-rich phase indicated that there were components containing sialic acid in this layer. The ganglioside content of the aqueous phases of grey and white matter extracts, measured both by the Svennerholm[5] and Warren[6] methods, was markedly elevated. As mentioned in case 1, the amino and neutral sugars obtained following the hydrolysis of the ganglioside fraction were quantified, and identified chromatographically as galactosamine, galactose and glucose. The amounts of gangliosides calculated on the basis that they contain about 9 per cent hexosamine and 24 per cent neutral sugars[7] were inconsistent with other data and again suggested either modifications of the gangliosides by the preparative procedures or the disease process, or the variability of methods of hydrolysis, isolation and measurement commonly employed. The remainder of the lipid analysis indicated that the total amounts of phos-

Table 1. ANALYSIS OF BRAIN TISSUE OF CASE 1 (AGE 4 YEARS) AND CASE 2 (AGE 22 MONTHS)

The tissue of case 1 was fixed in formalin, while that of case 2 was frozen immediately *post mortem*. Normal values are to be found in the following references: 11, 12, 13, 14. Grey matter was a sample of frontal cortex, and white the adjacent subcortical region. Phospholipids of grey matter examined by paper chromatography (ref. 4) revealed sphingomyelin in case 2 to be about 11 per cent of the total phospholipids and of a similar amount in case 1. *a*, Calculated value; *b*, method of Svennerholm (ref. 5); *c*, method of Warren (ref. 6). D.W., dry weight of tissue minus proteolipids

Components	Case 1 Grey (per 100 mgm. D.W.)	Case 1 White (per 100 mgm. D.W.)	Case 2 Grey (per 100 mgm. D.W.)	Case 2 White (per 100 mgm. D.W.)
Insoluble residue (mgm.)	63·7	60·4	50·5	58·8
Lipid weight (mgm.)	36·3	39·6	49·5	41·2
Lipid phosphorus (μM)	12·3	15·4	26·2	28·0
Plasmalogen (μM)	—	—	4·3	2·1
Lipid nitrogen (μM)	14·5	16·5	79·5	28·6
Lipid O-acylesters (μM)	23·8	30·8	26·0	46·0
Phosphatides (*a*) (mgm.)	10·2	12·4	21·0	21·8
Cholesterol (mgm.)	8·9	10·6	10·1	10·2
Per cent ester	12·4	17·4	8·0	8·5
Cerebroside (mgm.)	1·82	1·63	0·6	0·4
Hexosamine (mgm.)	0·570	0·370	0·912	0·558
CHCl phase	0·387	0·277	0·785	0·462
Aqueous phase	0·183	0·093	0·127	0·096
Gangliosides (mgm.)				
Aqueous phase (*b*)	2·11	1·34	4·04	2·54
Aqueous phase (*c*)	—	—	3·25	2·15

phatides were within normal limits. There was an increase in lysophosphatides in grey matter noted chromatographically. There was a decrease in plasmalogen and cerebroside content of white matter, suggestive of myelin atrophy.

The main chemical findings support the diagnosis of infantile amaurotic idiocy. The identification of the membranous cytoplasmic granules with the accumulated gangliosides must await isolation of these membranous units and their chemical analysis. Such granules seem to be unique to this condition for they have not been noted in our examination (Terry, R. D., unpublished observations) of other types of lipidoses, nor are they structurally similar to lipofuscin granules. Based on their appearance it is likely that if the membranous units do contain major amounts of gangliosides these glycolipids are associated with proteins to form complex membrane structures.

Whether or not the membranes are derivatives of a normal organelle surface or a coincidental physical formation assumed by excessive or abnormal gangliosides requires consideration. It should be emphasized that there does not seem to be any morphological differences between the granules present in the formalin-fixed tissue and in representative samples from frozen unfixed tissue. This is of particular interest since the sialic acid content of gangliosides decreases with fixation in unbuffered formalin.

There are a number of observations which might indicate considerable order in the molecular constitution of the cytoplasmic granules. There is only limited variation in their structure with two main types being found; their size ranges from 0·5 to 2·0 microns; whenever good resolution was afforded, regular spacing of the membranous elements of their bodies was seen. Some of these issues may be clarified by the study of fractions of homogenized cortical tissue submitted to gradient centrifugation, by which means we have obtained concentrates of these granules.

This work was supported by National Institutes of Health Grants *B*-2255 (*C*1) and *B*-1006 (*C*4). We are indebted to Dr. Bruno W. Volk, director of the Isaac Albert Research Institute of the Jewish Chronic Disease Hospital, for making the material from case 2 available for study.

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THE MOLECULAR DECOMPOSITION OF ALIPHATIC CARBONYL COMPOUNDS

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IT was first shown by Norrish *et al.*[1,2] that the photolysis of the aldehydes and ketones proceeds by two mechanisms, which for methyl propyl ketone are:

Type I $C_3H_7COCH_3 + h\nu = C_3H_7CO + CH_3$ (1)

Type II $C_3H_7COCH_3 + h\nu = C_2H_4 + CH_3COCH_3$ (2)

The first of these is a scission of the bond adjacent to the carbonyl group forming free radicals, and is common to all ketones. The type II reaction is a direct rearrangement into molecular products and is confined to the higher members of the series. This reaction is not limited to the ketones alone but occurs in many other compounds containing a carbonyl group and takes place not only on photolysis but also on thermal decomposition, radiolysis, and electron impact. It is the purpose of this article to assemble the evidence and discuss the nature of the intramolecular split, and to show how the results allow the designation of certain electronically excited states to these molecules.

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The Photochemical Breakdown

The type II reaction was first postulated by Norrish and Appleyard[1] in 1934 in a study of methyl butyl

ketone. Propylene was the major gaseous product and the reaction suggested was :

$$CH_3CH_2CH_2CH_2COCH_3 + h\nu = C_3H_6 + CH_3COCH_3 \quad (3)$$

Later, Bamford and Norrish[2] noted the equivalent reaction with *iso*valeraldehyde and di-*n*-propyl ketone which form propylene and ethylene as their respective olefinic products. As an extension to this work, the photolysis was carried out, both in the vapour phase and in hydrocarbon solution to ascertain the nature of the primary reactions. The method, which utilizes the principle of Frank and Rabinowitsch[3], relies on the free radicals formed in the primary act being confined together in a cage of solvent molecules. At low temperatures, recombination will predominate, lowering the quantum yield, while as the temperature is raised, the yields will be increased due to decomposition and hydrogenation of the free radicals. For a molecular split there is no difference on the change from vapour to solution. Although with di-*n*-propyl ketone, the type I reactions were shown to be exclusively free radical, the type II reaction, characterized by the quantum yield of ethylene, was entirely molecular, being invariant with environment and temperature.

More recently Blacet and Calvert[5] have photolysed butyraldehyde in the presence of iodine and, while the type I products were modified by the radical trap, the yield of ethylene remained unchanged. It was also shown[6] that although *n*-butyraldehyde decomposed intramolecularly, *iso*butyraldehyde formed no type II products. Thus three carbon atoms in a straight chain together with the carbonyl group are required for the reaction to occur.

$$CH_3CH_2CH_2CHO + h\nu = C_2H_4 + CH_3CHO \quad (4)$$

$$(CH_3)_2CHCHO + h\nu = \text{type I products only} \quad (5)$$

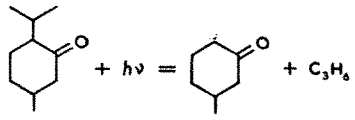
Although Wilson and Noyes[7] challenged the view that the type II reaction in the photolysis of methyl butyl ketone was intramolecular as the propylene to acetone ratio in their experiments was not unity, Nicholson[8], repeating the work, found that the ratio remained unity over a wide range of conditions including photolysis in the presence of nitric oxide.

McNesby and Gordon[9], after discovering a variation in product ratio with intensity in the photolysis of partially deuterated methyl propyl ketone, proposed a mechanism based on the interaction of two excited states. This is improbable in view of the solution work, where such a reaction is unlikely, and recently Ausloos and Murad[10], after repeating the experiments, reported no variation.

$$CD_3COCD_2CH_2CH_3 + h\nu = CD_3COCD_2H + C_2H_4 \quad (6)$$

These isotopic experiments indicate that the olefin is certainly formed from the β- and γ-carbon atoms in the molecule.

Experiments with cyclic ketones have thrown some further light on the mechanism: Bamford and Norrish[11] found that while *cyclo*hexanone is photolysed by a type I mechanism alone, 1-menthone almost entirely decomposes by a type II reaction.



(7)

The *iso*propyl group is free to rotate and bring the γ-carbon atom close to the carbonyl group as in a free chain. This condition is not fulfilled with *cyclo*hexanone.

The reaction is independent of temperature over a wide range : Masson showed that di-*n*-propyl ketone forms ethylene at a constant rate up to 160° C.[12], while Davies and Noyes showed that the quantum yield of acetone formation from methyl butyl ketone is constant up to 300° C.[13].

The type II split is not limited to the aldehydes and ketones but is also present in the acids and esters. Borrell and Norrish[14] have shown that ethylene is formed intramolecularly in the photolysis of both *n*-butyric acid and its methyl ester :

$$CH_3CH_2CH_2COOR + h\nu = C_2H_4 + CH_3COOR \quad (8)$$

There is no evidence of the reaction with *iso*butyric acid which is thus similar to the isomeric butyraldehydes[6]. Although the carbonyl group is modified by the introduction of a hydroxyl group, the absorption is due to the same transition[15] and the photochemistry should be similar. With a large group in the 'alcohol' position of the ester, another variation is possible : with ethyl acetate, for example, Ausloos[16] found that ethylene forms a large proportion of the gaseous products :

$$CH_3COOC_2H_5 + h\nu = CH_3COOH + C_2H_4 \quad (9)$$

Iodine has no effect on the yield in the vapour phase, and in solution ethylene is formed down to − 70° C.

In addition to the group in the α position having little effect, it is also evident that the reaction is independent of the β group. Ketene is formed in the photolysis of acetic anhydride[17] by the type II reaction :

$$CH_3COOCOCH_3 + h\nu = CH_2CO + CH_3COOH \quad (10)$$

Similarly, methyl ketene is produced from propionic anhydride. Even in very large molecules the reaction takes place, for Guillet and Norrish[18] concluded that the characteristic split occurs in the photolysis of polymethyl vinyl ketone :

$$\begin{array}{l} -CH_2-\underset{\substack{CO\\CH_3}}{CH}-CH_2-\underset{\substack{CO\\CH_3}}{CH}- + h\nu = \\ \qquad -CH_2-\underset{\substack{CO\\CH_3}}{CH_2} + CH_2:\underset{\substack{CO\\CH_3}}{C}- \end{array} \quad (11)$$

Wissburn has confirmed this result[19].

The photochemical studies show that the reaction is intramolecular, independent of temperature, environment and radical traps. It requires at least three carbon atoms in a chain together with the carbonyl group, although the α group may be methylene or oxygen, and the β group may be methylene or another carbonyl group. The cyclic studies indicate that the γ-carbon atom must be free to rotate into the proximity of the carbonyl group.

Thermal Decomposition

In 1876, Oppenheim and Precht pyrolysed ethyl acetate and found the products to be acetic acid and ethylene ; they postulated the reaction[20] :

$$C_2H_5OCOCH_3 = C_2H_4 + CH_3COOH \quad (12)$$

All the work carried out since then has confirmed the mechanism.

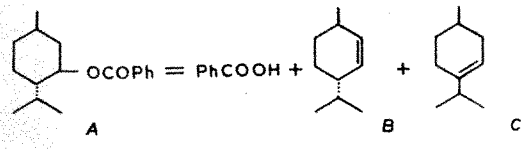
Hurd and Blunk[21], reinvestigating the reaction, pyrolysed several esters in a static system and found that 85 per cent of the decomposition of ethyl and propyl acetates proceeded by an intramolecular split, while *t*-butyl acetate decomposed exclusively by this mechanism. Anderson and Rowley[22] obtained similar results with various formates and showed the reaction to be first order. Blades[23] extended these studies using the toluene flow technique and could detect no evidence of a free-radical mechanism. The results are shown in Table 1.

Table 1

Compound	Activation energy (kcal./mole)	Activation entropy (e.u.)	Ref.
Ethyl formate	44·1	− 10·7	23
Propyl formate	50	− 18·7	22
*Iso*propyl formate	44	− 4·9	23
*Iso*propyl formate	46·3	− 5·35	22
Ethyl acetate	47·75	− 5·4	23
*Iso*propyl acetate	47	− 3·0	23
t-Butyl acetate	39·1	− 4·0	24

The entropies of activation are calculated on the assumption that the transmission coefficient is unity, which is true if no change of electronic state is involved. The activation energies are much smaller than that required for a split into free radicals, and in the absence of any evidence of a chain process, the reaction must be molecular.

Barton[25], in studies of *cis* elimination in terpenes, has pyrolysed (−) menthyl benzoate (*A*), which forms benzoic acid and a mixture of *p*-menth-2-ene (*B*) 36 per cent and *p*-menth-3-ene (*C*) 64 per cent.



(13)

The decomposition is homogeneous and first order; it is considered further in the discussion.

The pyrolysis of acetates has been used for the preparation of olefins and it has been suggested that the reaction forms the least substituted olefin[26,27]; for example, in the pyrolysis of methyl *iso*butyl carbinyl acetate, 4-methyl pent-1-ene is formed exclusively with no 2-olefin.

$$(CH_3)_2CHCH_2CH(OAc)CH_3 = (CH_3)_2CHCH_2CH : CH_2 + CH_3COOH \quad (14)$$

This conclusion, based on a number of studies, has recently been refuted by Royals[28] and Haag and Pines[29]. Reaction 14 in fact only forms 44 per cent of the 1-olefin, the rest being 4-methyl pent-2-ene. Similarly the pyrolysis of 2-butyl acetate yields 1-butene (60 per cent) and 2-butene (40 per cent):

$$CH_3CH_2CH(CH_3)OCOCH_3 \rightarrow CH_3CH_2CH : CH_2 + CH_3CH : CHCH_3 \quad (15)$$

*Iso*propyl chloroformate pyrolyses by two processes[30], one of which forms hydrochloric acid, carbon dioxide and propylene. A type II reaction is obviously occurring:

$$C_3H_7OCOCl = C_3H_6 + ClCOOH = C_3H_6 + HCl + CO_2 \quad (16)$$

but the conclusion should be treated with caution as ethyl chloroformate does not appear to decompose in this way[31].

These various reactions have been extensively studied because the products from pyrolysis are stable at the temperatures of decomposition. With ketones and other carbonyl compounds which may form an olefin and a lower member of the same series, this is not so, for the smaller fragment will decompose too.

As on photolysis (reaction 10), acetic anhydride pyrolyses to form ketene. The molecular nature of this decomposition has been shown by the absence of dibenzyl among the products when Swarc and Murawski studied it, using the toluene carrier gas method[32].

Some sealed-tube experiments with *n*-butyric acid and its methyl ester showed that here too the reaction is present. Ethylene formed a large proportion of the products with butyric acid at 550° C., while it was almost the only non-condensible product from methyl butyrate:

$$C_3H_7COOCH_3 = C_2H_4 + CH_3COOCH_3 \quad (17)$$

The activation energy for this reaction is approximately 34 kilocalories/mole.

The thermal decomposition of these compounds resembles the photochemical reactions. The type II split, which is intramolecular, is the low-temperature form of decomposition, while if the temperature is raised considerably, free-radical products are formed which are consistent with 'type I' reactions.

Electron Impact Studies

The widespread use of the mass spectrometer for analysis has necessitated the tabulation of large amounts of data on a variety of compounds. Sharkey and his collaborators[33] have studied rearrangement peaks in ketones: one significant group is formed by the scission of the β bond to the carbonyl group to form a charged lower ketone. The disadvantage of mass spectral studies is that only one fragment is generally detectable, the other being uncharged, but even so these results are important. Methyl *n*-propyl ketone and higher methyl ketones show a rearrangement peak at mass 58, probably formed by the reaction:

$$CH_3COCH_2(C_nH_{2n+1}) + e = (CH_3COCH_3)^+ + C_nH_{2n} + 2e \quad (18)$$

An analogy to the photochemical results is provided by the absence of a peak at mass 58 with methyl *iso*propyl ketone. Similarly 3-hexanone and larger ethyl ketones form a peak at mass 72 corresponding to the methyl ethyl ketone ion, and *iso*propyl ketones show a re-arrangement peak at mass 86 which corresponds to the methyl *iso*propyl ketone ion. Apparently the molecule splits into an olefin and a charged ketone.

Happ and Stewart, in an earlier investigation of the carboxylic acids[34], noticed a similar effect with *n*-butyric and the isomeric valeric acids which give peaks at mass 60, not formed by the lower acids or *iso*butyric acid. When carbon-13 was substituted into the carboxyl group the peak moved to mass 61, showing that the carboxyl group is present in the ion:

$$C_3H_7{}^{13}COOH + e = C_2H_4 + (CH_3{}^{13}COOH)^+ + 2e \quad (19)$$

Although there have been no other suitable systematic studies, some data are available from the American Petroleum Institute lists[35]. *n*-Butyraldehyde shows

a large peak at mass 44 as does 3-methyl butyraldehyde, which is not present with *iso*butyraldehyde.

$$CH_3CHRCH_2CHO + e = RCH:CH_2 + (CH_3CHO)^+ + 2e \quad (21)$$

Methyl butyrate forms a peak at mass 74 corresponding to the methyl acetate ion, which may be formed in a similar manner.

Esters with a large group in the 'alcohol' position (for example, ethyl acetate) form no significant peaks corresponding to the acid fragment, and any olefin is usually in a region already occupied by type I residues. Some information is provided, however, by chloro- and bromo-ethyl acetates. Chloroethyl acetate forms a peak at mass 62, corresponding to the chloroethylene ion, while bromoethyl acetate shows peaks at masses 106 and 108, consistent with the formation of bromoethylene from the two bromine isotopes:

$$^{79}BrCH_2CH_2OCOCH_3 + e = (^{79}BrCH:CH_2)^+ + CH_3COOH + 2e \quad (22)$$

These esters also do not show peaks corresponding to the acid ion, and it seems that fragmentation may take place in two ways depending on the presence of oxygen in the chain.

$$RCH_2CHR'CH_2COR'' + e = RCH:CHR' + (CH_3COR'')^+ + 2e \quad (23)$$

$$RCH_2CHR'OCOR'' + e = (RCH:CHR')^+ + R''COOH + 2e \quad (24)$$

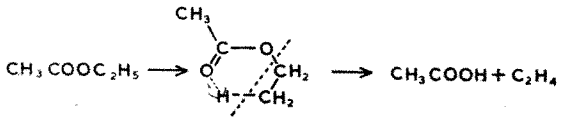
Although it is not possible to detect both of the fragments from electron impact, there seems ample evidence for a type II reaction here.

Radiolysis

In this comparatively new field there has been little interest in the molecules under consideration here. Some aldehydes have been examined but none which might give a type II reaction. However, Ausloos[36] has performed some experiments on ketones and has recorded that ethylene and propylene form a significant proportion of the products when methyl propyl ketone and methyl butyl ketone are radiolysed. Although nothing else has been examined, it is interesting to note that here, too, there is evidence of a type II split.

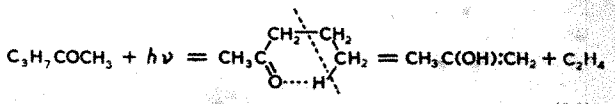
Mechanism of Rearrangement

It is clear that there is a form of decomposition occurring with these large carbonyl compounds, which is virtually independent of environment and conditions, and forms molecular products in a specific manner. For the reaction to be independent of the α and β groups, to break the β bond and to transfer a hydrogen atom from the γ- to the α-carbon atom requires a specific configuration. The most probable mechanism involves the formation of a six-membered ring as an intermediate and the separation of molecular products. This possibility was first put forward by Hurd and Blunk[21] in 1938 for the pyrolysis of esters:



(25)

For this mechanism to occur with a ketone, say, on photolysis, an enol would be formed which must isomerize.

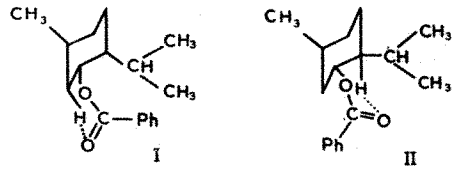


(26)

$$CH_3C(OH):CH_2 = CH_3COCH_3 \quad (27)$$

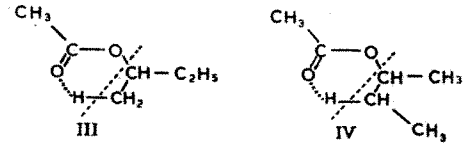
Srinivasan[37] has shown by his elegant isotopic work that this enol is indeed formed and isomerizes by exchange at the wall of the reaction vessel.

The cyclic intermediate explains the minimum size of the molecules required for this reaction, and provides an explanation for *n*-propyl substituents on the carbonyl group giving type II products while *iso*propyl derivatives do not. The advantage of the cyclic configuration over a flow of protons along the chain, which has also been suggested, is that it is independent of the α and β groups, which may be oxygen or carbonyl. The presence of an additional carbonyl group, as in acetic anhydride, would cause greater strain in the ring, but considering the activation energy required for this approximately thermoneutral reaction, and the transient nature of the intermediate, it should present no difficulty. Barton's work on the pyrolysis of (−) menthyl benzoate[25] is consistent with the ring: there are two positions in which *cis* elimination may occur from the terpene ring:



II is the only conformation available for the formation of menth-3-ene but there is an alternative *trans* linkage to I, which may be preferably formed. Consequently, when elimination occurs, there should be a greater proportion of *p*-menth-3-ene.

The work of Haag and Pines[29] on the pyrolysis of 2-butyl acetate (reaction 15) provides additional evidence, for again there are two possible intermediates:



In the case of III, which would form 1-butene, there are three hydrogen atoms available for transfer, while with IV there are only two to form 2-butene. Therefore, the yields of 1- and 2-butene should be in the ratio 3 : 2, as in fact is found.

Electronic States of the Larger Carbonyl Compounds

From the previous considerations, it is possible to assign some electronically excited states to these compounds, utilizing the Wigner spin conservation

rule and the results obtained in the photosensitized reactions of several of these compounds. In the mercury photosensitized decomposition of n-butyric acid, methyl butyrate, and n-butyraldehyde, type I products are formed, but there is no evidence of any intramolecular type II split[14].

There are two established electronic states in the carbonyl compounds, the ground-state and the first excited state. The ground-state is necessarily singlet, as is the upper state formed on absorption of radiation, which raises an electron from a non-bonding orbital localized near the oxygen atom to a less localized antibonding orbital. The transition, designated $n \rightarrow \pi^*$, is forbidden by local symmetry[38]. It is Mulliken's view that the upper state is not repulsive[39], and that photochemical dissociation takes place from other states reached by internal transition. The ground and excited states will be designated here as ^1M and $^1M^*$ respectively.

The type II reaction forms molecular products on photolysis through a mechanism which is independent of temperature or environment, and if spin is conserved the excited repulsive state must be singlet to give rise to singlet products. Although it is possible to postulate a triplet state forming a singlet olefin and a triplet ketone (or vice versa) it is known that triplet ethylene decomposes to form acetylene[40], while it is demonstrated below that triplet carbonyl compounds decompose to type I free-radical products. As it seems unlikely that the singlet 'type II' state is the vibrationally excited ground-state, for this would not be independent of phase and temperature, or the upper $^1M^*$ state, for no type I products would be formed, a separate singlet state ($^1M^{**}$) may be postulated.

The type I free-radical products may be formed from a singlet or a triplet state and the photosensitized results provide a means of distinguishing between the possibilities, for if spin is conserved then the reaction with excited mercury forms a triplet state ($^3M^*$):

$$Hg(^3P_1) + C_3H_7COOH(^1M) = Hg(^1S_0) + C_3H_7COOH(^3M^*) \quad (28)$$

The triplet state gives doublet free-radical products and it seems likely that it does so directly, rather than by internal conversion when type II products would also be formed.

These various conclusions may be conveniently summarized by means of a diagram (Fig. 1), where ethyl acetate is taken as an example. On photochemical excitation, $^1M^*$ state is formed, which gives rise to $^3M^*$ and $^1M^{**}$ states by internal conversion, forming type I and II products. On photosensitization the $^3M^*$ state alone is produced and forms free-radical products directly. Thermal decomposition is brought about by a molecule traversing point A from ^1M to $^1M^{**}$ to form type II products, while at higher temperatures the likelihood of crossing is increased and free-radical products are formed. Both electron impact and radiolysis obviously form the upper $^1M^*$ state, which in turn gives rise to type I and II reactions.

By consideration of spin alone, the transition time from the $^1M^*$ to the $^1M^{**}$ state should be faster than that for the $^1M^*$ to the $^3M^*$, and one would expect only type II products to be formed on photolysis. However, the $^1M^{**}$ requires a specific cyclic configuration and the time to form this may well be comparable

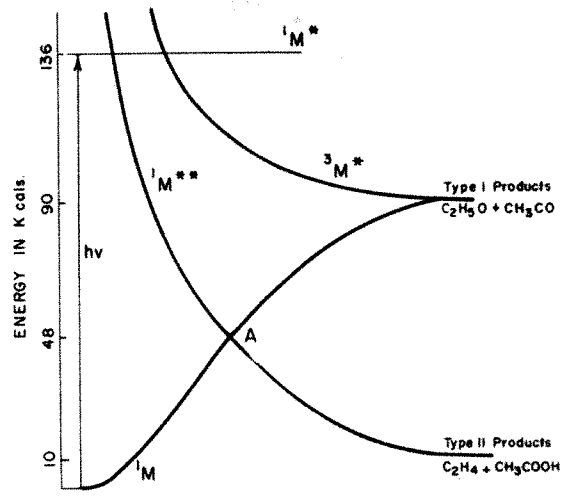


Fig. 1. Potential energy diagram for ethyl acetate

to that for spin reversal. In the photolysis of n-butyric acid[14] where the quantum yield is less than unity, it was found that added oxygen increased the yield of type I products while the type II yield decreased slightly. The collision of a free radical, such as oxygen, with the upper excited state might catalyse spin reversal to form a $^3M^*$ state decreasing the number of molecules lost to the ground-state by internal transition and also decreasing the number available for conversion to the $^1M^{**}$ (type II) state.

Although it has been possible to deduce something of the nature of the excited states in these carbonyl compounds, more work is required before their identities are finally settled. The effects of oxygen and other free radicals should provide some useful results, and a correlation of this work and that on the fluorescence of lower ketones may prove fruitful. The thermal decomposition, which is first order, may provide a needed addition to the available examples of unimolecular reactions and it would be useful to study the kinetics at low initial pressures. The change in electronic state in the thermal reaction may be of some theoretical interest.

I wish to express my thanks to Prof. R. G. W. Norrish for many encouraging discussions and to the Department of Scientific and Industrial Research for the award of a maintenance grant.

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SYNTHESIS OF MACROMOLECULES UNDER POSSIBLE PRIMEVAL EARTH CONDITIONS

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OPARIN[1] and Urey[2] have suggested that the primeval atmosphere consisted principally of methane with small amounts of ammonia and water vapour. Miller[3] has shown that when a high-frequency Tesla coil discharge is passed through such an atmosphere, a multitude of organic molecules are produced, including amino-acids. This demonstration of the production of amino-acids has been received with great interest by all those interested in the origin of life, because of their simple chemical relationship to protein material, which seems to hold a key position in present-day life processes. The next step in the sequence of chemical evolution is the production of macromolecules from these simple chemical substances. It is not possible, under ordinary conditions, for the amino-acids to join up spontaneously to form proteins, since the thermodynamic equilibrium is very much in the direction of amino-acids. Fox[4], however, has shown that polypeptides can be made under high temperature (160° C.) and anhydrous conditions. The work described in this communication shows how it would have been possible for macromolecules to have been produced on the primeval Earth.

The apparatus used (Fig. 1) is a 3-l. 'Pyrex' flask with tungsten electrodes sealed through the walls. A mixture similar to the composition which may have existed in the primeval ocean was made up thus: 10 gm. of baker's yeast was ashed at 600° C. and the ash dissolved in 100 c.c. water. Enough concentrated ammonia solution was added to make the solution 1 per cent in ammonia. A stream of hydrogen sulphide was then bubbled through the solution for 10 min. The resulting solution was then placed in the apparatus, evacuated and filled with methane to a pressure of 1 atmosphere. The output of a 40-kV. 50 c./s. transformer was then connected to the two electrodes. The voltage was controlled by a 'Variac' on the transformer primary winding and adjusted to be just below the arcingp oint (approx. 20 kV.). It was difficult to measure the power dissipated in the reaction vessel, but, from the voltage drop across a resistor in the secondary circuit, it was estimated to be of the order of 5 W. At first, after running for 1 hr., a surface-active material was produced, demonstrable by shaking the vessel to produce a foam. After 4 hr., an insoluble transparent film had formed on the liquid – gas interfaces. This material (see Fig. 2) can be produced in more than 10 per cent yield (based on methane). It is insoluble in organic solvents (for example, methyl alcohol, ethyl acetate, acetone, ethyl ether, hexane, benzene and carbon tetrachloride). It is infusible up to 400° C., and at this temperature slowly decomposes. On analysis, this material is found to have the composition C = 75·55, H = 7·33, N = 1·62, S = 0, ash = 3·79 per cent. The infra-red analysis is that of a highly cross-linked polyethylene-type structure with the presence of C=O bands. It has been found that this material will take dyes (for

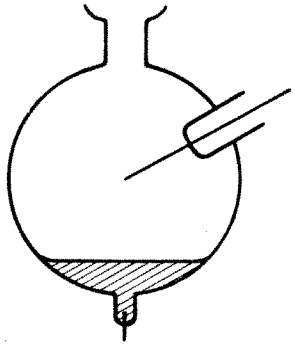

Fig. 1

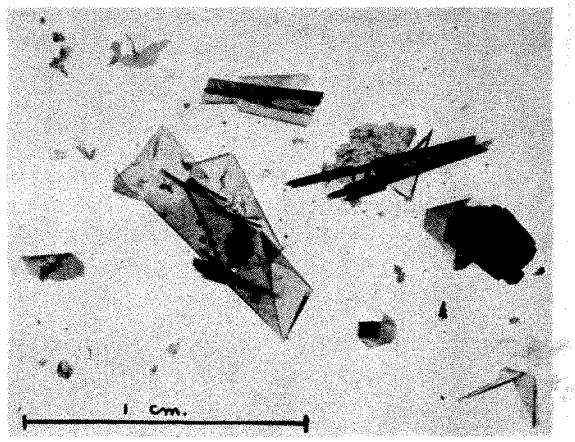

Fig. 2

example, methylene blue and fuchsin), is hydrophilic and more dense than water. (If the ammonia and hydrogen sulphide are omitted from the experiment, a product is obtained which is hydrophobic and cannot be dyed.)

The liquid in the flask was turbid, and when it was examined under the electron microscope, sheet-like molecules were observed (Figs. 3 and 4).

Under the conditions of the experiment, large sheet-like structures are produced. These range in size from large fragments (Fig. 2) through smaller material (Fig. 3) to very small structures (Fig. 4) which are, in fact, macromolecules. The analysis and determination of properties were carried out only on the larger material (Fig. 2), although it might be assumed that this is a reasonable approximation to composition of the material seen under the electron microscope. Thus, high molecular weight polymer is produced from methane, water and ammonia under the influence of an electrical discharge. The combustion results, infra-red spectra and general properties suggest that this polymer is essentially hydrocarbon in nature, and that its surface is covered with polar groups which enable it to be dyed and impart its hydrophilic character.

It seems at first surprising that it is possible to proceed from a simple one-carbon molecule (methane) to what is a product of very high molecular weight. One might expect larger and larger molecules to be built up until the products were no longer volatile, at which stage they would condense out as a liquid. Gas chromatographic analysis of the residual gas in the flask shows that a complicated mixture of $C_1 \rightarrow C_5$ compounds is indeed produced. However, it is difficult to understand how molecules larger than C_{20} could be synthesized without their precursors condensing out. Thus, a liquid product might be expected rather than a solid of very high molecular weight. I suggest that the electrical discharge produces surface-active molecules which form films on the gas – liquid surfaces. These molecules become cross-linked together either directly by the corona discharge itself or by atomic hydrogen produced in the discharge. This mechanism might be expected to produce large sheet-like molecules with one side polar and the other side non-polar. Experiments are in progress to produce similar sheet-like molecules from surface-active materials directly.

If one assumes that the primeval atmosphere of the Earth consisted largely of methane with smaller amounts of ammonia[2], it is reasonable to suggest on the basis of the above experiment that large quantities of hydrocarbons of high molecular weight with surface polar groups could have been synthesized during electrical disturbances on the surface of the primeval ocean and even perhaps on cloud and rain droplets caught in the corona discharge of thunderstorms. This no longer takes place on the Earth because it now has an oxidizing atmosphere, but perhaps it is taking place on the larger planets which still have reducing atmospheres. When one considers the very large number of polar groups of many different kinds all randomly orientated to each other, would it be possible that some of these groupings might be of the right kind and of the right geometrical orientation to endow the macromolecule with 'enzymatic' activity ? (The possibility of completely covering a cloud droplet with this material offers the possibility of having regions within the primeval ocean isolated by a membrane.)

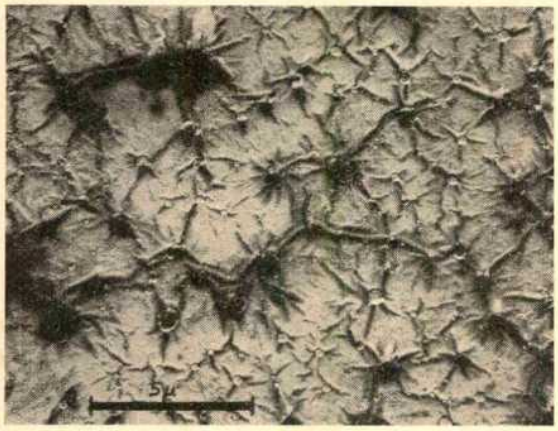

Fig. 3

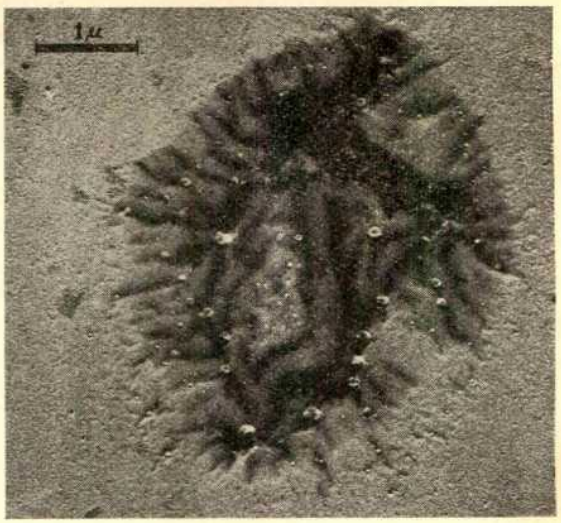

Fig. 4

Thus it is suggested that the early steps in the chemical evolution of life may have been based on catalysts or 'protoenzymes' in which the catalytic groupings were supported on material of hydrocarbon type. This 'hydrocarbon life' would then have evolved until it was sufficiently developed to be able to synthesize its own macromolecules, namely, protein, thus producing the beginning of our present-day 'protein life', where the catalytic groups of the enzymes are supported on protein material. Perhaps the petroleum and shale deposits in the Earth are the debris from the degradation of this material. (If, for example, these proto-enzymes attacked only polar groups and the process of degradation could not progress along the chain past a branch, the residue would be predominantly straight-chain hydrocarbons as are found in petroleum.)

The ease with which this material is produced would lead one to suppose that similar organic material of high molecular weight may be of frequent occurrence in unoxidized cosmic matter and, indeed, organic material of high molecular weight has been found in meteorites[5]. Do the clouds of Venus contain this material ? In this connexion it is interesting to suggest that the fluorescent material[6] found on the surface of the Moon is organic in nature. Also the

gas observed by Kosyrev erupting in Alphonsus[7] (a crater on the Moon) might be explained by the thermal cracking of lunar organic material by radioactive heating.

I wish to thank Dr. A. D. Campbell, of the University of Otago, for the combustion data, the Dominion Laboratory for the gas chromatographic and the infra-red analysis, the staff of the Electron Microscope Section, Dominion Physical Laboratory, for their kind co-operation, and Mr. F. B. Knox for interesting discussions. Much of this work was carried out in the Institute of Nuclear Science, Lower Hutt, New Zealand.

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PERCEPTION OF DISTANCE IN ANIMAL ECHO-LOCATION

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SINCE Griffin and Galambos[1] in 1940 discovered that bats orientate themselves by listening to the echoes from their own sounds, much information has accumulated about echo-location in bats and other animals[2]. Thanks to a number of studies in this field, we now have a fairly extensive knowledge of the acoustical properties of such sounds. There are, however, many questions raised by these studies which have so far received no satisfactory answer.

How, for example, can a bat separate the faint echoes of its own sounds—short, ultrasonic pulses of high intensity—from those emitted at the same time by hundreds or more of other bats? How can they detect and capture an insect when echoes from the ground and countless objects must be returned also? What is the reason for the failure of various attempts to interfere with the echo-locating process, such as trying to jam bats by means of intense noise covering the frequency-range of their pulses[3]?

All efforts to give an answer to these questions are likely to be fruitless while we are uncertain which properties of the echoes the animals utilize in judging distance. Is it the time interval between outgoing pulses and returning echoes or the intensity of the echo or some other property that varies with distance? Whatever the essential property, it is difficult to understand how bats and other echo-locating animals can make any use of the information in the echoes, bearing in mind that the time interval between pulse and echo is of the order of a few milliseconds.

There are, however, some findings from studies in human auditory perception that may help us to get an idea of the mechanism of echo-location. A few years ago Thurlow and Small[4] discovered that two pulse trains of identical repetition rate but slightly separated in time gave rise to a tone the pitch of which corresponded to the magnitude of the time separation. For example, if one train of pulses has a repetition rate of 100 per sec. and a second identical pulse train follows in 1/400th of a sec., the time separation pitch is that of a 400-c.p.s. tone. Decreasing the time separation gradually produces a tone that sweeps upwards (the authors call this phenomenon sweep pitch). Increasing the time separation makes the tone sweep downwards until the difference is half the pulse interval, when the time-difference pitch is the octave of the pulse-repetition frequency, 200 c.p.s. in the above example. A further increase of the time separation makes the tone increase in pitch again. The time-difference pitch thus always corresponds to the shorter time separation. One of the pulse trains may be considerably less intense than the other, particularly if the time separation is small[5]. At a sensation-level of 30 decibels the less-intense pulse train had to be reduced about 17 decibels before the effect disappeared.

There seems to be no reason why bats and porpoises should be different from us in this respect. They will consequently hear a tone the pitch of which corresponds to the time separation between the outgoing pulses and returning echoes, provided the echoes are not too weak. It is tempting to assume that they are also guided in their orientation by these very tones.

If this interpretation is correct, tones in a certain frequency-range have to them acquired a meaning of distance, so that, for example, a rising pitch signifies shrinking distance. If we take into consideration the fact that the echo will return slightly earlier if the animal is moving (although this will affect the result very slightly), a formula expressing the relations involved will be as follows:

$$f = \frac{c + v}{2s}$$

where f is the frequency in c.p.s. that corresponds to the perceived pitch, c and v are the velocity in cm./sec. in the medium (air or water) of sound and animal, respectively, and s is the distance in cm. from the animal's mouth to the object at the moment when the pulse is emitted.

A particularly attractive feature of this mechanism is that the rate of change of pitch is greater close to the object, where the need of accuracy is most acute. As a bat moves from 175 to within 155 cm. of an object, the pitch change will be from about 100–113 c.p.s., whereas an equal change of distance from 40–20 cm. will cause a rise of pitch from about 440–880 c.p.s.

As the lowest audible time-difference tone is unlikely to be much lower than 100 c.p.s., 2–3 metres is probably the greatest distance at which a bat can detect an object by this technique, the corresponding distance for animals living in water being 9–15 metres. This could explain why bats never give any signs in the form of increased pulse rate to show that they

have detected even large objects, such as walls, until they have come within this range. As also thin wires and other objects can be detected at a comparable distance it is possible that some factor other than the intensity of the echoes puts a limit to the distance of detection. Some puzzling results from experiments on a bat's ability to detect wires of different sizes strung across a room may be interpreted in this light. Increasing the size of the wires made the bats show signs of reacting at an increasingly greater distance. As the wire is increased from 1 to 3 mm., however, the distance of detection changes from just less than 2 to not more than about 2·25 metres, which is much less than would be expected[6]. One of the possible explanations for these observations given by the authors is that the bats detect the objects at a greater distance than their data indicate, but do not trouble themselves to increase the pulse rate until they come within a metre or two. For reasons already stated, however, it is possible that they cannot detect objects beyond a certain distance regardless of the strength of the echoes.

We are probably justified in assuming that the time-difference tone can be heard only as a result of a recurrent or a gradually changing pattern, although this aspect of the problem has not been investigated. Every time the animal approaching an object emits a pulse, the time-interval between pulse and echo will be slightly shorter, but the change will be a gradual one. This explains how an echo can be sorted out from among a large number of pulses, such as those from other animals. There is an infinitesimal chance that any two animals' pulses will have exactly the same repetition rate with a constant or gradually changing displacement in time, which are the necessary conditions for a time-difference tone. The pulse rate, moreover, is never absolutely constant, as Griffin's records for the bat *Eptesicus* show, but is slightly irregular even when the mean rate is nearly constant. This is of no consequence for the time-difference tone but makes the animal even less susceptible to interference from other pulses.

There is, however, every reason to believe that echoes from objects at different distances can each give rise to a separate tone, if the relation between pulse and echo is constant. As the pulse repetition rate is never exactly constant, a series of echoes the time lag of which exceeds one pulse-interval can produce no regular pattern and consequently no tone. The same reasoning can be applied to a series of echoes returning in the second half of the pulse interval. The echo will be too far removed from the original pulse, if the findings of Thurlow and Small are applicable under these conditions, and the relation to the next pulse will not be sufficiently constant.

Objects beyond a certain distance depending on the pulse rate can therefore not be detected, at least not by this method. This is probably the reason for the increase in rate as an animal starts to approach an object. As the rate goes up, the zone from which objects return echoes capable of producing a time-difference tone shrinks. At the maximum rate recorded, 200 per sec., a bat would thus not be able to detect anything beyond a distance of about 43 cm. A similar result may be obtained by emitting pulses of gradually reduced intensity or by a combination of both methods.

In this way the porpoise and many types of bats have at their disposal a means of increasing the acuity of their perception analogues to visual accommodation. Another way of excluding irrelevant echoes is to concentrate the emitted sound into a narrow beam. This method is used by some members of the family Rhinolophidae, which thereby compensate for a relatively low maximum repetition rate.

In the calculations above it has been tacitly assumed that the pulse is of negligible duration, and this is not strictly speaking correct. The calculations will scarcely be affected all the same, as Thurlow and Small have shown that the time-difference tone could be heard even when there was an overlap between the pulse trains. It is probably the time difference between the peaks of the sound pressure that determines the pitch. This conclusion is supported by observations recently made by me on pure tones bearing a simple mathematical relationship to one another, such as 1 : 2, 2 : 3, 1 : 3. Varying the phase of one of the tones produces, under certain conditions, a weak time-difference tone the pitch of which corresponds to the time separation between the closest peaks of the sine waves.

Perhaps the most baffling of all problems connected with echo-location has been how bats can discern the faint echoes from thin wires well enough to avoid them even in the presence of thermal noise of much higher intensity. As Thurlow and Small state that they were not able to obtain these tones when thermal noise of various intensities was presented simultaneously with the pulses, this might seem to be a serious objection to my hypothesis.

It is important to note, however, that these experiments were conducted at the relatively low sensation level of 30 decibels, whereas the sound pressure level of the pulses of bats often exceed 100 decibels. I have therefore investigated the effect of thermal noise on pulses of high intensity. The outputs of two pulse generators were led through a narrow band-pass filter and mixed with thermal noise. When the pulses had an intensity of 90 decibels r.m.s. the time-difference tone was clearly audible even when the intensity of one of the pulse generators was considerably reduced and that of the noise was at intermediate level.

Further investigation of the phenomena which have a bearing on the problem of echo-location in relation to rate, composition, and intensity of pulses and echoes is clearly needed. The pulse rate of bats is often only 10 per sec. or even lower, whereas the lowest rate tried on human beings is 25 per sec., when the tone sounded similar to pure tones of short duration[4].

The hypothesis outlined here seems compatible with the acoustical properties of sound produced by many different types of bats, as they are set forth in great detail in a recent paper by Novick[7]. It enables us to understand how these animals can achieve a high degree of precision in their orientation without any corresponding degree of precision in the sound production. The frequency composition, duration, intensity and regularity of the pulses from animals of different types and from one single animal can and do vary within wide limits without serious consequences. Far from being a shortcoming, the irregularity is often, as we have seen, an advantage.

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A SIALOMUCOPEPTIDE LIBERATED BY TRYPSIN FROM THE HUMAN ERYTHROCYTE

By G. M. W. COOK, Dr. D. H. HEARD and Dr. G. V. F. SEAMAN*

Department of Radiotherapeutics, University of Cambridge

DURING the course of a microanalytical examination of the action of trypsin on the surface of the saline-washed human erythrocyte it was found that a sialomucopeptide was liberated by this enzyme.

Ponder[1] has observed a decrease in the electrophoretic mobility of the erythrocyte on treatment with trypsin. The reduction in mobility corresponds to about a 20 per cent decrease in the net negative surface charge density and is accompanied by an increase in volume of the erythrocyte. Pondman and Mastenbrœk[2] suggested from analytical evidence that there is a loss of phospholipid from the erythrocyte on treatment with trypsin. Seaman and Heard[3] were unable to confirm this finding, and suggested that the decrease in mobility is the result of a diminution in the number of α-carboxyl groups effective at the electrophoretic plane of shear.

Trypsin is known to inactivate most mucoproteins which inhibit influenza virus hæmagglutination. Since sialidase inactivates all such inhibitory mucoproteins, presumably by the release of sialic acid[4], trypsin could therefore also release a bound sialic acid. Klenk[5] has demonstrated the presence of a sialic acid (N-acetylneuraminic acid) in the stroma of human erythrocytes.

Standard washed human erythrocytes[6], of phenotypes A Rh+ve, B Rh+ve, ORh+ve and −ve and AB Rh−ve, were examined. 10 c.c. of packed cells per experiment were treated with trypsin (50 μgm./ml.) according to a modification of the method of Morton and Pickles[7]. Appropriately controlled erythrocyte supernatants from each experiment were deproteinized with 20 per cent w/v aqueous trichloroacetic acid, filtered through a No. 50 Whatman paper, reduced to small volume at 50° C. under reduced pressure and the trichloroacetic acid extracted with diethyl ether. The aqueous phase was again reduced in volume and desalted electrolytically.

Finally, these processed supernatants were reduced to dryness and the residues taken up in a few drops of 10 per cent v/v aqueous *iso*propanol. These solutions were examined by descending paper chromatography (Whatman No. 1 paper, butan-1-ol : acetic acid : water (4 : 1 : 5) organic phase). The air-dried chromatograms were dipped in 0·2 per cent w/v ninhydrin in acetone and developed at 90° C.

Fig. 1 shows schematically the appearance of a ninhydrin-positive compound (purple complex) of R_F 0·65, designated compound 1, from the supernatant of trypsin-treated red cells. This compound is not present in any of the controls. Fig. 2 is a photostat copy of a chromatogram showing components as in strip 1 and strip 5 of Fig. 1.

Compound 1 was eluted with 10 per cent v/v aqueous *iso*propanol from an air-dried untreated controlled chromatogram. The ultra-violet absorption spectrum of eluates of compound 1 shows absorption over the wave-lengths 215–300 mμ with a minor peak at about 270 mμ. Acid treatment of compound 1 produces an increase in the absorption over the range 270–290 mμ (see Fig. 3) and on alkaline treatment there is an increase at 260 mμ (Fig. 4). This spectral behaviour does not suggest trichloroacetic acid contamination and is characteristic of materials containing sialic acid[8].

Microchemical estimations were performed on solutions of compound 1 in 10 per cent v/v aqueous *iso*propanol. The nitrogen content of the eluates was determined colorimetrically by the Nessler method of Johnson[9] and the carbohydrate content was assayed using an anthrone reagent[10]. Sialic acids were determined colorimetrically by the resorcinol–hydrochloric acid method of Svennerholm[11] and the 2-thiobarbituric acid technique of Warren[12]. It was

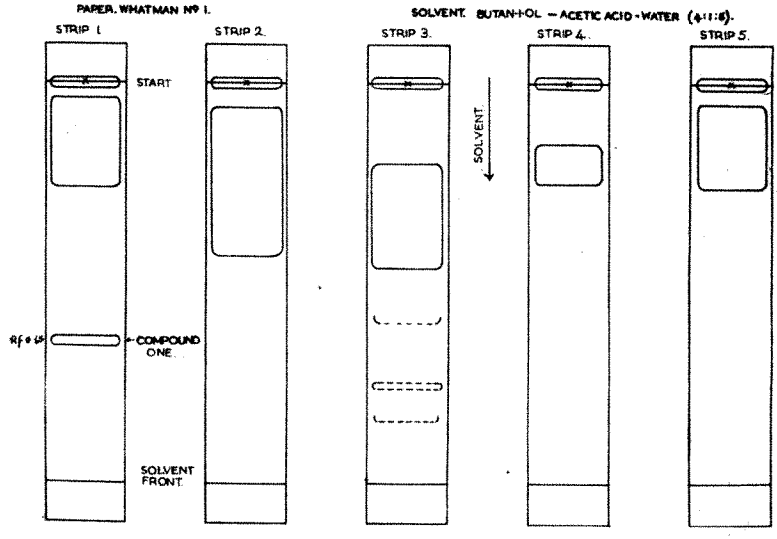

Fig. 1. Map showing regions of ninhydrin-positive material on the chromatograms. Strip 1, supernatant from trypsin-treated human erythrocytes (conc. 50 μgm./ml. total of 2 mgm. trypsin); strip 2, autolysis of trypsin (conc. 50 μgm./ml. total of 2 mgm. trypsin); strip 3, impurities in trypsin (total of 25 mgm. trypsin); strips 4 and 5, supernatants from normal human erythrocytes; (4) incubated in saline (vol. of saline = vol. of saline in strip 1 experiment); (5) supernatant obtained as in strip 4, re-incubated with trypsin (conc. = 50 μgm./ml.). Electrophoretic mobility of untreated erythrocytes = 2·78 ± 0·08μ sec.$^{-1}$ V.$^{-1}$ cm. Electrophoretic mobility of trypsin-treated erythrocytes = 2·30 ± 0·06μ sec.$^{-1}$ V.$^{-1}$ cm.

* Beit Memorial Research Fellow.

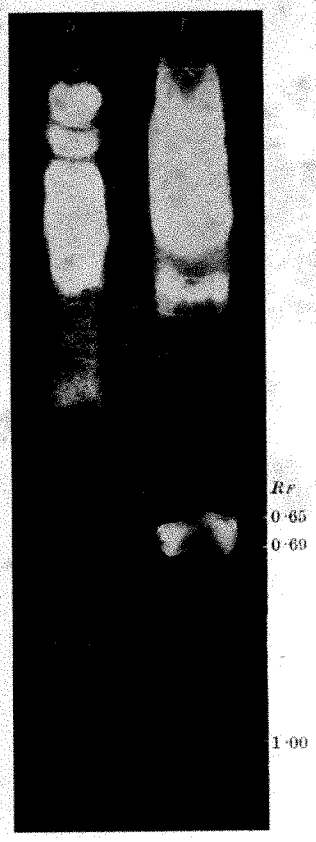

Fig. 2. Photostat copy of chromatograms developed with ninhydrin, from experiments strip 1 and strip 5. Compound 1 present only in experiment strip 1

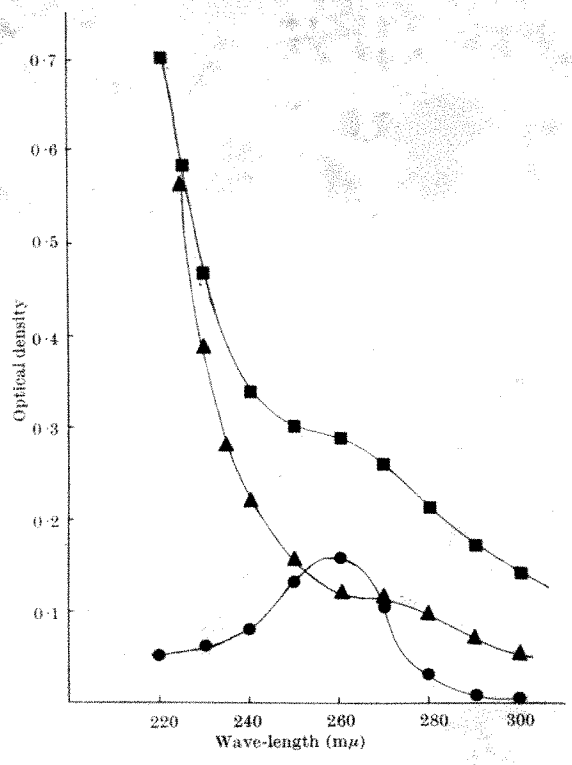

Fig. 4. Ultra-violet absorption spectra in 10 per cent v/v aqueous *iso*propanol of: ▲, eluate containing compound 1 (sialic acid content, 16 μgm. in 5 ml.), *p*H 5·1; ■, above material reduced to dryness and treated with *N* sodium hydroxide (0·075 ml.) at 105° C. for 17 hr., dissolved in water (5 ml.) adjusted with hydrochloric acid to *p*H 5·8; ●, 2 carboxypyrrole (1 μgm./ml.), *p*H 4·9

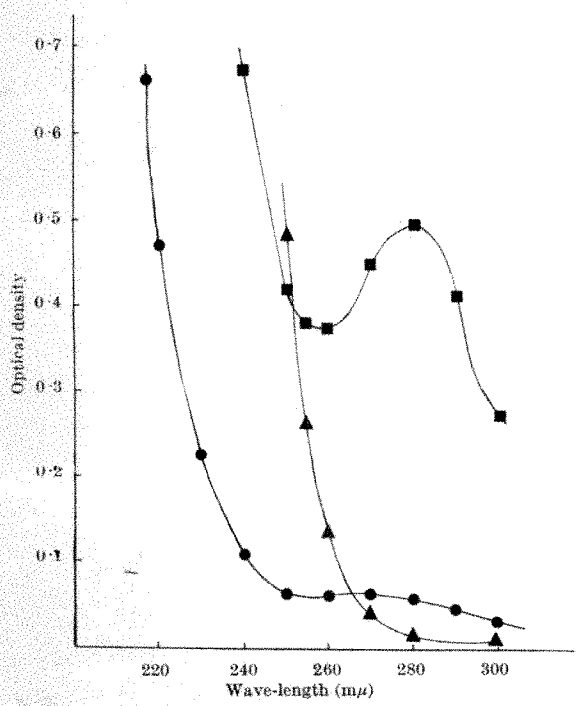

Fig. 3. Ultra-violet absorption spectra in 10 per cent v/v aqueous *iso*propanol of: ●, eluate containing compound 1 (sialic acid content, 1 μgm./ml.), *p*H 6·1; ■, eluate containing compound 1 (sialic acid content, 1 μgm./ml.) after heating for 10 min. at 90° C., *p*H 2·8; ▲, trichloroacetic acid solution (1,000 μgm./ml.), *p*H 2·0

found that in compound 1 the ratio of nitrogen to carbohydrate (as glucose) to N-acetylneuraminic acid (after treatment with 0·1 *N* sulphuric acid at 80° C. for 1 hr.) was as 18 : 10 : 1 by weight. The high nitrogen content coupled with the appearance of a purple complex with ninhydrin is indicative of a peptide character for compound 1, which would be expected from the known specificity of trypsin. The release from the periphery of the erythrocyte membrane of this sialomucopeptide, probably structurally analogous to that suggested for ovine submaxillary gland mucoprotein by Gottschalk[13], could account for the decrease in electrophoretic mobility of the erythrocyte observed after treatment with trypsin.

We wish to thank the Medical Research Council for financial assistance, Prof. D. D. Eley and Prof. J. S. Mitchell for useful discussion and Mr. E. W. Mitchell for the photography.

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LETTERS TO THE EDITORS

PHYSICS

Use of an Artificial Satellite to test the Clock 'Paradox' and General Relativity

An interesting and promising test for the effects of gravitation and motion on the relative rates of a satellite clock and an earthbound clock was proposed four years ago by S. F. Singer[1]. For this purpose Singer used the Schwarzschild metric for the Earth's field and considered a circular satellite orbit. The neglect of the ellipticity of the Earth has been justified by B. Hoffmann[2], provided that the mean radius is used. Neglecting also the rotatory motion of the Earth clock Singer found for the red shift of the satellite clock relative to the Earth clock the expression:

$$\Delta = \frac{dt_S - dt_E}{dt_E} = \frac{\gamma M}{2c^2 R}\left(\frac{1 - 2\,h/R}{1 + h/R}\right) \qquad (1)$$

where R is the radius of the Earth, M its mass, h the height of the satellite above the surface of the Earth, and γ and c have their usual meanings.

However, Singer's calculation is open to criticism, as is also the work of H. Nariai and Y. Ueno[3], who calculate the result for an elliptic orbit following Singer's procedure, since the dt_S, dt_E here are the co-ordinate time-intervals corresponding to unit ticks of the respective clocks. Singer justifies this procedure on the ground that, since t measures proper time for an observer at rest at great distance from the Earth, Δ will therefore measure this observer's view of the relative rates. This is not so since we do not have flat space-time near the Earth where the clocks are. Furthermore, this expression for Δ is not invariant. If we performed a Lorentz transformation at infinity we should find a different value of Δ in terms of the new co-ordinate t'. Finally, we remark that the view of an observer at great distance is not relevant to the practical procedure which Singer suggests for carrying out the test, that is, to make a direct comparison by radio of the cumulative number of oscillations of the two clocks after a suitable number of revolutions of the satellite.

We shall obtain here an invariant form for the expression that Singer desired to measure. As it happens it agrees with Singer's result, but it appears difficult to justify Singer's method of analysis until implied assumptions are clarified. In view of past controversy over the clock paradox, and the need for tests of general relativity, it is thought that a different approach to Singer's test will be of interest.

We formulate in the first instance a slightly different problem from that proposed by Singer. Let a rocket, equipped with a cæsium atomic clock, leave the Earth at a given point and ascend to a suitable height where it goes into free circular orbit about the Earth. Let the rocket complete a suitable number of revolutions and thereafter make a controlled descent to land at the same point of the Earth at which it started. Supposing that the times for ascent and descent are small compared with the time in orbit, we wish to compare the cumulative number of oscillations of the rocket clock with the cumulative total on a similar clock at the rocket base on the Earth.

Following Singer we adopt the Schwarzschild metric for the Earth's field:

$$ds^2 = (1 - 2m/r)dt^2 - \frac{1}{c^2}\left\{\frac{dr^2}{1 - 2m/r} - r^2 d\theta^2 - r^2 \sin^2\theta\, d\varphi^2\right\} \qquad (2)$$

in which $m = \gamma M/c^2$. If we put:

$$v^2 = \left(\frac{dr}{dt}\right)^2 \Big/ (1 - 2m/r) - r^2\left(\frac{d\theta}{dt}\right)^2 - r^2 \sin^2\theta \left(\frac{d\varphi}{dt}\right)^2 \qquad (3)$$

then the element of proper time as registered on the rocket clock will be:

$$ds_{\text{rocket}} = \left(1 - \frac{2m}{r} - \frac{v^2}{c^2}\right)^{\frac{1}{2}} dt \qquad (4)$$

To adequate approximation v is the Newtonian velocity relative to the Earth. Let the orbit be characterized by $\theta = \pi/2$, $d\varphi/dt = \omega$ (constant), $r = a$ (constant). Then the total proper time registered on the rocket clock during the whole journey will be:

$$[s]_{\text{rocket}} = \int_{t_1}^{t_2}\left(1 - \frac{2m}{a} - \frac{\omega^2 a^2}{c^2}\right)^{\frac{1}{2}} dt + \int_{t_0}^{t_1}\left(1 - \frac{2m}{r} - \frac{v^2}{c^2}\right)^{\frac{1}{2}} dt + \int_{t_2}^{t_3}\left(1 - \frac{2m}{r} - \frac{v^2}{c^2}\right)^{\frac{1}{2}} dt \qquad (5)$$

where t_0 is the co-ordinate time of leaving base, t_1 the time of going into orbit, t_2 that of leaving orbit, and t_3 the co-ordinate time of landing at the base. In the last two integrals of (5) r and v will be functions of t.

Similarly, the total proper time registered on the base clock will be:

$$[s]_{\text{base}} = \int_{t_0}^{t_3}\left(1 - \frac{2m}{R} - \frac{V^2}{c^2}\right)^{\frac{1}{2}} dt \qquad (6)$$

where V is the velocity of the base point arising from the Earth's rotation.

But $t_1 - t_0$, $t_3 - t_2$ can be made arbitrarily small compared with $t_2 - t_1$, and so we are able to take:

$$t_2 - t_1 \simeq t_3 - t_0 \qquad (7)$$

and neglect the last two integrals in (5). Furthermore, the geodesic equations of general relativity, as well as the Newtonian theory, yield:

$$\omega^2 a^2 = m\,c^2 \qquad (8)$$

Hence, to sufficient approximation:

$$[s]_{\text{rocket}} \simeq \left(1 - \frac{3m}{2a}\right)\left(t_2 - t_0\right) \qquad (9)$$

and since $V^2 \ll \omega^2 a^2$ for a satellite orbit :

$$[s]_{\text{base}} \simeq \left(1 - \frac{m}{R}\right)\left(t_3 - t_0\right) \qquad (10)$$

Therefore, the invariant fractional excess of the registered time on the Earth clock over that registered on the rocket clock is :

$$\frac{[s]_{\text{base}} - [s]_{\text{rocket}}}{[s]_{\text{rocket}}} \simeq m\left(\frac{3}{2a} - \frac{1}{R}\right) \qquad (11)$$

which, if $a = R + h$, is :

$$\frac{\gamma M}{2c^2 R}\left(\frac{1 - 2h/R}{1 + h/R}\right) \qquad (12)$$

This result has the same interpretation as Singer's. That is, the rocket clock registers the smaller time if $h < \frac{1}{2}R$, and the greater time if $h > \frac{1}{2}R$, or a net red shift and violet shift respectively of order 1 c./s. of the cæsium line.

We could, of course, avoid the necessity of a relatively short period of ascent and descent by requesting the satellite to telemeter its 'readings' for comparison with the base clock from the time of going into orbit to the time of completing a suitable number of circuits, as suggested by Singer. Our result (11) would still apply. But to emphasize that this is a test of the familiar clock paradox, or problem of identical twins, we have chosen to reunite the two clocks at the same space-time event.

In so far as we have deduced the result from the Schwarzschild metric it is also a test of general relativity, that is, of the curvature of space-time that general relativity predicts for the case of a spherical mass.

More strictly, this experiment tests that part of general relativity usually referred to as the principle of equivalence, together with certain features of the Schwarzschild metric which might have been predicted from Newtonian gravitation, in agreement with a view of the Schwarzschild metric recently expressed by H. Bondi and C. W. Kilmister[4].

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DR. DAVIDSON is quite right in remarking that it is not necessary to introduce an observer at great distance from the Earth in order to measure proper time. But neither is it necessary to bring the two clocks into space-time coincidence at the beginning and at the end of the experiment, as he has done in his derivation. In fact, the experimental method for doing the measurement requires only a comparison of the time intervals necessary to accumulate a large number of ticks on the two clocks, and this comparison could be done by any third observer.

What is interesting is the fact that our derivations do give the same result, as does the derivation superimposing the simple 'red shift' and second-order Doppler shift (from the special theory of relativity). This agreement is not accidental, as Davidson implies. It depends on the fact that the observer at a great distance from the Earth does not carry out any irregular motion; hence his introduction appears to be correct and entirely equivalent to having, for example, the Earth clock signals themselves determine the co-ordinate time. The reason for this is that the signals travel along null geodesics in a time-independent metric.

I am indebted to my colleague Prof. J. Weber for useful discussion.

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Theoretical Magnetic Moments of Proton and Neutron

RECENTLY it was shown that the equation :

$$E = 38{\cdot}46\ [l(l + 1) + s(s + 1)]\ \text{MeV}. \qquad (1)$$

provides a correlation of empirical particle masses[1] and of nucleon excitations[2].

The prediction of a resonance energy E_r at 750 MeV. in free protons has now been fully confirmed[3,4]. The maximum for π^+ scattering reported to lie at 1·3 or 1·35 MeV.[3,5] appears to be a doublet as can be seen from Table 1.

Table 1. CALCULATED AND OBSERVED RESONANCE ENERGIES (MEV.) FOR PHOTOPIONS AND FOR PION SCATTERING FROM HYDROGEN

Transitions $^6F_{1/2} \rightarrow$	$^6F_{1/2}$		$^6G_{3/2}$		$^6G_{1/2}$		$^6H_{5/2}$	
Pairs created	$2\pi^0$	$2\pi^-$		^2D		^4D		^2F
E_r calculated	270	279	308	520	577	750	961	980
E_r observed (cm.)	263	279	299	543	574	750	958	983·5
	$\gamma\pi^+$	$\gamma\pi^0$	$\pi^\pm$	$\gamma\pi^+$	$\pi^-,\gamma\pi^0$	$\pi^-,\gamma\pi^0$	π^+	π^+

This table gives the energies for the transitions from the core particle $^6F_{\frac{1}{2}}$ to the indicated higher levels, and the energies needed for the formation of pairs, all calculated according to equation (1). The last line of figures gives the observed resonance energies in photo-production and scattering of pions from free protons.

Equation (1) provides thus a numerical interpretation of all observed resonance energies. The agreement is in several cases within 1 per cent, less than the estimated error.

Equation (1) also contains quantum numbers which are essential for calculating the magnetic moments of the proton and the neutron. In particular, in Table 1, the state $^6F_{\frac{1}{2}}$ plays an important part as the core particle of the proton.

The anomalous magnetic moments of proton and neutron are generally believed to be caused by the contributions of charged (virtual) pions. The magnetic moment of the free pion, however, must be zero. The parity of the pion is odd. Thus it must possess an internal angular momentum, most probably $l = 1$. The correlated magnetic moment is compensated by the anomalous magnetic moment connected with the spin $s = \frac{1}{2}$ of the electric charge. Also the total angular momentum of the pion is zero.

Since the charged pion is required to contribute to the magnetic moment of the nucleon, it cannot be bound in an S-state.

The next simplest case is $l = 1$ for the pion orbital. Then the contribution of the pion to the magnetic moment is one pion magneton :

$$\mu_\pi = (m_P/m_\pi)\ \mu_0 = 6{\cdot}72\ \mu_0 \qquad (2)$$

where μ_0 means one nuclear Bohr magneton and m_P and m_π are the rest masses of proton and pion respectively.

The core particle ^6F can be assumed to have total angular momentum $I = \frac{1}{2}$ as the ground-state because the system will have minimum energy if the total angular momentum has its minimum value, since then the energy due to the magnetic field connected with the angular momentum will be a minimum.

The ground state of the nucleon is $I = \frac{1}{2}$. The addition of a pion with orbital $l = 1$ to the state $^6F_{\frac{1}{2}}$ can lead again to a state with $I = \frac{1}{2}$ as required.

In the case of the neutron the core particle $^6F_{\frac{1}{2}}$ can exchange its positive charge with the bound negative pion, since the pion must contain two spins $s = \frac{1}{2}$ to compensate the internal angular momentum to zero. Therefore one spin $s = \frac{1}{2}$ is not occupied by charge.

The probabilities for finding the positive charge at the core or at the pion can be expected to be in the ratio:

$$(2I + 1) : (2l + 3) = 2 : 5 \qquad (3)$$

counting for the statistical weight of the boson, $2 + 1 = 3$ for the bond orbital $l = 1$, another unit for the internal angular momentum $l = 1$ indicated by the odd parity of the pion, and another unit, the sum of the two spins $s = \frac{1}{2}$ which compensate the internal angular momentum of the pion to zero.

The magnetic moment μ_N of the neutron can thus be expected to be:

$$\mu_N = (2/7)\ \mu(^6F_{\frac{1}{2}}) - (2/7)\ \mu_\pi \qquad (4)$$

The magnetic moment of the core particle $\mu(^6F_{\frac{1}{2}})$ is not known. The contribution $\mu(F)$ of the F-term ($l = 3$) has to be three core magnetons:

$$\mu(F) = 3(m_P/m_C)\ \mu_0 = 3{\cdot}527\ \mu_0 \qquad (5)$$

The core mass m_C of the state $^6F_{\frac{1}{2}}$ is given by equation (1).

Systems with rotational motions belonging to half-integral quantum numbers were investigated by Weyl[6]. In his case, the half-integral quantum numbers are due to the combination of an intrinsic spin $s = \frac{1}{2}$ and an integral quantum number of the type of angular momenta. The magnetic moment due to the spin $s = \frac{1}{2}$ is anomalous, namely, one full unit of a magneton. The quantum number 5/2 should thus lead to three core magnetons and therefore to the same absolute value as given in equation (5). In the state $^6F_{\frac{1}{2}}$, however, the two contributions have opposite signs, thus:

$$\mu(^6F_{\frac{1}{2}}) = 0 \qquad (6)$$

Then, together with (4) and (2):

$$\mu_N = -\ (2/7)(m_P/m_\pi)\ \mu_0 = -1{\cdot}92_0\ \mu_0 \qquad (7)$$

This value deviates by less than $\frac{1}{2}$ per cent from the empirical value $\mu_N = -1{\cdot}91_3\ \mu_0$. This small difference is probably caused by the relativistic increase of the mass of the pion owing to its kinetic energy.

The result of equation (7) justifies the assumptions made above and leads to the conclusion that the pion is not virtually created but permanently present, and in a well-defined state. The same conclusion was also reached from the mass difference of the nucleon and of the core particle[1].

In the case of the proton, the bound pion has to be neutral. This is the case if the two spins $s = \frac{1}{2}$ within the pion are occupied by opposite charges. Then there is no spin $s = \frac{1}{2}$ free of charge and the exchange of a single charge between core and pion which occurs within the neutron is no longer possible within the proton.

According to equation (1), however, there is the possibility of resonance between the isobaric states $^6F_{\frac{1}{2}}$ and $^2G_{7/2}$. The probabilities for finding the core particle in these states are in the ratio 2 : 8, due to the respective values of $2I + 1$.

Then the resulting magnetic moment of the core should be:

$$\mu_C = (0{\cdot}2)\ \mu(^6F_{\frac{1}{2}}) + (0{\cdot}8)\ \mu(^2G_{7/2}) \qquad (8)$$

The magnetic moment of the state $^2G_{7/2}$ must be $4-1 = 3$ core magnetons, incidentally the same value as given in (5). This value together with (6) and (8) leads to:

$$\mu_C = (0{\cdot}8)3(m_P/m_C)\ \mu_0 = 2{\cdot}82\ \mu_0 \qquad (9)$$

This value deviates only about 1 per cent from the empirical value of the magnetic moment of the proton $\mu_P = 2{\cdot}79\ \mu_0$. The difference is presumably due to diamagnetism of the neutral pion contained in the proton.

In the resonance process between the isobaric states of the core, the total angular momentum would not be conserved. This condition can be fulfilled in the case of the proton if the angular momentum of the bound neutral pion changes from $l = 1$ with core $^6F_{\frac{1}{2}}$ to $l = -3$ with core $^2G_{7/2}$.

The neutral pion can be bound to the core by the exchange of the positive charge of the core and of the positive charge which neutralizes the negative charge in the neutral pion. This process would not change the magnetic moment of the system.

The resonance process within the proton between the two isobaric core states $^6F_{\frac{1}{2}}$ and $^2G_{7/2}$ introduces also an unsharpness of the two states and widens the energy range in which resonance can occur.

If the bound pion were not neutral, additional energy would be required to build up the magnetic field connected with the orbital $l = 3$. This would destroy the condition for resonance which exists for the system of core and bound neutral pion. In fact, the ensuing magnetic moment would also destroy the agreement with the empirical values.

Thus the resonance process between the isobaric states $^6F_{\frac{1}{2}}$ and $^2G_{7/2}$ appears to be possible only in the case of the proton with its neutral pion, but not for the neutron as a compound of a positive core and a negative pion. In this way one can understand the exceptional stability of the proton.

Like the proton, the Ξ-particle appears to contain a neutral pion. The rest energy of the charged Ξ-particle is 1,319 MeV., and this is quite near the sum of a $^2H_{9/2}$ particle and of a neutral pion, namely, $1{,}182 + 135 = 1{,}317$ MeV.

The agreement between calculated and empirical values of the magnetic moments of proton and neutron indicates that the half-integral quantum numbers s in equation (1) refer really to Weyl's relativistic system of spherical harmonics with spin.

The quantum numbers of equation (1) must belong to internal degrees of freedom of extended particles, and this equation appears now to be relevant to the calculation of the masses of the 'elementary'

heavy fermions, of the internal excitation energies of the free proton and of the magnetic moments of proton and neutron.

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Generation of Water Waves by the Wind

THE spectral energy density φ of small deep-water waves increases with wind speed and fetch, for a given frequency-band, only up to a certain value. For larger wind speed or fetch the energy density appears to become saturated, as was noticed by Burling[1] and by Phillips[2]. Having recently completed a detailed analysis of two sets[1,3] of data on φ, I can now give quantitative evidence for this apparent saturation. (I am indebted to Dr. Burling and to the Imperial College of Science and Technology, London, for permission to use the original data published in his thesis.)

For the purposes of the analysis I assumed φ to be of the form:

$$\begin{aligned} \varphi &= b_1 V^{r_1} F^{s_1} f^{t_1} \qquad f \leqslant f_0 \\ &= b_2 V^{r_2} F^{s_2} f^{t_2} \qquad f > f_0 \end{aligned} \tag{1}$$

where V, F, and f are the independent variables in the experiments, that is, the average wind speed, the average fetch, and the wave-frequency. The eight parameters, b_1, b_2, r_1, r_2, s_1, s_2, t_1, and t_2, are at our disposal in making the best fit to the experimental data. On the basis of earlier analyses we can expect that r_1, s_1, t_1 and $-t_2$ will be positive, the opposite signs of t_1 and t_2 implying that the largest value of φ, for given V and F, is reached at $f = f_0$. The value of f_0 is given by the equation:

$$b_1 V^{r_1} F^{s_1} f_0^{t_1} = b_2 V^{r_2} F^{s_2} f_0^{t_2} \tag{2}$$

For a frequency $f < f_0$, the spectrum is unsaturated. For a frequency $f > f_0$, the spectrum is saturated with respect to increases of wind speed or fetch if the absolute values of r_2 and s_2 are small compared to one. (Phillips refers to the saturated part of a spectrum as the "equilibrium range".) More complete descriptions of wave generation than these equations afford would require the specification, for example, of the velocity profile above the water and the directional spectra of the wind and of the waves.

Burling's data consist of 463 measured values of φ for various combinations of frequency, average wind speed, and average fetch in the ranges:

$$0{\cdot}4 \leqslant f \leqslant 1{\cdot}8 \text{ c.p.s.}, \; 5{\cdot}0 \leqslant V \leqslant 8{\cdot}8 \text{ m./sec.}, \text{ and } 400 \leqslant F \leqslant 1{,}350 \text{ m.}$$

All the wave systems that he studied were thus in the gravity wave regime. My data consist of 273 measurements of the wave energy, observed through octave-wide filters centred at 0·75, 1·5, 3, 6 and 12 c.p.s., for various combinations of average wind speed and average fetch in the ranges:

$$0{\cdot}15 \leqslant V \leqslant 10{\cdot}2 \text{ m./sec. and } 5 \leqslant F \leqslant 625 \text{ m.}$$

Most of the waves that I measured also were in the gravity wave regime. Integration of the function φ in equation (1) over the power transfer function of the filter yields energy values which can be compared with my experimentally determined values. For each of the two sets of data a least-squares fit was made to find the best values of the eight parameters in equation (1). Afterwards, 10 sub-sets of data were chosen at random from each set of data, and least-squares fits, starting with randomized values of each parameter, were made for each of the 20 sub-sets. I shall discuss here the results of my analysis only for the parameters r_2, s_2, t_2 and b_2.

In Table 1 are listed, for each set of data, the best values of these four parameters and the probable errors, parameters and errors both being derived from the randomly chosen sub-sets.

Table 1

	r_2	s_2	t_2	$\log_{10} b_2$*
Burling	0±0·02	0±0·01	−5·69±0·04	−3·10±0·02
Present author	0·41±0·14	−0·14±0·05	−4·66±0·12	−2·78±0·22

* m.sec. units.

For the limited range of frequency in Burling's data r_2 and s_2 may be taken equal to zero with a high degree of certainty. For the larger frequency-range of my data, r_2 and s_2 may also be taken to be about equal to zero. In fact, if in the least-squares analysis of my data $r_2 = s_2 = 0$, the best values of the other two parameters are essentially unchanged from the values given in Table 1. It may be concluded then that the saturation effect noted by Burling and by Phillips does indeed exist and that it extends over a frequency-range that is more than a decade wide.

The two values of $\log_{10} b_2$ given in Table 1 differ by but little more than the sum of the probable errors. The exponents t_2 from the two sets of data do not agree within their combined probable errors. The value -5 or $-2{\cdot}33$ for this exponent is to be expected for pure gravity waves or pure capillary waves, respectively, if the wave growth is affected only by the acceleration of gravity or by the capillary constant. That t_2 for my experiments is smaller in absolute value than for Burling's experiments may reflect the fact that some of the waves I measured are in the capillary–gravity wave regime. It should also be pointed out that the air boundary layers, for the same wind speed and fetch, were probably rather different in Burling's experiments and in mine.

Small gravity waves may well form a naturally occurring dynamical model of the larger wind waves on the ocean. If a dynamical similarity does exist, then it would be expected that ocean waves will show a saturation effect similar to that of the smaller waves and that wind waves of the two scales will be alike in many other respects. Model work on small waves on lakes and reservoirs would then provide, with but a small effort, data on wind wave generation that are significant for the waves both on lakes and on the sea. The critical question is: How complete is the supposed dynamical similarity between the generation by the wind of large and small gravity waves?

The CSL measurements were made by E. A. Huber and C. G. Whittenbury. Calculations were made on *Illiac*, the digital computer of the University of

Illinois. G. Berg and C. W. Mendel wrote most of the *Illiac* programmes used in the data reduction. This work was supported by a Tri-Services Contract of the Department of Defense.

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Standard Unit of Pressure in Vacuum Physics

DR. N. A. FLORESCU[1] proposes to use in vacuum physics a unit of pressure = 10^3 dynes cm.$^{-2}$, which he suggests should be called a 'vac'. A unit of this magnitude, however, has already been designated and used under the name 'millibar', and is equal to 100 newtons m.$^{-2}$. It therefore seems to me useless to invent a new name, particularly at a time when attempts are being made to limit the introduction of special names for units derived from systems in current use.

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[1] *Nature*, 188, 303 (1960).

MANY readers of Dr. Florescu's communication in *Nature* of October 22, p. 303, on the standard unit of pressure in vacuum physics will see in it a powerful plea for the extended use of the absolute unit of pressure, the bar equal to 10^6 dynes/cm.^{2}. They will of course recognize that the proposed 'vac' is none other than the existing millibar (see, for example, British Standard 2520 (1954). Barometer Conventions and Tables). Now that the internationally adopted prefixes to abbreviations for the names of the metric units are coming increasingly into use (see for example B.S. 1991, Part 1 (1954), Symbols, Signs and Abbreviations, p. 32) there should be no difficulty in applying them to the bar and thus realizing the objective which Dr. Florescu has in mind. There is no need to introduce a new unit. For example, we have:

1 vac = 10^{-3} bar = 1 millibar (mb)
10^{-3} vac = 10^{-6} bar = 1 microbar (μb)
10^{-6} vac = 10^{-9} bar = 1 nanobar (nb or mμb)
10^{-9} vac = 10^{-12} bar = 1 picobar (pb or $\mu\mu$b)

(In each instance the abbreviation 'b' for bar can, according to a 1948 decision of the General Conference of Weights and Measures, be replaced by the complete word 'bar'.)

Regarding Dr. Florescu's plea that the millibar (or 'vac') should be recognized as granting a special significance to the value 980·7455 cm./sec.^{2} for gravity, this should be approached with considerable reserve, bearing in mind the confusion which existed for many years between various other values associated with the term standard gravity (see B.S. 2520 (1954), p. 6). This confusion was resolved in 1950 by the International Committee of Weights and Measures when the value 980·665 cm./sec.^{2} was re-affirmed as standard. This value is now accepted as standard for all purposes, and it is to be hoped that no action tending towards further confusion will now be taken.

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GEOPHYSICS

Effects of Diffusion of Electrons near the Magnetic Equator

IN a recent interesting communication, Dr. E. R. Schmerling[1] has discussed the possible effect of vertical diffusion in the ionosphere in the presence of the geomagnetic field. He claims that the effect of diffusion is to increase the electron density below the electron peak, so that near the magnetic equator the electron density N at a given height h should be less than in slightly higher latitudes, since the magnetic field at the equator is horizontal and precludes vertical diffusion. Dr. Schmerling, however, assumes in this derivation that the rate of ion production is independent of latitude and therefore of the magnetic dip.

If we assume that the ionization is produced according to the Chapman law, this is certainly not the case, the rate of ionization increasing as the magnetic equator is approached. The two effects therefore tend to cancel each other out, and according to our calculation it seems that the increase in ionization at lower geomagnetic latitudes exceeds any decrease due to the effects of diffusion described by Dr. Schmerling. This is illustrated in Fig. 1, which shows the variation of electron density with geomagnetic latitude about an hour after midday at heights of ½, 1 and 1½ scale heights above the level of maximum ion production. The graph of maximum electron density (N_m) follows very closely the highest curve in Fig. 1, and we must conclude that the $F2$ model under discussion, based on a hypothesis of

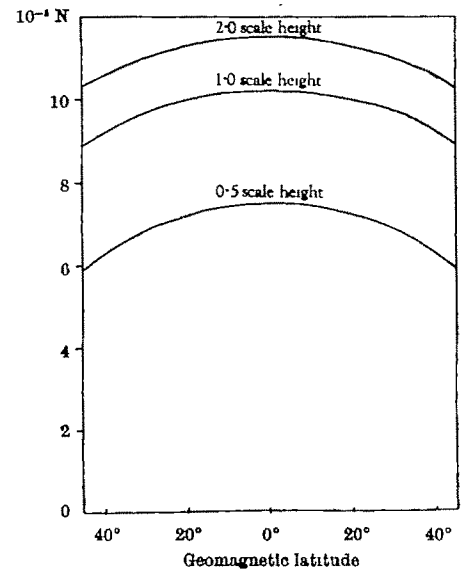

Fig. 1

vertical diffusion, does not account for the Appleton anomaly. It will be seen from this figure that the variation of electron density at midday is rather insensitive to changes of geomagnetic latitude. It has been suggested by various writers, however, that horizontal diffusion may affect the vertical distribution of ionization, and near the magnetic equator the tendency would be for ionization to diffuse away north and south from the equator and pile up on opposite sides of it. We are at present investigating the magnitude of this effect.

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Evidence of Quasi-Perpendicular Propagation of Hydromagnetic Waves caused by Nuclear Explosions over Johnston Island

IN previous reports[1,2] one of us (H. M.) has suggested that the initial phase of artificial magnetic storms due to high-altitude nuclear explosions over Johnston Island (16·5° N.; 169·5° W.) may be interpreted by hydromagnetic waves propagated through the high atmosphere from the explosion point. Such a suggestion has also been made by many other workers. The purpose of this communication is to exhibit evidence supporting such a suggestion. (Quite recently, Berthold *et al.*[3] have also found similar effects due to *Argus*.)

Fig. 1 shows replotted recordings of the induction magnetograph around 10h. 50m. G.M.T. on August 1, and around 10h. 30m. G.M.T. on August 12, 1958, at Shimosato (33·6° N.; 135·9° E.) and Onagawa (38·4° N.; 141·5° E.) in Japan. As has been estimated by Maeda[2], the explosion time (and altitude) is 10h. 50m. (150 km.) on August 1, and 10h. 30m. (70 km.) on August 12, respectively. On examining carefully the magnetic traces, one finds peculiar changes around the explosion time on each day. The changes seem to consist of two parts, the first and the second arrivals, and each of them starts at the time indicated by arrows, and comes to an end about 30 sec. later. An almost complete similarity between the changes on both days at each station seems to provide the evidence that these changes are the direct effect of the Johnston Island explosions. Numerical detail of the changes read from magnetograms is summarized in Table 1.

It seems likely from these results that the changes found at Japanese stations are due to hydromagnetic waves propagated in the high atmosphere across the lines of geomagnetic force from the explosion point. If so, the propagation velocity is estimated at about 540 km./sec. for the first arrival, and about 300 km./sec. for the second arrival, on the average. Moreover, if we assume that the initial change at Honolulu is also caused by hydromagnetic waves, the average damping distance in which the wave is attenuated by a factor e^{-1} is estimated at about 1,650 km.

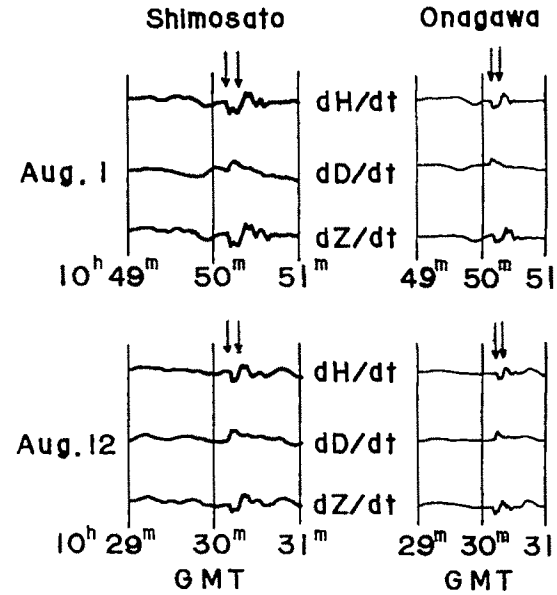

Fig. 1. Replotted recordings at Shimosato and Onagawa, Japan, showing geomagnetic effects due to Johnston Island nuclear explosions on August 1 and 12, 1958

As seen in Fig. 2, the propagation path is across the lines of geomagnetic force at about 90° (that is, quasi-perpendicular propagation), so that the waves seem to be a modified Alfvén mode. Theoretical treatment of the propagation of hydromagnetic waves in a partially ionized plasma has been carried out by Akasofu[4], Dungey[5] and Piddington[6,7]. According to Piddington's formulæ, the propagation velocity and the damping distance depend closely on altitude in the ionospheric region. The damping distance of about 1,650 km. estimated here corresponds to an altitude of about 300 km. On the other hand, the propagation velocity at this altitude is about 10 km./sec. This value is much smaller than that deduced here. Such a disagreement results from a very simple assumption that the hydromagnetic waves are propagated along a path of constant height in the ionosphere. The actual conditions of propagation, however, seem to be much more complicated.

Thus, although it seems, at present, to be difficult to find any precise interpretation of the phenomena, the following preliminary picture may be drawn. Simultaneously with high-altitude nuclear explosions, very strong shocks are caused and propagated with high velocity. These shocks are attenuated after travelling some distances, and degenerate into hydromagnetic waves (of the modified Alfvén mode

Table 1. NUMERICAL DETAIL OF GEOMAGNETIC CHANGES AT SHIMOSATO

	First arrival				Second arrival				Last time of arrival (sec.)
	Time of arrival (sec.)	dH/dt	Amplitude dD/dt (γ/sec.)	dZ/dt	Time of arrival (sec.)	dH/dt	Amplitude dD/dt (γ/sec.)	dZ/dt	
August 1	9	0·058	0·045	0·080	18	0·090	0	0·135	41
August 12	11	0·051	0·042	0·060	18	0·066	0	0·105	40
Mean	10	0·055	0·044	0·070	18	0·078	0	0·120	41

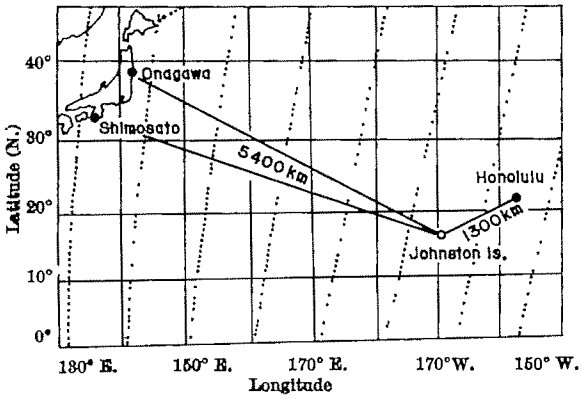

Fig. 2. Distance and direction from Johnston Island to observed stations, where dotted lines indicate the geomagnetic meridian

in the present case). The hydromagnetic waves will be propagated through the upper ionospheric region in the following manner: a highly ionized plasma produced by explosions pushes the geomagnetic field away, as it expands, so that a magnetic barrier may be formed in a height where the magnetic pressure of the compressed geomagnetic field equals the kinetic pressure of the plasma. Because of such a barrier, the waves may tend to be propagated horizontally; and its height seems to be lower (probably around 900 km.) than that suggested by Bomke *et al.*[8], because both the height and the latitude of Johnston Island explosions are lower than those of *Argus*. The first and the second arrivals found here would not be due to the difference of propagation mode, but due to the difference of propagation path. If several induction-type magnetographs of high sensitivity had been used, the effects of the explosions would also be detected at more distant stations than Japanese ones.

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RADIATION CHEMISTRY

Radiation-induced Carboxylation of Organic Compounds: Formation and Reactions of the Carboxyl Radical Ion

WE have recently reported[1] some results on the reduction of carbon dioxide and bicarbonate in aqueous solution by cobalt-60 γ-rays and X-rays, leading to the formation of formic acid, aldehydes and small quantities of oxalic acid.

It has been found also that under these conditions the yields of molecular hydrogen were low when carbon dioxide or bicarbonate was present in the solution. From work on these reactions under different *p*H conditions, one is led to the conclusion that the negatively charged polarons $(H_2O)^-$, formed by the action of the radiation on water[2], which can react, for example, with protons according to: $(H_2O)^- + H^+ \rightarrow H + H_2O$, can, in the presence of carbon dioxide or bicarbonate, react as follows[2]:

$$(H_2O)^- + CO_2 \rightarrow CO_2^- + H_2O \quad (1)$$

$$(H_2O)^- + HCO_3^- \rightarrow CO_2^- + OH^- + H_2O \quad (2)$$

The existence of the CO_2^- radical ion in aqueous systems has recently been postulated also from polarographic evidence[3].

Some of the reduction products observed in the radiolysis of solutions of carbon dioxide or bicarbonate are the result of further reactions of the CO_2^- primarily formed (or the corresponding COOH radical with which it will be in equilibrium according to: $CO_2^- + H^+ \rightleftharpoons CO_2H$); for example, dimerization of these radicals can lead to oxalic acid.

Furthermore, direct proof of the presence of CO_2^- has been obtained from experiments in which oxygen-free aqueous solutions containing suitable organic solutes (for example, alcohols, acids, aliphatic hydrocarbons, etc.) are irradiated in the presence of carbon dioxide or bicarbonate. Under these conditions, it has been clearly demonstrated that the reduced carbon dioxide can be built into the organic molecules with the formation of the corresponding carboxylic acids.

For example, irradiation of aqueous solutions of ethanol (10^{-3} *M*) in the presence of carbon dioxide (0·5 atm.) or sodium bicarbonate (10^{-2} *M*) with cobalt-60 γ-rays (dose-rate $1 \cdot 8 \times 10^{17}$ eV. ml.$^{-1}$ min.$^{-1}$) gave lactic acid; the yields obtained were dependent upon *p*H, varying between $G \sim 1$ (molecules/100 eV.) at the lower *p*H to $G \sim 2$ at the higher *p*H. The lactic acid was identified by paper chromatography. Similar experiments were also carried out with carbon dioxide or bicarbonate labelled with carbon-14; in the latter case identification and analysis were carried out by isotope dilution technique.

Under similar conditions, irradiation of aqueous methanol gave glycollic acid, and irradiation of dilute acetic acid solutions gave malonic acid. When a solution of a 1 : 1 mixture of methane and carbon dioxide (total pressure 1 atm.) was irradiated with γ-rays, acetic acid was found to be one of the radiation products. Irradiation of 10^{-2} *M* formic acid in the presence of carbon dioxide labelled with carbon-14 (2×10^{-2} *M*) at *p*H 3 5 gave oxalic acid with a yield of $G \sim 1 \cdot 2$, calculated as ^{14}COOH.COOH (unpublished results of N. Getoff and M. Simic).

All these experiments were carried out in deoxygenated solutions; this is of importance, because otherwise the negative polarons may be scavenged to a greater or lesser extent by molecular oxygen according to: $(H_2O)^- + O_2 \rightarrow O_2^- + H_2O$, as shown previously[2].

In general, the carboxylation process depends on the formation of a free radical from the organic solute by the action of the OH or $(H_2O)^+$ formed by the ionizing radiation acting on the water, and association of the organic free radical with the CO_2^- radical ion formed according to reactions (1) or (2).

In the formation of lactic acid from ethanol, one has the following reactions:

$$CH_3CH_2OH + OH \rightarrow CH_3CHOH + H_2O \quad (3)$$

$$CH_3CHOH + CO_2^- \rightarrow CH_3CHOH\ CO_2^- \quad (4)$$

Similarly, glycollic acid is formed via the radical CH_2OH produced by dehydrogenation of methanol.

The production of acetic acid from methane and carbon dioxide would involve a CH_3 radical as follows[4]:

$$CH_4 + OH \rightarrow CH_3 + H_2O \quad (5)$$

$$CH_3 + CO_2^- \rightarrow CH_3\,CO_2^- \quad (6)$$

Formation of malonic acid from acetic acid is according to the following reactions:

$$CH_3\,CO_2H + OH \rightarrow CH_2CO_2H \quad (7)$$

$$CH_3\,CO_2H + CO_2^- \rightarrow {}^-O_2C\,CH_2\,CO_2H \quad (8)$$

It has been shown also that irradiation of more complex polymer molecules, such as histones and nucleoproteins, in aqueous systems, in the presence of carbon dioxide, leads to the introduction of carboxyl groups into the molecules; this has been demonstrated using carbon dioxide or bicarbonate labelled with carbon-14 (Appleby, Emmerson, Scholes and Weiss, unpublished results).

Carboxylations with CO_2 in the gaseous state or in mixtures with solid carbon dioxide under the action of 2-MeV. electrons have been reported recently; in these cases the carboxyl compounds appear to be relatively minor reaction products as they are only formed with yields of $G = 0{\cdot}01 - 0{\cdot}1$ (ref. 5).

It is clear that in this way it is possible to produce labelled carboxylic compounds and, in particular, to produce some carboxylic acids labelled with carbon-14 which may be difficult to obtain in any other way.

Another application of this method of radiation-induced carboxylation would be its use in the identification and characterization of free radicals produced by radiation, as in this way the radicals could be converted into carboxylic acids which may then be identified as such, for example, by an isotope dilution technique, if carbon dioxide or bicarbonate labelled with carbon-14 is used for the carboxylation process.

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CHEMISTRY

Heats of Chemisorption of Simple Diatomic Molecules on Metals

THERE have been suggestions recently that the heats of formation of compounds are related to the catalytic activity of metals and heats of chemisorption[1-3]. Fahrenfort, van Reijen and Sachtler have shown that for the decomposition of formic acid on metals there is a definite correlation between the activity of the metal and the heat of formation of the metal formate. A relationship between heats of oxygen chemisorption and heats of oxide formation is suggested by the recent results of Brennan, Hayward and Trapnell.

Table 1. HEATS OF FORMATION ARE TAKEN FROM "SELECTED VALUES OF CHEMICAL THERMODYNAMIC PROPERTIES" BY ROSSINI

Compound	$-\Delta H^\circ_f$ (298·16° K.) kcal. mole^{-1}	$-\Delta H$ (calorimetric) kcal. mole^{-1}	Ref.
NiH	2·7	35	4
NiO	58·4	110	3
FeO	63·7	130	3
CoO	57·2	110	3, 5
MnO	92·0	150	3
PdO	20·4	67	3
RhO	21·7	76	3
TaN	58·2	130	4
WO_2	136·3	190	3
TiO_2	218	235	3
CrO_2	138·4	170	3
AlO_2^-	218·6	210	3
NiS	17·5	—	

If, as a first approximation, the assumption is made that during chemisorption of diatomic molecules a two-dimensional surface compound is formed of simple stoichiometry, it would be anticipated that a correlation should exist between the heat of formation of that compound and the heat of chemisorption. Table 1 gives values for the heats of chemisorption (ΔH) of simple diatomic gases on metals determined calorimetrically and the corresponding heat of formation (ΔH°_f) of the stoichiometrically simplest compound. For example, in the oxidation of cobalt the heat of chemisorption is compared with the heat of formation of CoO and not Co_3O_4. An interesting example is the oxidation of aluminium where the heat of formation of AlO_2^- is used and not that of Al_2O_3. There does not appear to be any reason *per se* why the chemisorbed oxide layer on aluminium should not, in fact, have the composition AlO_2^-. In Fig. 1 are plotted the heats of chemisorption (experimental accuracy $\pm$ 5 kcal. mole^{-1}) and the corresponding heats of formation of the stoichiometrically simplest compound.

Since values for the heats of chemisorption of gases are somewhat limited the correlation shown in Fig. 1 allows estimates to be made of such heats if the

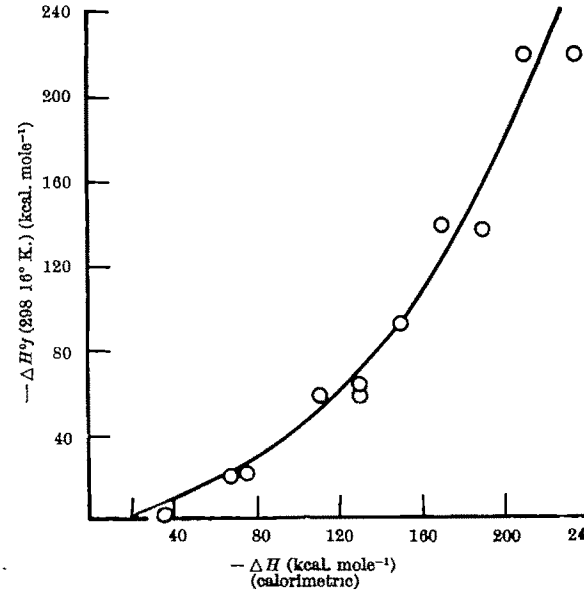

Fig. 1. Correlation between the heats of chemisorption of simple diatomic gases on metals and the heat of formation of the corresponding simple stoichiometric compounds

corresponding heat of formation is known. Recent work (Kemball, C., Wyn Roberts, M., and Saleh, J. M., unpublished results) on the sulphiding of metals has suggested that the binding energy of sulphur to nickel at − 80° C. is somewhat greater than the corresponding heat of hydrogen chemisorption ($\sim$ 35 kcal. mole^{-1}). If the chemisorbed layer simulates nickel sulphide we would expect, on the above hypothesis, a value of about 50 kcal. mole^{-1} for the heat of sulphur chemisorption since the heat of formation of nickel sulphide is − 17·5 kcal. mole^{-1}.

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Heat of Adsorption of Hydrogen on Tungsten at Elevated Temperatures

RECENT work[1,2] has shown that when certain hydrides are adsorbed on tungsten filaments at low pressures, and temperatures around 1,750° K., part is apparently desorbed as a negative ion, and a residual hydrogen atom is left bound to the tungsten surface. At the low surface coverages prevailing under the conditions of experiment, the migration of these residual hydrogen atoms to adjacent sites is relatively slow, so that the process of desorption is energetically isolated from that giving rise to negative ions. The approximate strength of the tungsten–hydrogen bond formed in this process has been put at 73·5 kcal /mole (refs. 3 and 4) based on measurements at room temperature, and this value was used in deducing the mechanism outlined above, but as an order of magnitude only. Several results have now been obtained, and the argument may be inverted, to use these results in conjunction with established electron affinities and heats of atomization, to deduce the strength of the W—H bond at these elevated temperatures. Briefly, the apparent electron affinity, E', is related to the true electron affinity, E, the heat of atomization of the substrate, D, and the tungsten–hydrogen bond energy Q_r by the relation :

$$E' = E - D + Q_r$$

The values of E and D have been adjusted to a temperature of 1,750° K., the original data being taken from compilations[5,6] except for the electron affinity of oxygen, taken from Branscomb and Smith[7]. The mean value of Q_r is 73 ± 1 kcal./mole, which is practically identical with the value at lower temperatures. If there was a loss of three translational degrees of freedom of the hydrogen atom in forming the W—H bond, the bond-energy would be expected to rise by 5 kcal./mole at the higher limit of temperature, which is well outside the limits of experimental error, and the fact that the value is the same as, or slightly lower than, the room-temperature value suggests that there is a considerable degree of vibrational freedom in the adsorbed film. Two fully excited bending modes would lower the bond-energy to 72·0 kcal./mole from a value of 73·5 at room temperature, which is so close to the values obtained from the more reliable experiments with the halogen acids as to indicate that this is the true value at high temperatures. The differential heat of adsorption of molecular hydrogen on tungsten at limiting low surface coverage may readily be calculated to be 40 kcal./mole at 1,750° K., compared with 45 kcal. at room temperature.

Table 1

Substrate	E'	E	D	Q_r
Hydrochloric acid	61	93	104	72
Hydrobromic acid	70	86	88	72
Water	−32	40	221	2 × 74

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Identification of Organic Compounds by Gas Chromatography

THE identification of unknown compounds separated by gas chromatography is often effected by comparison of their retention values with those of known compounds together with infra-red spectrophotometry or mass spectrometry. For this purpose graphs are prepared of log r against boiling point or log r on one stationary phase against log r on another stationary phase, where r is the retention time, relative retention time or the retention volume. Both non-polar and polar stationary phases are used to indicate the nature of the unknown substance. Wehrli and Kovats[1] have shown a relation between the structure of the substance and its retention values on two such phases. Stationary phase liquids which can take part in electron donor–electron acceptor interactions have also been used by Langer *et al.*[2] and Janak and Hrivnac[3] to separate closely similar pairs of compounds. I have also found[4] three different stationary phases to be useful in identifying components of a brown coal tar.

A method has been developed for the identification of compounds by gas chromatography alone using three stationary phases; one non-polar, one an electron donor and one an electron acceptor.

If r_1, r_2 and r_3 are the retention times (or volumes) of a substance on the three stationary phases 1, 2 and 3 under fixed conditions, we can define an 'affinity fraction' A of the substance for each phase. For phase 1 we have $A_1 = r_1/(r_1 + r_2 + r_3)$. This enables the data for a particular substance to be plotted as a point on a triangular graph.

The retention value r_b of a compound a on stationary phase b under a fixed set of conditions is proportional to $RT/(\gamma^0_a p^0_a)$, where γ^0_a is the activity coefficient of a at infinite dilution in b and p^0_a is the vapour pressure of a at column temperature. For ideal solution behaviour r_b is governed by p^0_a. In non-ideal solution the value of γ^0_a is governed by the balance of interaction energies E between like

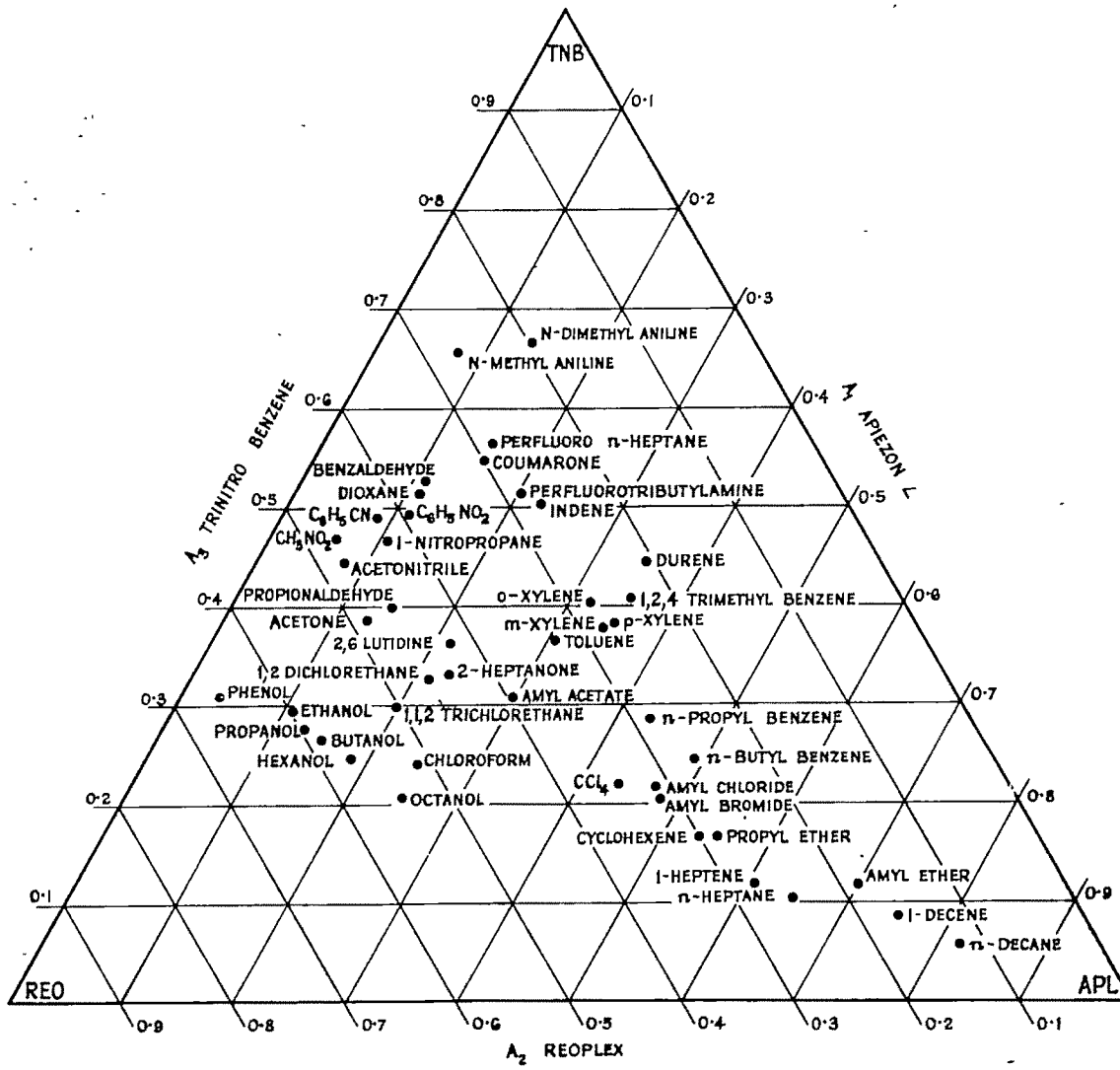

Fig. 1

and unlike molecules. For the simple case of a regular solution $\gamma^{\infty}_a = \exp(w/RT)$, where w is proportional to $(E_{aa} + E_{bb} - 2E_{ab})$. Thus a strong specific interaction of donor-acceptor type between the substance and the stationary phase liquid leads to a large retention value.

Retention times were measured for a number of substances at 125° C. on three 2·5-m. columns each containing 1·5 gm. of stationary phase on 9 gm. of 'Celite 545' using a nitrogen inlet pressure 1,000 mm. mercury above the outlet pressure, which was atmospheric. The A values for the substances were calculated and are shown in Fig. 1, where A_1 refers to 'Apiezon L', A_2 to 'Reoplex 400', polyester (electron donor) and A_3 to 1,3,5-trinitrobenzene (electron acceptor). Substances with low polarity have high values of A_1; $1/A_1$ is approximately proportional to the dielectric constant of the substances chromatographed. Compounds with a protonic function (electron acceptors) have high values of A_2 and substances which can act as electron donors have high values of A_3. Thus each compound has a position on the graph governed by its electron acceptor–donor properties and the group of points for each homologous series of compounds lie on a line pointing towards the 'Apiezon L' apex.

This method, together with the use of the three individual retention values, is being applied to the identification of the components of coal tar and should prove useful in the identification of the degradation products of other substances of low volatility. The method should prove useful in studying the electron donor and acceptor properties of volatile substances and of non-volatile liquids used as stationary phases. Further applications may be possible in interpreting and predicting the course of organic substitution reactions which are governed by the electron distribution in the reacting molecules.

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Some Experiments on Rice's Blue Material: Colours on Jupiter

Clarke and McTurk[1] have recently claimed that Rice's blue material can be prepared by passing ammonia through an electrical discharge tube and partially freezing out the decomposition products on a cold finger, placed about 2 cm. from the nearest electrode.

Since this observation conflicts with the results of extensive experiments carried out earlier by Rice and Freamo[2], we repeated the work of Clarke and McTurk; but, in spite of intensive effort, we have been unable to produce the blue material from ammonia. We realize, of course, that the negative results reported in this communication, as well as those of Rice and Freamo, do not prove conclusively that the blue material cannot be formed from ammonia using the above technique, since the conditions may be very critical and difficult to duplicate.

In our experiments we used tank anhydrous ammonia as supplied by the Matheson Co. The ammonia was passed, at pressures varying from 0·1 to 2·0 mm. of mercury, through an a.c. discharge powered by a transformer rated at 10,000 V. and 50 m.amp. current. The power supply to the discharge tube could be diminished at will be means of a Variac placed between the primary coil of the transformer and the power source. The products from the discharge were partially frozen out on a cold finger at 77° K., which was about 2 cm. from the nearest electrode. In each series of experiments a discharge tube of different dimensions was used, the length being varied from 9 in. to 8 ft., the diameter from 1 to 3 cm. The electrodes were of iron except for a few experiments in which aluminium electrodes were used.

If hydrazoic acid were substituted for ammonia, we always obtained the characteristic blue deposit on the cold finger except when the current density was sufficiently high to decompose all the hydrazoic acid. Whenever this occurred, we could always obtain the blue colour by diminishing the voltage supplied to the primary of the transformer.

Since Clarke and McTurk report: "In one experiment the uncondensed gas was sampled and found by mass spectrograph to be largely hydrogen, with small amounts of nitrogen and oxygen in the ratio of 4 : 1", we assumed that air leaked into their apparatus, and that possibly nitrogen trioxide was formed; this is blue when condensed on a surface cooled with liquid nitrogen. We, therefore, did a whole series of runs in which mixtures of ammonia and air were passed through the discharge tube, but we never succeeded in obtaining a blue deposit. We did a few experiments in which we mixed nitric oxide with small quantities (about 10 per cent) of air and passed the gas mixture, without any discharge, on to the cold finger. Under these conditions we did obtain a blue deposit of nitrogen trioxide which in colour and in its behaviour on warming could have been mistaken for the blue material. However, we never succeeded in finding any conditions under which nitrogen trioxide could be frozen out from mixtures of ammonia and air or nitrogen and water vapour on passage through a discharge tube.

These experiments on nitrogen oxides are of some importance in connexion with colours on Jupiter[3]. Recently, Kiess *et al.*[4] have shown that oxides of nitrogen are present on the atmosphere of Mars, and the suggestion has been made that the colours on Jupiter are due to frozen-out oxides of nitrogen, even though Jupiter is a 'reduced' planet. It is conceivable that non-equilibrium conditions exist on Jupiter and that the violent electrical storms might possibly result in the freezing-out of oxides of nitrogen formed by reaction of nitrogen atoms and oxygen atoms. The oxygen atoms would presumably result from the dissociation of water which may be whirled about in the turbulent Jovian atmosphere as tiny ice particles.

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BIOCHEMISTRY

Metabolism of β-Sitosterol and Other Lipids in the Presence of Acetate-2-^{14}C by Blowfly Larvæ

It has been shown recently that the ability to convert C_{28-29} sterols to cholesterol is likely to be a general attribute of phytophagous insect larvæ[1]. In the case of β-sitosterol, this conversion could occur either by removal of the side-chain and *de novo* synthesis of the cholesterol side-chain or by elimination of the supernumerary carbon atoms to yield the *iso*-octyl side-chain. Enzymes capable of cleaving the side-chain of sterols are known to occur in mammals[2] and certain bacteria[3].

Although blowfly larvæ are not as efficient in converting sitosterol into cholesterol as obligatory plant feeders, they were selected for the present work because they grow sufficiently rapidly to avoid randomization of the isotopic carbon; they also grow readily on a synthetic diet and under aseptic conditions.

Larvæ of *Calliphora erythrocephala* were reared at 29° aseptically[4] at a density of seven animals per 10 gm. of a synthetic diet[5] in which cholesterol was replaced by purified β-sitosterol (m.p. 140°; $[\alpha]_D$–36). Sodium acetate-2-^{14}C was diluted with carrier acetate and 2·5 mgm. added to 40 gm. of this diet, amounting to a concentration of 6·25 mgm. per cent; the specific activity of the sodium acetate was 12 μc./mgm. The diet was continuously aerated with air free from carbon dioxide and kept in darkness during the 6 days of larval growth. At the end of this period the 27 surviving animals had attained their maximum body-weight (mean larval weight, 92 mgm.) and were used for analyses; the radioactivity of the samples was measured with a thin end-mica window tube with an accuracy of ± 5 per cent and corrected for self-absorption in the usual manner.

The desiccated larvæ (578 mgm.) contained 19·7 per cent of ethylether – chloroform – acetone-extractable lipids, of which 83·6 per cent consisted of fatty acids and 11·5 per cent of unsaponifiable matter; of the latter, 10·7 per cent were recovered as sterols, precipitable by digitonin. Table 1 shows the radioactivity of the various fractions. The most

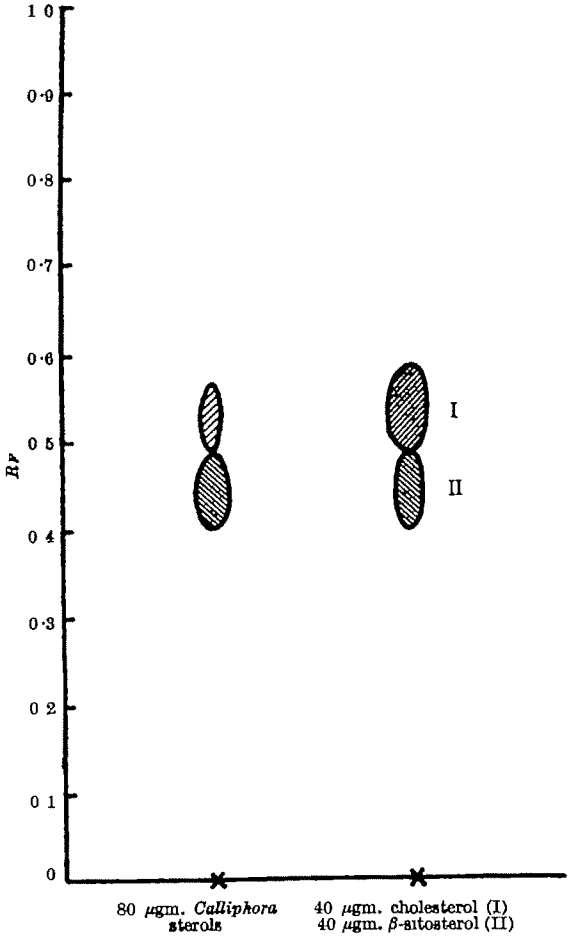

Fig. 1. Reversed-phase chromatogram of *Calliphora* sterols on Whatman paper No. 3, impregnated with 5 per cent paraffin, B.P.; ascending run for 17 hr. in ethylene glycol–mono-ethyl ether – abs. methanol – n-propanol – water (32 . 5 . 35 : 15 : 17 5). Chromatogram sprayed with antimony trichloride solution in chloroform and warmed for 2 min. on hot plate

striking feature is the negligible activity of the sterols. Moreover, the latter, when chromatographed on paraffin-impregnated filter paper[6] to separate the newly formed cholesterol from β-sitosterol (Fig. 1), did not show any radioactivity on X-ray films ('Kodirex'), after an exposure of 6 weeks. These findings not only confirm that *Calliphora* larvæ, like *Dermestes vulpinus*[7], are unable to synthesize sterols from ^{14}C-acetate, but indicate also that the cholesterol side-chain is not formed by re-synthesis from acetate, but rather by de-ethylation of the β-sitosterol side-chain at position C_{24}. An analogous de-methylation of ergosterol has been shown to occur in nymphs of *Blattella germanica*[8]. On the other hand, it has been claimed that adult *Periplaneta americana* incorporate ^{14}C-labelled acetate into their tissue sterols[9].

The results in Table 1 suggest that acetate is being utilized at least as efficiently for the biosynthesis of fatty acids as for the biosynthesis of the unsaponifiable matter, other than sterols; about 2·3 parts of acetate were incorporated into 1,000 parts of fatty acids. The remainder of these must be derived from other carbon sources, which in the absence of glucose in the diet[5] are obviously amino-acids. A similar observation has been made with housefly larvæ reared on a carbohydrate-free medium[4]. Adults of *Prodenia eridania* have been found to synthesize long-chain fatty acids also from acetate, which was better utilized than glucose[10].

Table 1. DISTRIBUTION OF RADIOACTIVITY IN BLOWFLY LARVÆ GIVEN ACETATE-2-^{14}C IN THE DIET

Material	Radioactivity		
	Specific activity (mμc./mgm.)	Total (mμc.)	Percentage of dietary acetate-2-^{14}C
Total lipids	25 3	2,884	9 6
Unsaponifiable matter	22 4	293	1 0
Digitonin-precipitable sterols	0 3	0 4	0·001
Digitonin-non-precipitable	21 1	181	0 6
Fatty acids	27 8	2,649	8 8
Lipid-free residue	1 0	464	1 5
Total carbon dioxide expired by larvæ	—	314	1 0

Significant amounts of carbon-14 were incorporated into the unsaponifiable lipids, other than sterols; this uptake amounted to an incorporation of 1·7 parts acetate in 1,000 parts of the digitonin-non-precipitable, unsaponifiable matter. This fraction could be separated by reversed-phase paper-chromatography[6] into 4 radioactive spots, *A*—*D*, with R_F 0·65, 0·74, 0·89 and 0·97, respectively; the spots *B* and *C* were the most radioactive ones (Fig. 2). Preliminary infra-red analyses on this fraction, kindly performed by Dr. N. Sheppard, showed a spectrum of a compound with an aliphatic hydrocarbon chain, particularly of a long-chain carboxylic acid (shoulder towards 2,650 cm.$^{-1}$ due to stretching of —OH, peak at 1,707 cm.$^{-1}$ of —C=O from —COOH, shoulder at 1,415 cm.$^{-1}$ for —CH_2—[C=O], peak at 1,287 cm.$^{-1}$ with shoulders due to —C—OH of —COOH, and peak at 933 cm.$^{-1}$ due to —OH of —COOH, angle-bending

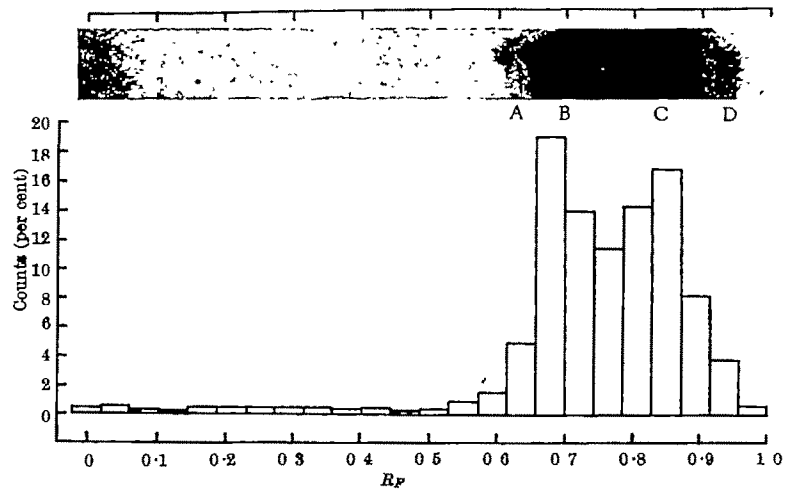

Fig. 2. Autoradiogram and counts of the reversed-phase chromatogram of the unsaponifiable, digitonin-non-precipitable matter (790 μgm.) of *Calliphora* larvæ. Whatman paper No. 3, impregnated with 5 per cent paraffin, B.P.; ascending run for 17 hr. in abs. methanol–n-propanol–water (80 15. 5)

vibration). There was no indication of the presence of an aldehydic or keto group. Branched —CH_3, if any, were few (a small peak at 1,377 cm.$^{-1}$). The presence of double bonds could not be ruled out as the —C=C— frequency could have been hidden by the large —CO peak centred at 1,707 cm.$^{-1}$. Peaks at 717, 1,465, 2,850 and 2,930 cm.$^{-1}$ indicated a fair amount of CH_2 groups in an alkyl chain of considerable length. The nuclear resonance spectrum was consistent with that obtained by infra-red light; four peaks were observed (a weak one in the position of —CH=C, stronger bands due to —CH_2—[C=O], alkyl chain —CH_2 and a few terminal —CH_3) The ultra-violet spectrum showed ill-defined shoulders at 220 and 250 mμ.

The larvæ still contained significant amounts of radioactivity after removal of their lipids; one can therefore assume that acetate was used also for the synthesis of non-lipidic constituents of the body. The ability of *Calliphora* larvæ to incorporate ammonia into alanine, glutamic and aspartic acids[5] should be recalled in this respect.

The total barium carbonate derived from the expired carbon dioxide was 2·48 gm. for 27 surviving larvæ during 6 days. The expired carbon dioxide amounted thus to 20·5 mgm./6 days/larva or to an average of 3·2 μmoles (72 μl.) carbon dioxide/hr./larva, out of which, according to the carbon-14 count, only 1 part in 2,000 could have been derived from acetate-2-^{14}C, the rest from other carbon sources.

We wish to thank Dr. N. Sheppard for the analyses and interpretation of the infra-red and nuclear resonance spectra. One of us (Z. H. L.) wishes to acknowledge a Sir Simon Marks Fellowship awarded by the Research Council of Israel.

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Immunoelectrophoresis of Human Sera with Antiserum to Raben Growth Hormone

During investigations in progress using the immunological method for the assay of growth hormone in human serum[1,2], attempts have been made to show a reaction between human sera and rabbit antiserum to the Raben preparation of human growth hormone, made in Cambridge, in Ouchterlony plates and on electrophoretic strips.

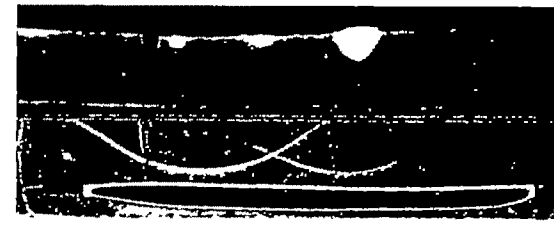
On micro-immunoelectrophoresis in agar gel[3], human serum gave a precipitin line with the antiserum in a position corresponding with the albumen band. This line was found when normal sera and when various sera including those from acromegalic and myxœdemic patients were tested against antiserum prepared from each of four rabbits. Serum from normal non-immunized rabbits and from rabbits injected with the adjuvant mixture alone did not give this line.

Each of the four rabbits was immunized by a primary injection of 1 mgm. of Raben human growth hormone in water-in-oil emulsion ('Arlacel *A*'/'Bayol *F*') containing 200 μgm. of purified glycolipid of *Mycobacterium tuberculosis* strain 'Test', followed by a secondary injection at multiple sites six weeks later of a total of 0·5 mgm. of Raben growth hormone adsorbed to aluminium phosphate. The sera from animals bled 10 days later yielded hæmagglutination titres[2] of 1/800–1/9,600.

The line described above does not appear after absorption of the antiserum with Raben growth hormone, and evidently its formation is dependent on antibody formed against a component of Raben growth hormone. No reaction has been found against other components of human serum, such as were described by Hirschfeld *et al.*[4] using antisera to a Li and Papkoff[5] preparation of human growth hormone.

By the Ouchterlony technique, Li *et al.*[6] described reactions of identity between human growth hormone and pituitary mash put up against rabbit antiserum to growth hormone. On immunoelectrophoresis of Raben growth hormone mixed with human serum the present investigation has shown the formation of single precipitin lines against both the albumen and the Raben growth hormone bands. Identical lines were obtained on immunoelectrophoresis of human pituitary mashed in saline. Addition of human serum to the pituitary mash before immunoelectrophoresis failed to produce more than one line against the albumen band, so that the appearance of this line in the pituitary mash could be due to the contained serum. These lines clearly crossed in each of the above experiments (Fig. 1), indicating non-identity of the antigen antibody systems. In Ouchterlony plates the precipitin lines against human serum and Raben growth hormone failed to show a reaction of identity.

It is of interest that Gemzell[7] has reported biological growth hormone activity in a precipitate of human serum proteins composed mainly of albumen. Human serum albumen (kindly provided by the Lister Institute) was found to react with the four rabbit



A *B*

Fig. 1. Immunoelectrophoresis of human pituitary mashed in saline, with the rabbit antiserum to Raben human growth hormone, showing precipitin lines against the growth hormone (*A*) and albumen (*B*) bands, which clearly cross Half an identical electrophoretic run is shown stained with nigrosin to demonstrate the protein bands

antisera. After absorption of the antisera with the albumen, precipitin lines still appeared against the Raben growth hormone but not against the albumen band in serum. Following pituitary destruction in two cases in which the immunological assay for growth hormone fell considerably, the precipitin line against the albumen spot cannot be demonstrated.

These results could depend on the contamination of Raben human growth hormone with human serum albumen; but these investigations have not excluded the possibility that a component of human growth hormone is carried *in vivo* on the serum albumen or that the second protein present in the Raben growth hormone is also dependent on the pituitary.

The presence of an immunologically active contaminant in the growth hormone used as antigen might invalidate an immunological method of assaying growth hormone in human serum, unless the non-specific antibody could be absorbed out, as seems possible from the experiment described above. If the reactive material in serum is considered to be growth hormone then it is so immunologically distinct from that prepared from the pituitary that the immunological assay using pituitary growth hormone as a standard may not give absolute or even comparative values for levels of growth hormone in serum.

Various investigations are in progress for the elucidation of these phenomena.

I thank Prof. C. Wilson for his encouragement and advice and Dr. R. G. White and Dr. A. Stuart Mason for much constructive guidance and criticism. The Raben preparation of human growth hormone was kindly made available by the Medical Research Council Committee on Human Growth Hormone.

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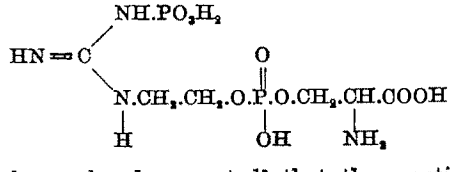
Synthesis of N-Phosphoryl-D- and L-Lombricine

THE isolation of the phosphagen of the earthworm in an impure form was reported by Thoai *et al.*[1] in 1953. The compound was Sakaguchi-negative[2] and on mild acid hydrolysis yielded equimolar proportions of phosphoric acid and lombricine (2-amino-2-carboxyethyl 2-guanidinoethyl hydrogen phosphate). It was concluded that the compound had the following structure:



We have already reported[3] that the reaction of N-phosphoryl-O-methylurea[4] with 2-amino-2-carboxyethyl 2-aminoethyl hydrogen phosphate (serine ethanolamine phosphodiester) leads to the formation of a compound with properties similar to those of the substance isolated from earthworms by Thoai *et al.*[1]. The product resulting from the use of L-serine ethanolamine phosphodiester in this reaction has now been isolated by fractionation of the reaction mixture on 'Dowex-50 (H^+)' ion-exchange resin. It was obtained in 70 per cent yield as an amorphous ammonium salt, which was converted to a microcrystalline powder by recrystallization from aqueous methanol. Titration and elementary analytical data are in agreement with this material, being a mixture of the mono- and di-ammonium salts of L-2-amino-2-carboxyethyl 2-N-phosphorylguanidinoethyl hydrogen phosphate. Analysis: calculated for a mixture of 1 part of the monoammonium salt ($C_6H_{15}O_9N_4P_2.NH_4.\frac{1}{2}CH_3OH$) and 4 parts of the diammonium salt ($C_6H_{14}O_9N_4P_2.2NH_4.\frac{1}{2}CH_3OH$): C, 19·67; H, 5·94; N, 20·47; P, 15·61 per cent; found: C, 19·55; H, 5·96; N, 20·10; P, 15·54 per cent. pK_a values (potentiometric): *c.* 2, 4·6 and *c.* 8·8; as the substance was in the form of its ammonium salt the pK_a of the guanidino group could not be determined. It had main infra-red absorption peaks at 777, 969, 1,056, 1,084, 1,220, 1,309, 1,349, 1,413, 1,458, 1,628, 3,020 and 3,180 cm.$^{-1}$.

The product did not react with the Sakaguchi[5] or α-naphthol/diacetyl[6] reagent, but did react with ninhydrin and the molybdate reagent[7] for phosphate. On paper chromatography in a number of solvent systems it was homogeneous in respect to the latter two reagents. Hydrolysis in 0·1 *N* hydrochloric acid for 1 min. at 100° caused complete conversion to phosphoric acid and a guanidine base behaving as lombricine on paper chromatography. The base was further characterized as lombricine by its behaviour on nitrous acid degradation[3]. Thus, guanidination with N-phosphoryl-O-methylurea occurs preferentially, as it does with O-methylurea[2,3], at the terminal amino group of serine ethanolamine phosphodiester.

Direct phosphorylation of D-lombricine (isolated from earthworms) with phosphoryl chloride in strongly alkaline solution gave in 13 per cent yield a product (isolated similarly as an essentially diammonium salt) which was Sakaguchi- and α-naphthol/diacetyl-negative and had an infra-red spectrum and R_F and pK_a values identical with those found for the product described above. The isolation of natural material for comparison with the synthetic compounds is in progress.

The method of synthesis of the product obtained from serine ethanolamine phosphodiester establishes that the phosphoryl residue is located on one of the two unsubstituted nitrogen atoms of the guanidino group of lombricine; because of resonance within the zwitterionic phosphorylguanidinium group[9] these two positions are identical. That the phosphoryl residue in the product obtained by the phosphorylation of lombricine occupies a similar position is shown by the identity of the infra-red spectra of the two compounds. It may be concluded, therefore, that both products have the structure shown.

The general question of the precise location of the phosphoryl group of phosphagens derived from monoalkylguanidines, and of the identity of the natural and synthetic preparations, will be discussed at greater length in a subsequent communication. It is, however, relevant to point out here that with

the exception of the two synthetic preparations described above and the N-phosphorylglycocyamine recently synthesized by Cramer and Vollmar[10] via N-diphenylphosphoryl-S-methylurea, the accepted position for the phosphoryl residue in all these preparations—on one of the unsubstituted nitrogen atoms of the guanidino group of the parent base—although perhaps correct, remains unproved. Thus it appears that the only direct evidence in support of this formulation is based on the fact that phosphagens do not give a colour reaction with the α-naphthol/diacetyl reagent, and on the supposition[11] that N-phosphorylguanidines will show the same specificity towards this reagent as do simple alkylguanidines, of which only the mono- and *asym* di-substituted react[12]. That this supposition is unwarranted follows from an observation made in the course of the present work that phosphorylguanidine itself (prepared by the method of Cramer and Vollmar[9], or by treating N-phosphoryl-O-methylurea with aqueous ammonia) gives no colour reaction with this reagent.

With the exception noted above[10], previous syntheses of phosphagens derived from monoalkylguanidines have invariably involved the reaction of phosphoryl chloride with the guanidine base in a strongly alkaline medium. It would seem likely, by analogy with the structure of the phosphorylation product of lombricine, that the phosphoryl group of these products is, indeed, in the accepted position, that is, on one of the unsubstituted nitrogen atoms of the guanidino group of the parent base. Although these synthetic preparations have been claimed[11] to be identical with the natural, there seems insufficient evidence available at present to warrant any definite conclusion on this point.

These questions are now under investigation and the results, together with a complete account of the present work, will be published elsewhere, but already from the work reported here, the potential value of the synthetic method involving N-phosphoryl-O-methylurea and its derivatives in orientating the phosphoryl residue throughout this group of naturally occurring compounds is clear.

We are indebted to Dr. J. E. Fildes and staff, to Dr. E. Spinner and Mr. D. T. Light, and to Dr. D. Perrin and Mr. H. Satrapa, of the Department of Medical Chemistry, for microanalyses, infra-red spectra and pK_a determinations, respectively.

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Synthesis of Thiamine and Folic Acid by *Nocardia rhodnii*, the Micro-symbiont of *Rhodnius prolixus*

STRONG suggestive evidence[1] exists to support earlier proposals[2] that *Nocardia rhodnii*, the extracellular symbiont of *Rhodnius*, contributes essential food factors to its host. In recent years, however, the evidence has been conflicting, particularly where it concerns the nature of these factors. In 1954, Geigy, Halff and Kocher[3] isolated a micro-organism from *Triatoma infestans* similar to *N. rhodnii* and found that whereas it synthesized thiamine and other vitamins in minimal amounts, there was a 2,500-fold hyper-production of folic acid. Bewig and Schwartz[4], however, later claimed that this organism was not *N. rhodnii*, and was not symbiotic. They showed that pure cultures of *N. rhodnii* on an elaborate semi-synthetic medium synthesized minimal amounts of folic acid, no vitamin B_{12} and no folininic acid. They found too that injection of vitamins into sterile *Rhodnius* failed to induce moulting. In 1956 Baines[5], using feeding and injection techniques, came to the conclusion that *Rhodnius* is dependent on *N. rhodnii* for pyridoxine, calcium pantothenate, nicotinamide and thiamine, but that biotin and folic acid are present in adequate concentration in the host blood to meet the requirements of *Rhodnius*.

The two experiments described here attempt to throw further light on the synthesis of folic acid and thiamine by *N. rhodnii* and *Rhodnius*. Techniques involving the injection of vitamins into insect or mammalian host were avoided. In the first experiment, the vitamins were fed artificially to sterile bugs using my technique[6], and in the second the synthesis of the two vitamins by *N. rhodnii* was determined microbiologically[7].

Exp. 1. The effect of rabbit blood supplemented with folic acid and/or thiamine, as a diet for sterile 4th instar *Rhodnius*.

Sterile insects do not respond well to artificial feeding, and only small volumes of blood are usually ingested. This difficulty was overcome by adding the test vitamins to oxalated horse blood in such concentrations that the small amount of blood taken in would contain approximately the quantity of vitamins required for the experiment. The weight of blood ingested, and hence the amount of vitamin, was determined by rapidly weighing the bugs before

Table 1. EFFECT OF FOLIC ACID AND/OR THIAMINE ON THE MOULTING OF STERILE 4TH INSTAR *Rhodnius* FED ON SMALL AMOUNTS OF HORSE BLOOD CONTAINING THE VITAMINS, FOLLOWED BY CAPACITY MEALS ON THE RABBIT EAR

Group	Diet	No. used	Mean amount of vitamins introduced (μgm.)	Effect
A	(Horse blood) + full feed on rabbit	8	—	No moults in 70 days
B	(Horse blood + folic acid) + full feed on rabbit	2	0·035	No moults in 70 days
C	(Horse blood + thiamine) + full feed on rabbit	2	0 18	Both moulted in 41 and 53 days
D	(Horse blood + folic acid + thiamine) + full feed on rabbit	2	0 02 folic acid 0 075 thiamine	Both moulted in 15 and 26 days
E	Full feed on rabbit (normal, infected bugs)	98	—	Mean moult period: 15·5 days

and after feeding. The amount of blood ingested represented about 25 per cent of a capacity blood meal. After weighing, the bugs were placed on the ear of a rabbit when they fed to repletion. The results show that the amount of horse blood introduced into the bugs before the rabbit feed does not affect the time of moulting of the experimental insects.

The results analysed statistically show that the delay in groups *A* and *B* compared with the control, *E*, is readily apparent. It is also significant, in the main, for group *C*; for group *D*, any delay in moulting must remain in doubt. It also seems apparent that folic acid and thiamine together have a far more significant effect than either vitamin alone.

Exp. 2. Quantitative microbiological estimations of thiamine and folic acid synthesis by *N. rhodnii* in sterile horse blood.

Pure cultures of *N. rhodnii* were isolated from infected bugs and kept at 30° on nutrient agar slopes. Microscopical examination did not show any accompanying organisms. Sterile horse blood was chosen as the culture medium as blood is the natural substrate of *N. rhodnii* in the *Rhodnius* gut. 1 day before the commencement of the experiment, a sub-culture from the original agar slopes was transferred to a liver peptone broth and incubated at 30°. On the first day the culture from this broth was washed with, and suspended in, isotonic saline. Three drops of this pure culture in suspension were used as the inoculum, and were added to two of three tubes of 5 ml. freshly drawn, sterile horse blood. The third sample of blood was not inoculated and served as the control.

Levels of thiamine and folic acid in control and inoculated groups were determined at the beginning of the experiment and after 3 and 7 days (Table 2).

Table 2. VITAMIN SYNTHESIS BY *N. rhodnii* IN HORSE BLOOD (Values expressed as mγ/ml.)

Time in days after inoculation	Thiamine		Folic acid	
	Normal blood control	Inoculated blood	Normal blood control	Inoculated blood
First	36	—	28	—
Third	33	35	32	71
Seventh	41	96	29	122
	37 (mean)	—	30 (mean)	—

The results show that by the seventh day there is a 2·6-fold increase in the thiamine-level in the inoculated blood over that in pure, *Nocardia*-free blood, and a 4-fold increase of folic acid. Using Bewig and Schwartz's figure[6] for the folic acid requirements of *N. rhodnii* as 0·1 mγ/cm.^{3}, it can be seen that in the present experiments this organism produces about 920 times its own requirements of folic acid. Without knowing the thiamine requirements of the organism, it is not yet possible to determine what excess of this vitamin is produced.

It therefore seems likely that both folic acid and thiamine are synthesized by *N. rhodnii* in such amounts that the excess over the organism's own requirements could be made available to its host for its satisfactory growth and development.

This work forms part of a study for the degree of Ph.D. of the University of London, and was carried out under the late Prof. P. A. Buxton, whose helpful criticisms, together with those of the present head of the Department, Prof. D. S. Bertram, I much appreciate. It was financed by the South African Council for Scientific and Industrial Research, the support of which I wish to acknowledge.

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Effect of Degeneration on the 'Albumin' Components of Human Muscle Extracts

JACOB[1] showed that a fast-moving group of proteins, which he called group III, was observed when low ionic strength extracts of rabbit striated muscle were subjected to moving boundary electrophoresis. The group consisted of a major and a minor component; the major component, unlike the minor, was soluble in distilled water and he considered that it probably corresponded to the myoalbumin described by Bate-Smith[2]. Subsequent reports[3-5] have claimed that this group increases relative to other proteins in the muscle extracts when the striated muscle of various species, including man, degenerates as a result of pathological and experimental lesions. The increase has been attributed to an increase of myoalbumin. Recently, Corsi and Buscaino[6] have pointed out that much of the group III fraction is likely to consist of serum albumin. However, since the electrophoretic techniques used previously appear to have resolved only one albumin component, interpretation of the results is ambiguous. In view of this the following preliminary observations may be of interest.

I have recently described[7] the use of starch-gel electrophoresis by Smithies's method[8] for the separation of the human muscle proteins which are soluble at low ionic strength. At that time the occasional separation of the albumin fraction into two components was reported; in this context, by the albumin fraction is meant the fastest-moving fraction seen after starch-gel electrophoresis and which has albumin-like solubility characteristics. When separation occurred the slower component moved at the same speed as serum albumin. Further investigation has defined the conditions under which the albumin fraction of muscle extracts can be invariably separated into two components. Both components, like the major component of Jacob's group III, are soluble in ion-free water. Although the relative amounts of the two components vary considerably, some peroxidase activity is always associated with the faster component, but not with the slower under the conditions of the present experiments. The significance of this observation is as yet unknown, and it is included merely as indicating a

dissimilarity, other than in electrophoretic mobility, between serum albumin and the muscle protein.

The factors influencing the speed of migration of proteins on starch may be rather complex[8]; nevertheless, the relative mobilities are such as to suggest that the faster component may be myoalbumin, since Bate-Smith[2] showed that this had a lower isoelectric point than the corresponding serum albumin.

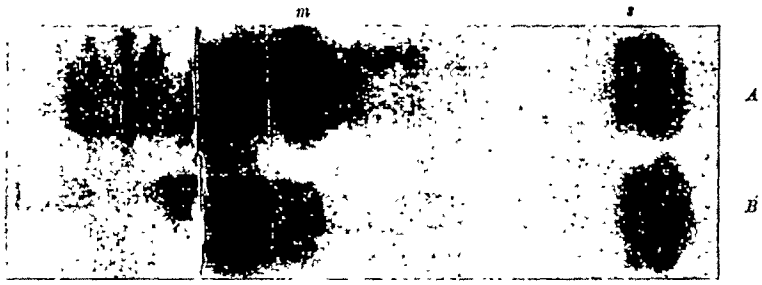

Fig. 1. Starch electropherogram of two muscle extracts run in parallel: *A*, Normal muscle; *B*, atrophied muscle. Buffer, 0·03 *M* *tris*-(hydroxymethyl) amino methane/hydrochloric acid, *p*H 7·7. *m*, Myoglobin; *s*, serum albumin

Fig. 1 is a photograph of a starch-gel electropherogram in which low ionic-strength extracts of a normal (*A*) and an atrophied human muscle (*B*) have been run side by side. Atrophy in this case had resulted from severe chronic denervation. Several components, for example the myoglobin band, have largely disappeared from the electropherogram of the atrophied muscle; but the bands due to the albumin components are of similar intensity in the two cases and hence these components are proportionately increased. Although the relative amounts of the two albumins are not always quite the same as in the example shown, nevertheless, when muscle degeneration is accompanied by a marked reduction in the intensity of certain characteristic bands on the starch electropherogram, no obvious reduction in the intensity of either albumin band occurs. The proportionate increase in serum albumin probably reflects a decrease in the intracellular space relative to the extra-cellular space resulting from destruction of muscle cells. On the other hand, the increase in the faster component, which may be human myoalbumin, is understandable if it represents, as Fischer[3] has suggested, a breakdown product of other muscle proteins.

This work, which is continuing and will be reported in detail elsewhere, was supported by a research fellowship of the Mason (Chiswick) Medical Research Trust.

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Characterization of Deoxyribonucleic Acid from *Anacystis nidulans*

THE chemical nature of deoxyribonucleic acid in blue-green algæ was not known until very recently[1-3]. This communication deals with a quantitative study of deoxyribonucleic acid from *Anacystis nidulans* and its characterization in respect to that from other sources. *Anacystis nidulans* and *Chlorella ellipsoidea* were grown in continuous culture chambers as described earlier[4,5]. The algal cells were treated with cold 10 per cent trichloracetic acid, 95 per cent alcohol, alcohol/ether (3 : 1) and finally with ether until all the pigments except phycobilins were fully extracted. Deoxyribonucleic acid was isolated by one of the following procedures: (*a*) with 10 per cent sodium chloride (2 ml./10 mgm.) three times by refluxing at 80° C. for 1 hr. each time[6]; (*b*) with 1 *N* potassium hydroxide at room temperature[7]; (*c*) with 0·5 *M* perchloric acid[8]. Purification of deoxyribonucleic acid from protein and polysaccharide was done according to the methods described earlier[9]. Chromatographic analyses were done according to Wyatt[10]. Purines and pyrimidines were estimated by maximum extinction technique[11]. With different procedures of extraction it has been observed that the yield of purified deoxyribonucleic acid varies from 3·7 to 4·7 per cent of the dried cells after ether wash. The fresh weight of the cells was found to be 5 times that of the dried ether-washed cells and hence deoxyribonucleic acid constitutes 0·73–0·94 per cent of the fresh weight of the cells. Nitrogen content varies from 13·9 to 14·3 per cent and that of phosphorus from 6·8 to 8·2 per cent with different procedures of isolation. Deoxyribonucleic acid is found to have an absorption maximum at 257 mμ and minimum at 230 mμ. The infra-red spectrum of deoxyribonucleic acid from *Anacystis* does not show any remarkable deviations from those of other sources. The main peaks are at 3, 6·1, 8·1 and 9·3–9·8μ. The percentage of molar ratios of constituent bases, guanine, adenine, cytosine and thymine, in deoxyribonucleic acid of *Anacystis* was found to be 29·5, 23·3, 24·8, and 22·3 respectively. The ratios of G/C, A/T and Pu/Py were 1·19, 1·04 and 1·12 respectively. The average values only have been recorded here. The deviation of unity in base ratio in this case is very difficult to explain at present, though the presence of single-stranded deoxyribonucleic acid which has recently been isolated from bacteriophage[12] cannot be ruled out. The (A + T)/(G + C) ratio may be used as a species parameter. In the case of *Anacystis nidulans* this was found to be about 0·82.

The deoxyribonucleic acid from *Anacystis nidulans*, *Chlorella ellipsoidea* and sperm (obtained from Nutritional Biochemical Corporation, Cleveland, Ohio) was degraded with deoxyribonuclease in the following way. 48 mgm. deoxyribonucleic acid, 1·28 mgm. deoxyribonuclease in 0·003 *M* magnesium sulphate and 0·02 *M* phosphate buffer *p*H 7·6, total volume being 4·8 ml., was incubated at 37° C. for 24 hr. The deoxyribonuclease hydrolysate was chromatographed in *iso*propanol/water (7 : 3) with ammonia in vapour phase[13]. The incubation of

Table 1. MOLAR PROPORTIONS OF BASES IN THE FIRST BAND AFTER CHROMATOGRAPHIC SEPARATION OF DEOXYRIBONUCLEASE HYDROLYSATE AND IN THE CORE AFTER 24 HR. OF DEOXYRIBONUCLEASE TREATMENT AND DIALYSIS

	Source	G	A	C	T	G/C	A/T	Pu/Py
First band	*Anacystis nidulans*	32 5	23·5	25 5	18 5	1·27	1·27	1·27
Core, 18–20 per cent	*Anacystis nidulans*	33 5	23 2	24 5	18·7	1 37	1·24	1·31
First band	*Chlorella ellipsoidea*	33·0	22·0	23·0	22 0	1 50	1 00	1 22
Core, 18–20 per cent	*Chlorella ellipsoidea*	32 6	23·5	22 5	21·4	1·44	1·10	1·28
First band	Sperm	20 5	36 0	15 5	28 0	1 32	1 28	1·30
Core, 34–40 per cent	Sperm	20·8	39 2	17·6	22 4	1·18	1·75	1·50

First band of deoxyribonuclease hydrolysate after chromatographic separation (*iso*propanol–water, ammonium) was eluted in 0·1 *N* hydrochloric acid, hydrolysed with 12 *N* perchloric acid and the proportion of bases was determined spectrophotometrically. The methylcytosine in the case of sperm deoxyribonucleic acid was not detected after perchloric acid hydrolysis. Core signifies the non-dialysable fraction when digestion was carried out in dialysis tubes against 500 ml. of distilled water. 48 mgm. of deoxyribonucleic acid was used.

Table 2. ELECTROPHORETIC SEPARATION OF CHROMATOGRAPHIC BAND 3 OF THE DEOXYRIBONUCLEASE HYDROLYSATE

Spot No.	Electrophoretic mobility (cm.)	Identity	Source
1	0	pC	*Anacystis*, *Chlorella*, sperm
2	2 5–3 5	pApC	*Anacystis*, *Chlorella*, sperm
3	4 5–5·5	pGpC	*Anacystis*, *Chlorella*, sperm
4	6 5–7·0	pApG	*Anacystis*, sperm
5	12·0–14·0	pT	Sperm

Electrophoresis was carried out at 4° C. in citrate buffer *p*H 3 5 and voltage gradient 15 V./cm. for 2 hr. pC, deoxycytidylic acid; pApC, dinucleotide of deoxyadenylic and deoxycytidylic acids; others are similarly assigned. No sequence of nucleotides is indicated in the case of dinucleotides. The ratio of two bases in the case of dinucleotides was found to be approximately unity.

deoxyribonucleic acid with deoxyribonuclease in the dialysis tube showed that the core, that is, non-dialysable fraction in the case of sperm deoxyribonucleic acid, contains 36–40 per cent of the original deoxyribonucleic acid whereas in the case of *Anacystis* and *Chlorella* it is only 18–20 per cent. In separate experiments deoxyribonucleic acid was incubated with deoxyribonuclease similarly without dialysis and the hydrolysate was chromatographed[12]. Three distinct bands were detected under ultra-violet light and those were designated as band 1, 2, 3 according to their higher migration in the chromatogram. The first band was analysed after elution with 0·1 *N* hydrochloric acid. Molar proportion of bases in the first chromatographic band of hydrolysate and in the core is given in Table 1. In all the samples the ratio of purine to pyrimidine is higher both in the first band and the core. The third chromatographic band was subjected to electrophoresis[13] in citrate buffer *p*H 3·5 and voltage gradient 15 V./cm. for 2 hr. using Spinco paper electrophoresis apparatus. It was observed that the third band after electrophoresis was separated into four spots in the case of *Anacystis*, three spots in the case of *Chlorella* and five spots in the case of sperm. The spots were designated as 1, 2, 3, 4 and 5 according to their higher electrophoretic mobilities. The electrophoretic mobilities of the spots and their probable identities are given in Table 2. Spot 4, which has been identified as dinucleotide of deoxy-adenylic and deoxy-guanylic acids, is absent in the case of *Chlorella*, indicating the occurrence of less adenine guanine linkage than that in *Anacystis* or sperm deoxyribonucleic acid. From this point of view sperm deoxyribonucleic acid differs from that of *Anacystis* in containing a distinct thymidylic acid spot in the third band. In short, it appears that the deoxyribonucleic acid of *Anacystis nidulans* contains more adenine–guanine linkages than that of *Chlorella ellipsoidea* and fewer thymidylic acid units than that of sperm. The analyses of other portions of deoxyribonucleic acid may reveal more differences in the arrangement of the nucleotides in deoxyribonucleic acid of blue-green algae from those of other sources which have chemically identical composition.

Details of this work will be published elsewhere.

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RADIOBIOLOGY

In vitro Uptake of Iodine-131 by Tissues of Rainbow Trout

RECENTLY, it has been shown that *in vitro* uptake of iodine-131 by the lactating mammary tissue of rat was 10–15 times that of liver, muscle or boiled mammary tissue. Further, the data on the *in vitro* uptake of iodine-131 by different tissues of rat indicate that iodide concentration mechanism in the mammary, salivary and gastric glands but not in liver or placenta appears to be similar to that of thyroid gland in the rat[2]. In the case of fish, it has been shown that the thyroid hormone is not involved in the regulation of oxidative metabolism, and thus it was decided to study the *in vitro* uptake of iodine-131 by different tissues of rainbow trout (*Salmo gairdnerii*)[3]. Tissue slices from one-year-old rainbow trout were incubated for 2 hr. at 13° C. in flasks containing 2 ml. Nandi and Bern medium[4]. The *T/M* values (counts per min. per 100 ml. tissue divided by counts per min. per 0·1 ml. medium) for different tissues were calculated.

The values of the ratio T/M for *in vitro* uptake of iodine-131 by different tissues of rainbow trout indicated that only thyroid follicles present in the lower jaw concentrated iodine-131. The T/M value was higher in the case of the posterior part of the lower jaw than the anterior part, indicating that the thyroid follicles are comparatively more numerous in the posterior part. Uptake of iodine-131 was higher in the lower part of the gill than the upper part and this may be due to the presence of some thyroid follicles at the base of the gills where they are attached to the lower jaw. Addition of thiouracil (0·02 mgm./ml.) to the medium did not affect uptake of iodine-131 by thyroid follicles, whereas potassium thiocyanate blocked such uptake by thyroid follicles. The T/M values for uptake of iodine-131 by different organs of the digestive system, kidney, head kidney, liver, spleen, heart muscle, skeletal muscle or brain were less than 1·0, indicating that these organs or tissues have a relatively poor ability to concentrate iodide *in vitro*.

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PHYSIOLOGY

Protein and Lipid Content of *Chlorella vulgaris* in Relation to Light

INCIDENTAL to other work, we have observed an effect of light on *Chlorella vulgaris* which can be interpreted as indicating an influence of different spectral regions on the synthesis of protein and lipid.

A strain of *Chlorella vulgaris* which has been maintained in this laboratory since 1938 was cultured in an inorganic medium consisting of potassium nitrate, 0·025 M; crystalline magnesium sulphate, 0·02 M; potassium dihydrogen phosphate, 0·018 M; crystalline ferrous sulphate, 0·00005 M; and potassium citrate, 0·00005 M. Air, enriched with 5 per cent carbon dioxide, was bubbled through the culture solutions continuously. Duplicate sets of flasks, with an initial population of 100 cells/mm.^{3}, were illuminated continuously at a total incident radiation of 600 foot candles, as measured with a Weston illumination meter, model 603. Illumination for one set was provided by daylight fluorescent lamps and for the other set by tungsten filament lamps.

The wave-length distribution of the radiation was such that, although both sets of cultures received equal total amounts of incident visible radiation, the 'filament' cultures received one-half as much radiation as the 'fluorescent' cultures in the 440–455 mμ region of the spectrum (60 f.c. vs. 120 f.c.) and twenty times as much radiation in the 655–700 mμ region (71 f.c. vs. 3·55 f.c.). Despite the differences in the ratio of red to blue intensities incident on cultures under these light sources (1·18 for the 'filament' and 0·029 for the 'fluorescent'), the total incident radiation in the two regions combined was about the same for both sets of cultures (131 foot candles for the 'filament' and 123·55 for the 'fluorescent').

All cultures were maintained at 23 ± 1° C.

Cell counts were made in duplicate for each culture at approximately 24-hr. intervals by means of a hæmocytometer. Total packed volumes and dry weights were determined in the conventional ways at the end of each experiment (15 days). Total nitrogen and total protein were determined as described by Umbreit[1] and total lipid was determined by the method of Stekol *et al.*[2].

Table 1 shows that the final population achieved, total packed volume, and proteins formed were substantially greater in cultures exposed to the filament source than in those exposed to the fluorescent source. However, the yield of lipid (expressed as per cent of dry weight) was lower in the 'filament' than in the 'fluorescent' cultures. But, despite the difference in percentage yield of lipid, the yield in absolute terms was about 3·4 times greater in the 'filament' cultures because of the greater total growth (2·28 mgm. of lipid/ml. of culture versus 0·67 mgm./ml. of culture).

Table 1. RELATION OF CERTAIN CELL CHARACTERISTICS TO LIGHT SOURCE IN *Chlorella vulgaris*

Characteristic (15-day culture)	Light source: Filament	Light source: Fluorescent	Filament / Fluorescent
Population (cells/mm.^{3})	100,070	70,000	1·43
Packed volume (mm.^{3}/ml.)	14·50	9·00	1·61
Dry weight (mgm./ml. of culture)	10·31	2·31	4·46
Total protein (per cent of dry weight)	49·86 ± 5·23	39·64 ± 5·41	1·26
Total lipid (per cent of dry weight)	22·2 ± 2·89	29·0 ± 1·82	0·76
Total carbohydrate (by difference)	26·48	25·55	1·04

The differences in protein and lipid contents of cells grown under the two different light sources are clearly significant within 95 per cent confidence limits. The critical ratio of protein from 'filament' versus 'fluorescent' cultures was 4·48 (t 0·05 = 2·086). The corresponding value for lipid content was 3·96 (t 0·05 = 2·048).

Peaks in photosynthetic efficiency occur in the 440–455 mμ and in the 650–700 mμ regions[3]; but what effect, if any, these wave-lengths may have on subsequent biochemical conversion of the primary products of photosynthesis is not known. The present experiments show that, with the light sources and total radiation employed, the relative protein content is higher and lipid content is lower in *Chlorella vulgaris* cultured under light conditions relatively deficient in the 440–455 mμ region and distinctly richer in the 650–700 mμ region (filament source) than in cells exposed to a light source that is rich in the blue wave-lengths and relatively deficient in the longer wave-lengths. However, the experiments do not indicate which of these regions is more important in determining the protein and lipid contents and the protein/lipid ratio in the cells or whether the determining factor is the ratio of blue to the longer wave-lengths or, indeed, whether other wave-lengths have an important role. These facets of the problem are being investigated.

Two-dimensional paper chromatography showed no qualitative difference in the amino-acid content of

protein from 'filament' and 'fluorescent' cultures. Alanine, arginine, aspartic acid, glutamic acid, glycine, *iso*leucine, leucine, serine, threonine, and valine were identified in the protein from both sources.

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Interaction between Repetitive Nerve Stimulation and Twitch-potentiating Agents at the Neuromuscular Junction

THE indirectly developed maximal twitch tension of vertebrate muscle is sometimes augmented after periods of tetanic nerve stimulation, an effect generally called post-tetanic potentiation. This effect is further increased by the administration, prior to tetanic conditioning, of physostigmine in doses which in themselves are too small to facilitate twitch tension[1]. Physostigmine[2] and also other agents which elicit twitch potentiation, for example neostigmine[3] and *m*-hydroxy phenyltrialkylammonium ions[4], have been shown to possess an action on motor nerve terminals which is revealed by bursts of repetitive antidromic nerve discharge appearing after single orthodromic volleys. Furthermore, this presynaptic activity is greatly facilitated by tetanic conditioning of the motor nerve[5]. Within the context of these observations, it seemed important to compare drug-induced twitch potentiation before and after periods of repetitive motor nerve stimulation.

Drugs dissolved in isotonic saline were injected into the arterial supply of the cat gastrocnemius muscle before and at different intervals after a 10–20 sec. period of motor nerve stimulation at frequencies of 50–400/sec. Except for these periods of tetanic conditioning, the nerve was stimulated by single supramaximal shocks at a rate of 1 every 6 sec. Antidromic nerve discharge was displayed on a cathode-ray oscilloscope. A monopolar recording electrode was placed on an *L*7 ventral root filament and an indifferent electrode on the skin. All cats were anæsthetized with chloralose. Two groups of drugs were used as test agents. Group I comprises *m*-hydroxy and *p*-hydroxy phenyltrialkylammonium ions and neostigmine; Group II consists of phenyltrialkylammonium ions and a variety of aliphatic quaternary ammonium ions including tetraethylammonium. A characteristic feature of Group I agents is the perfect correlation exhibited between their twitch-potentiating potencies (on single shock stimulation) and *in vitro* anticholinesterase activities[6]. The Group II compounds lack such a correlation and most of them are relatively much weaker than the other agents as either twitch potentiators or cholinesterase inhibitors. In contrast to Group I agents, the compounds of Group II rarely elicited post-activation antidromic motor nerve discharges; they did, however, regularly produce this neural response after 10-sec. periods of tetanic conditioning (200 per sec.) or on stimulation every 7 sec. with paired shocks separated by 1–3 msec., conditions which also facilitate the post-activation neural response to Group I agents[5].

In twenty nerve-muscle preparations, consistent results were obtained when agents of Group I and Group II were injected after periods of tetanic stimulation: drug-induced twitch potentiation greatly exceeded that obtained in response to equal, or smaller, doses administered prior to the tetanic conditioning. A characteristic result is illustrated in Fig. 1. Repeated administration of a test dose at different intervals after tetanic conditioning permitted determination of time course and duration of the post-tetanic enhancement of pharmacological response. Using *m*-hydroxy phenyldiethylmethylammonium and its non-hydroxy analogue as test agents, enhancement of drug-induced twitch potentiation in 8 different nerve-muscle preparations endured for 10–80 min. after one conditioning tetanus (200/sec. for 20 sec.). In 5 of these preparations, the time of return to pre-tetanic drug response exceeded 20 min. The maximal pharmacological effect was always produced by the first post-tetanic injection of drug, usually made within 30 sec. after cessation of the tetanus. From then on, the effect decayed in an

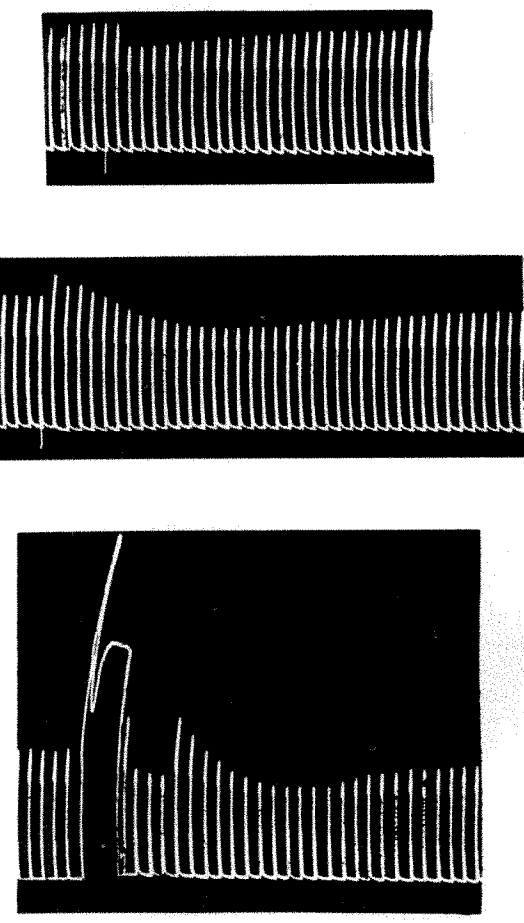

Fig. 1. Effect of *m*-hydroxy phenyltrimethylammonium ion on isometric twitch tension before and after tetanic conditioning. Chloralosed cat. Single maximal shocks applied to posterior tibial nerve every 6 sec. as square waves of 0·5 msec. duration; marks at bottom of trace indicate time of injection. Top, Response to test agent, 1 μgm./kgm. intra-arterially; middle, response to test agent, 5 μgm./kgm. intra-arterially; bottom, response to test agent, 1 μgm./kgm. intra-arterially after tetanic nerve stimulation at 300 sec. for 20 sec. Note that injection was made during a post-tetanic depression of twitch tension

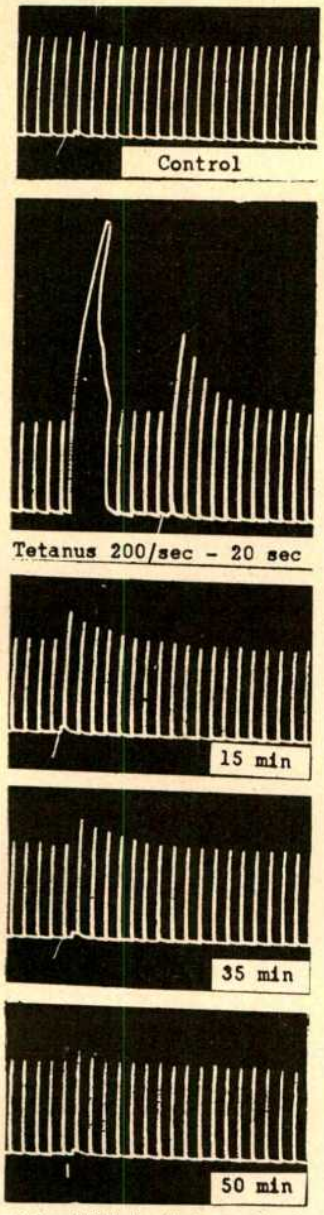

Fig. 2. Effect of phenyldiethylmethylammonium ion on isometric twitch tension before and at various intervals after tetanic conditioning. See legend to Fig. 1 for technical details. All injections were 50 μgm./kgm. intra-arterially. Note that first injection of test agent after tetanus (20 sec.) was given during post-tetanic potentiation of twitch tension. Not shown here is response to test agent 75 min. after tetanus; this response was same as shown in top tracing

exponential manner until the pre-tetanic level of response was attained (Fig. 2).

This increase in pharmacological response produced by tetanic conditioning was observed irrespective of whether the post-tetanic twitch tension in the absence of drug was potentiated, depressed or unchanged relative to pre-tetanic tension. This increase is, therefore, not contingent on the selection of stimulus parameters which result in post-tetanic potentiation *per se*.

The duration of enhanced drug-induced twitch potentiation observed after tetanic conditioning is considerably longer than that of other post-tetanic phenomena previously studied: decurarization[7,8], increase in miniature potential discharge-rate[9], twitch potentiation[1]. These latter events, subsiding within 5–10 min. at the most, have been attributed to an action on presynaptic terminals which augments transmitter output[8,9]. The increased drug-induced twitch potentiation seen after repetitive nerve stimulation also appears to have a presynaptic origin; this suggestion is supported by the finding that twitch-potentiating compounds, including those which are not cholinesterase inhibitors, produce a post-activation antidromic motor nerve discharge which is markedly facilitated in frequency and duration by tetanic conditioning. Perhaps the post-tetanic increase in pharmacological response constitutes a more sensitive measure of the duration of presynaptic changes consequent to repetitive nerve stimulation than is provided by changes in miniature potential discharge-rate, post-tetanic decurarization and twitch amplitude. Alternatively, the post-tetanic increase in drug-induced twitch potentiation may result from changes in neuromuscular transmission which are unrelated to these other more transient post-tetanic phenomena.

In the absence of further information concerning the nature of the presynaptic alterations involved, we may conclude that the effects of repetitive nerve stimulation and of twitch-potentiating compounds on presynaptic terminals are interchangeable and additive.

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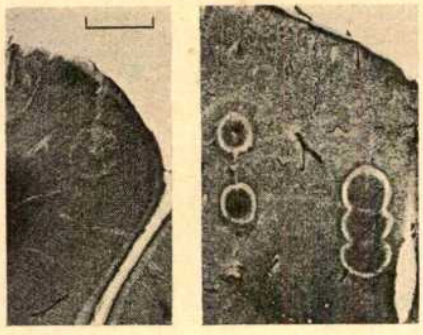
Locating Capillary Microelectrode Tips within Nervous Tissue

FOR the identification of structures generating potentials recorded by micropipettes it is necessary to locate the position of the micropipette in the tissue. The method most frequently used to obtain this information consists in depositing a marker at the tip of the micropipette. Most authors employ an electrolyte of good conductivity the composition of which does not disturb the functions of the cells but which leaves a trace when a small amount of it is extruded from the electrode by electrophoresis. Thus, crystal violet in hydrochloric acid[1], lithium carmine in potassium chloride[2], silver nitrate[3] and potassium ferrocyanide[4,5] have been used for markings in the retina, whereas gold trichloride in potassium chloride (von Baumgarten, R., personal communication) and ferrous ammonium sulphate[6] were used



A B

Fig. 1. Frozen sections, 100μ, according to the plan of the penetrating electrode. Hæmatoxylin–eosin stain. *A*, Single mark in cat cortex (suprasylvian gyrus); *B*, multiple marks in pigeon telencephalon; left, two sites of marking at 1 mm. distance; right, three sites at 0·5 mm. Index : 1 mm.

for the central nervous system. To our knowledge, none of these methods is used routinely. This is probably due to the irregularity of the results and also to the difficulty of finding the very small mark left in the tissue.

To obviate the above-mentioned difficulties, we have devised a method in which the extruded marking ions are complex anions containing copper and citrate. The advantage of complexing the copper is that a too drastic fixation of copper on to the proteins of the nervous tissue is thereby avoided. It is well known that if a solution of a simple salt of a heavy metal is used as an electrolyte, the release of metal cations provokes a considerable and almost immediate increase in the electrode impedance. This inhibits the current-flow, and, in most cases, the result is that the coagulated proteins adhere to the tip of the micropipette, so that it is impossible to remove the micropipette without removing at the same time the marking deposit. If, however, the copper is complexed, the impedance of the electrode remains constant during the entire time of current-flow and the tip of the electrode remains clean, no coagulum being seen on inspection under the microscope.

In practice we use an electrolyte containing complex anions of copper and citrate, obtained by dissolving 811 gm. (2·5 moles) of tripotassium citrate monohydrate and 213 gm. (1·25 moles) of cupric chloride dihydrate in 1 litre of water and adjusting the *p*H to 7 with the necessary amount of strong potassium hydroxide solution. In the 0·5, 1·5μ micropipettes (4–40 MΩ) this solution can be conveniently substituted for the electrolytes (potassium chloride, sodium chloride) generally used for the detection of spikes. (We are grateful to Prof. P. Souchay (Department of Chemistry, Sorbonne, Paris) for his advice on the preparation of complex ions.)

After recording, the marking is obtained by passing a continuous 2-μamp. current with microelectrode negative, for 2 min. The specimen is then fixed in 10 per cent neutral formol and embedded in paraffin (or sliced frozen). Nissl or panoramic staining is then carried out by the usual techniques. The method was tested on pigeon and cat brains. In both cases, after staining the tissue, a well-defined, colourless ring appears, having a diameter varying with the preparation from 300μ to 800μ. Examination of serial sections shows that this ring results from the cutting of a sphere (or ellipsoid), the centre of which is the tip of the electrode. When the section passes through a diametrical plane, a colourless spot having a diameter of 50–100μ likewise appears in the centre of the ring. An examination at higher magnification shows that the absence of staining in the ring and in the centre corresponds to tissue lysis, due probably to denaturation of the proteins by the copper. This assumption is supported by the fact that perfusion with an acidified Ringer solution before killing the animal prevents the formation of the ring whereas an alkaline perfusion favours it. It is known that metal-protein bonding is facilitated by an increase in *p*H. We think that the formation of the ring around the central point is due to a passive diffusion of the product after its release from the tip of the electrode, since the intensity of the current and the time of its application have little influence on the diameter of the sphere.

It seems to us that this method is likely to be useful to neurophysiologists for the following reasons :

(1) Its simplicity : the classical routine histological methods can be used without modification.

(2) The marks can be easily found, and, because of the presence of the halo around the central point, are not liable to be confused with artefacts.

(3) Its reliability : whereas many methods give very irregular results, we have found that with this method the number of failures is very small.

We hope that an extensive use of this method will confirm these results.

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Mechanisms of Nerve Impulse Initiation in a Pressure Receptor (Lorenzinian Ampulla)

ELASMOBRANCHS have a well-developed system of large tubular sense organs, the Lorenzinian ampullæ[1–4]. In the dogfish, each ampulla consists of a bulb-like swelling, about 0·7 mm. in diameter, located deeply in the head of the fish, and a jelly-filled tube, several mm. long, that opens in a skin pore (see inset of Fig. 1). The ampulla is innervated by a bundle of 4–8 nerve fibres that end inside the swelling. Since the findings of Sand[5] and Hensel[6] that the stationary frequency of impulses discharged by the Lorenzinian ampulla has a high temperature coefficient (Q_{10} = 2–3), the organ has been generally regarded as a thermo-receptor. But at that time, it was not yet known that not only thermo-receptors but also mechano-receptors may have such a high temperature coefficient without losing their mechano-receptor specificness[7,8]. The general morphology of the Lorenzinian ampulla suggests a mechano- rather

than a thermo-receptor function. In any event, its deep location in the head, and the relatively low thermal conductivity of the jelly of its tube, argue strongly against its being a thermo-receptor. In fact, Murray[9] has recently shown in *in situ* experiments that probing of the ampulla pore with a bristle causes a brief change in the frequency of the nerve impulses discharged. In this communication evidence will be given that the ampulla is sensitive to pressure; it produces generator potentials which increase with the internal pressure of the ampulla.

Single isolated ampullæ of the dogfish (*Mustellus canis*) were set up in a pressure chamber (Fig. 1). The tubule was cannulated and connected to a pump. Thus, the internal and/or external pressure of the ampulla could be varied over a wide range. Single axons were dissected up to the point of axon emergence from the ampulla, and the electrical activity led off that point. Under these conditions generator and action potentials of the order of 0·1 mV. are recordable.

When the internal pressure of the ampulla is raised above its external pressure, generator potentials are produced. The amplitude of the generator potential increases with the pressure differential. The relation between pressure and generator potential is best seen when the site of nerve impulse initiation is blocked by an anæsthetic[10]. This prevents the generator current from being short-circuited at that site, and the generator potential is found to increase over a wide range of pressure (Fig. 2).

In the non-anæsthetized preparation the effect of an increment in generator current is to increase the frequency of nerve impulses. At normal atmospheric pressure on either side of the ampulla, relatively few units produce generator potential sufficiently large to set up nerve impulses. But as the internal pressure is raised, the generator potential is driven to the critical firing-level, and impulses are discharged rhythmically and continuously. When the internal pressure is raised abruptly to a new level, the discharge has a dynamic and a static non-adaptive phase. The frequency of both phases increases as a function of the pressure differential (Fig. 2).

The structures that convert pressure into generator potentials are located inside the ampulla swelling. The ampulla tube and most of the tissue of the ampulla swelling can be removed by micro-dissection[11]

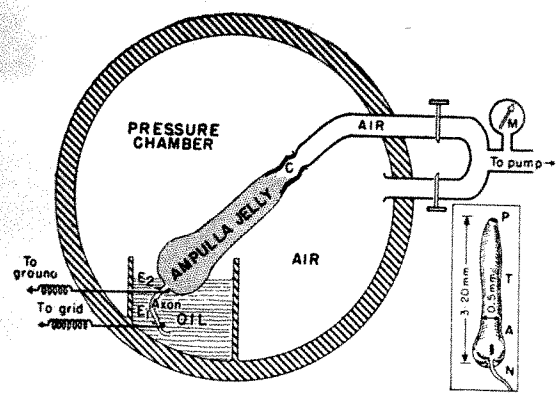

Fig. 1. The Lorenzinian ampulla is drawn over a metal cannula (c). Its internal and/or external pressures are varied and the corresponding generator and action potentials are led off a single axon with electrodes E_1 and E_2. Inset, some anatomical characteristics of an ampulla. *P*, Pore; *T*, tubule; *A*, ampulla swelling which contains the receptor endings; *N*, bundle of 4–8 nerve fibres

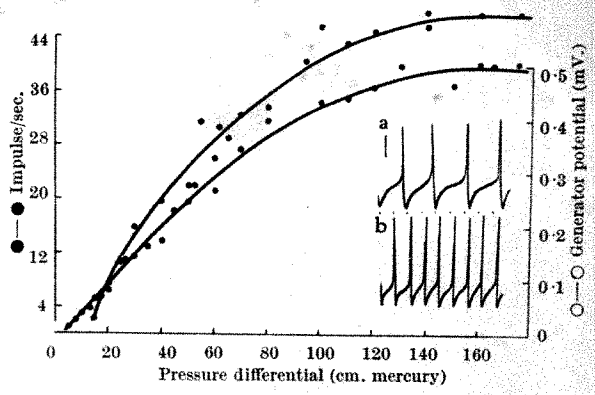

Fig. 2. Generator potential and impulse frequency as a function of pressure. The internal pressure of the ampulla is varied at constant external pressure of 1 atmosphere, and the pressure differential (abscissæ) is plotted against the amplitude of the resulting generator potential and impulse frequency (static phase). Generator potential and impulse frequency were determined in successive runs. In order to obtain a complete pressure–generator potential curve, uncomplicated by action potentials, the latter were abolished with procaine (0·08 per cent). Inset, response patterns of generator and action potentials at *a*, 40 cm. and *b*, 95 cm. pressure differential. Calibration, 50 μV.; 25 msec.

without impairment of the convertor process. The generator potential originates in, or in the immediate neighbourhood of, the nerve terminals, at a site more peripherally located than that at which the nerve impulse is started. This situation resembles that of other mechano-receptors[11–14]. The generator structures are excited effectively by an increase in the internal ampulla pressure that involves stretching, but not by increasing equally and simultaneously the internal and external pressures. A change in temperature causes an increase in the rate of rise of the mechanically elicited generator potential and thereby causes an increase in impulse frequency. But a temperature change, *per se*, produces no excitation: if the internal ampulla pressure is low so that no detectable generator potential is produced, a change in temperature, however steep its gradients, elicits no electrical response.

The Lorenzinian ampulla may thus possibly serve as a receptor of hydrodynamic pressure. In the dynamic phase of impulse discharge, the sensitivity of the receptor at about 10 metres of water (the normal cruising range of the fish) is from 5 to 12 impulses/second per metre of water pressure.

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Elevated Serum Insulin associated with Leucine-induced Hypoglycæmia

SINCE the original description of leucine-induced hypoglycæmia in 1956[1], much interest has been aroused concerning the mechanism by which the administration or ingestion of L-leucine or leucine-containing proteins produces a profound lowering of blood sugar-levels in susceptible individuals. Our previous experiences with two leucine-sensitive children have been reported in detail elsewhere[2,3]; the present communication deals with new and pertinent observations.

Payne and Woolf[4] reported a high blood-level of insulin-like activity following administration of leucine when compared to a fasting-level obtained a few days previously. Drs. Renold and Steinke of Boston and Drs. Yalow and Berson of New York have kindly determined for us the levels of insulin-like activity using the epididymal fat pad method[5] and the level of circulating insulin by an immunochemical technique[6], respectively.

In these experiments the L-leucine was injected intravenously[2] at a dose of 75 mgm./kgm. Zero time on Figs. 1 and 2 represents the end of a 2-hr. fasting period at which time the leucine was given. Blood samples were drawn serially during the subsequent hour. Sugar-levels were obtained for capillary blood using the method of Nelson-Somogyi[7]. Sera from venous blood were used for the determination of insulin and insulin-like activity-levels.

In Fig. 1 is shown the levels of insulin-like activity obtained by the method of Renold. The stippled bar along the ordinate indicates the limits of the values obtained in Renold's laboratory in ten normal infants less than two years of age. The maximum level was 1,450 micro-units and the mean level was 513 micro-units per ml. of serum. The solid black circles represent the results obtained on a control patient. There was no effect on the blood sugar-level (92 mgm.–86 mgm. per cent) or on the insulin-like activity. The

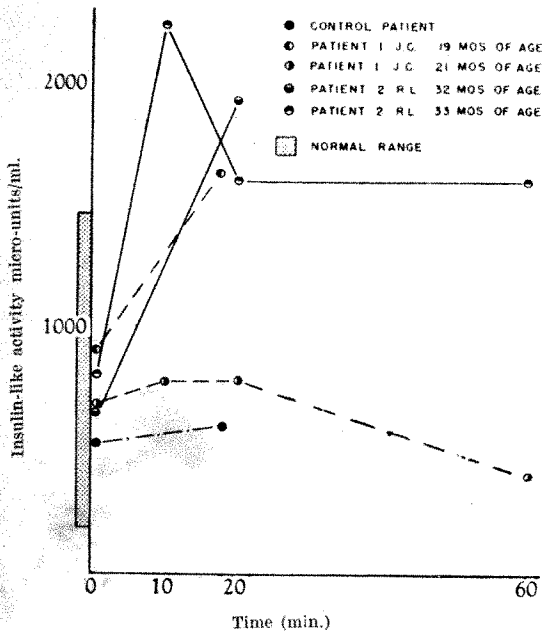

Fig. 1. Blood insulin-like activity following L-leucine administration. Method of Winegrad and Renold (ref. 5)

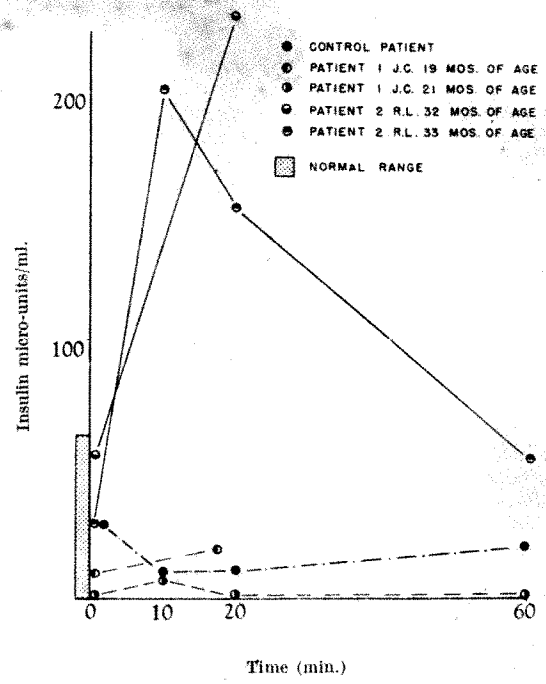

Fig. 2. Blood insulin-levels following L-leucine administration. Method of Yalow and Berson (ref. 6)

interrupted lines depict results obtained on two occasions on patient 1 (J. C.). At 19 months of age there was an increase in insulin-like activity to a level slightly above the normal range and the blood sugar-level was decreased from 84 mgm. to 38 mgm. per cent. When the test was repeated two months later, the insulin-like activity was unaltered during the course of the experiment although we observed a decline in the blood sugar-level. The solid lines depict our experiences in patient 2 (R. L.). The first test, at 32 months of age, demonstrated a significant increase in circulating insulin-like activity and the blood sugar-level decreased from 38 mgm. to 6 mgm. per cent. One month later, a second test again demonstrated a marked increase in insulin-like activity concomitant with a fall in the blood sugar-level.

In Fig. 2 are shown levels of insulin obtained by Yalow and Berson on aliquots from the same specimens from which the data on Fig. 1 were obtained. The stippled bar along the ordinate indicates the normal insulin-levels obtained by the immunochemical technique which range from virtually zero to 66 micro-units per ml. of serum. A control patient is again represented by solid circles. There was no change in either blood sugar-levels or in the circulating insulin-level during the 1-hr. test period. Patient 1 (J. C.) showed no significant changes in insulin-levels on two occasions. Patient 2 (R. L.) demonstrated very dramatic increases in circulating insulin-levels on each occasion.

Thus, we have demonstrated a significant increase of both insulin and insulin-like activity on duplicate samples of serum on two occasions in one patient with leucine-induced hypoglycæmia following the intravenous administration of leucine. In each instance there was an appropriate decrease in the blood sugar-level. In the other patient, there was no demonstrable change in the insulin-level on either of

two occasions, and the insulin-like activity was increased on only one of the two times measured.

Although we have demonstrated marked leucine sensitivity of each patient on repeated occasions, we are unable to explain the difference between these two patients with respect to the response of circulating insulin and of insulin-like activity to the administration of leucine. Other investigators have obtained data showing an increase in circulating insulin-levels in three other children with leucine-induced hypoglycæmia after the administration of leucine. These results have been communicated to us by Yalow and Berson, in whose laboratory the analyses of insulin-levels were performed. A rise of "insulin or insulin-type activity" after the administration of leucine has been reported in yet another child[8].

It would appear that in the majority of children sensitive to leucine the blood-sugar depressant activity of this amino-acid is mediated via increased synthesis and/or release of insulin. The exact mechanism by which leucine increases the circulating insulin-level is unknown. It is remarkable that in one of our two patients, hypoglycæmia followed the administration of leucine without an associated significant increase in insulin-level. The discrepancy may be explained by the presence of circulating insulin in a 'bound' form not readily detectable by the techniques employed. Other possible explanations also are now being tested.

This investigation was supported in part by research grants from the National Institutes of Arthritis and Metabolic Diseases (*A*–3581 (*A*)) and Mental Health (*M*–2673), U.S. Public Health Service.

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ANATOMY

X-ray Diffraction Study of Acellular Teleost Bone

THE osseous endoskeletons of the higher orders of teleost fish are noteworthy in that they are totally devoid of enclosed osteocytes (Fig. 1)[1,2]. The osseous tissue of other fish, like that of all other vertebrates, contains enclosed osteocytes. Although acellular bone, *per se*, is phylogenetically a very ancient tissue[3], its appearance as the sole osseous element in the skeletal systems of the most highly evolved and successful fish suggests that possession of such a tissue confers an adaptive value to the organism in a marine environment.

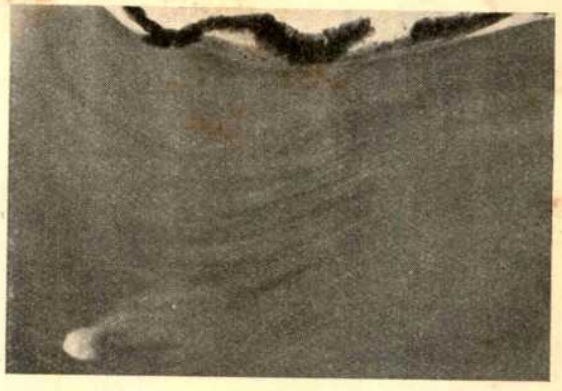

Fig. 1. Operculum of the zebra fish (*Pterois volitans*), a typical acellular bone form. Note the absence of enclosed osteocytes. (× 450)

A taxonomic classification of the distribution of these two bone tissue types in fish is under way. Preliminary observations by Moss[4] indicate that the classification of Kölliker[1] and of Berg[5] require further study.

The histogenesis of acellular bone is also unusual. The osteoblastic cells become incorporated within a matrix of their own production. There is an almost immediate cellular necrosis following which the cell spaces totally disappear, becoming filled with a substance indistinguishable from that of the surrounding calcified matrix. A more complete description of the osteogenic and reparative processes of this tissue will be published elsewhere.

An X-ray diffraction study was undertaken to seek further information on the structure of piscine bone. Two fish were used, Spanish mackerel (*Scomberomorus maculatus*) which has acellular bone, and the carp (*Cyprinus carpio*) which has cellular bone tissue. The skulls of several adults of each species, freshly caught, were soaked in water, scraped and cleaned. The separate samples were pulverized in a Waring blender and dried over calcium chloride. The material was then ground by hand in a mullite mortar for X-ray diffraction examination.

The X-ray diffraction powder patterns (Fig. 2) were taken on a 'Norelco' diffractometer using nickel-filtered copper *K*-radiation, with a 1-deg. slit system, and an argon-filled Geiger–Müller counter as a

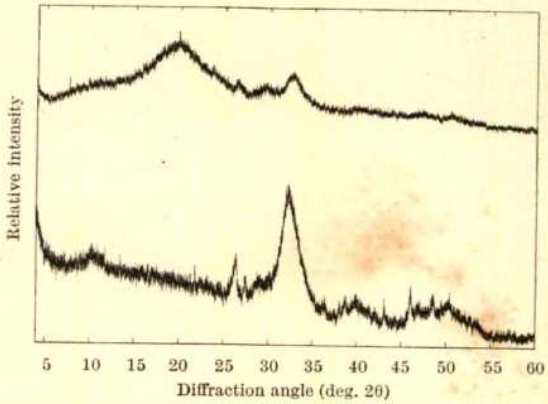

Fig. 2. Comparison of X-ray diffraction powder patterns of acellular (Spanish mackerel) fish bone (upper) and cellular (carp) fish bone. Nickel-filtered copper *K*-radiation was employed. The broad peak on upper pattern at about 20° 2θ is probably due to a large collagen component in the acellular bone

detector. The latter was set to travel through the goniometer arc at a speed of $\frac{1}{2}°$ 2θ per min.

Fig. 2 shows typical X-ray diffraction patterns of the two specimens. Both patterns indicate the presence of a finely divided hydroxyapatite phase. The apatite crystals in the acellular bone (upper curve) appear to be smaller and/or more strained than the cellular bone crystals (lower curve) as evidenced by the broader X-ray diffraction maxima due to apatite seen at about 26° 2θ, 29° 2θ, and 32° 2θ. There is a much larger organic fraction, probably collagen, in the acellular bone than in the cellular bone. This is shown by the prominent, broad peak at about 20° 2θ which appears in the acellular pattern but not in the cellular X-ray diffraction pattern.

The role of acellular bone in the mineral homeostasis of the fish and the structure of such bone is being further investigated[6].

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A Microscopic Method of determining Rates of Bone Growth

THE measurement of accretion-rates of bone by a non-toxic, non-radioactive, direct method based on the intravital marking of growing surfaces would be of value[1]. I have been studying intravital staining of growing-bone surfaces in man, dogs, and rats, using many agents including alizarin red *S*, chlorazol fast pink[2], chlorazol sky blue, calcium fast purple, naphthamine brilliant blue *RR* and the tetracyclines. My aim was to be able to define microscopically the amount of growth in a stated time interval. By far the most satisfactory are the tetracyclines. Chlortetracycline, oxytetracycline and tetracycline are selectively incorporated into new bone deposits and can be identified by their fluorescence. They remain detectable for at least six mon'hs[3].

Fig. 1 shows the growth of two canine osteons over a twelve-week period. The outer ring in each system is a deposition of alizarin red *S*, which is less suitable for this work than tetracyclines because of its systemic toxicity. Next is a chlortetracycline ring (33 mgm./kgm. intravenously given four weeks later). The next ring is a marker of oxytetracycline (62·5 mgm./kgm. intravenously, 8 weeks after the alizarin). The last line is made by 33 mgm./kgm. intravenously of chlortetracycline 12 weeks after the alizarin and 72 hr. prior to killing the animal. The

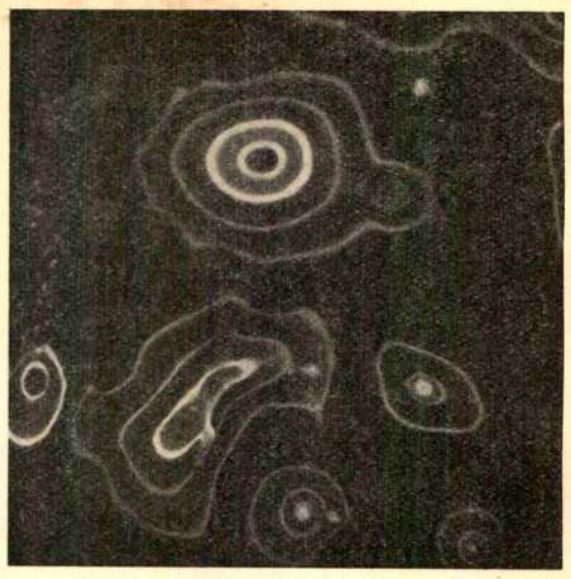

Fig. 1

upper system in the illustration demonstrates growth varying from 28 to 60 microns during the first four-week period, from 28 to 52 microns during the second, and from 26 to 48 microns during the third.

The width of the line of initial uptake may be wider than the subsequent width of that line (compare the second and fourth lines, which both result from a dose of 33 mgm./kgm.). The relationship of this to changes occurring in the osteoid and at the calcification front is not yet known.

Ghosez[4] and Ponlot[5] have shown that the microscopic localization of tetracycline uptake is strongest at the peripheral portion of the pre-osseous layer, that is, the calcification front and region just preceding it.

The submicroscopic specific site of tetracycline uptake is unknown. However, so long as measurements are made between two tetracycline lines, this information is not required for measurements of the area of new bone deposit.

62·5–80 mgm. of tetracycline intravenously produce less-suitable lines because of their width and the flare that accompanies more intense deposits. Moreover, these doses may produce a partial inhibition of mineralization (unpublished work). Chlortetracycline, but not oxytetracycline or tetracycline, can occasionally produce a minimal decrease in mineralization of canine bone at doses as low as 33 mgm./kgm. intravenously. Therefore, 20 mgm./kgm. intravenously of oxytetracycline is recommended for work with dogs. In recent experiments with rats, demethylchlortetracycline showed greater intensity of fluorescence than identical doses of the other three. This may be related to its sustained blood-levels. A satisfactory mark is given in human bone by two oral doses of 1 gm. of any of the tetracyclines, 6 hr. apart.

Undecalcified sections must be used, since the tetracyclines are removed by acid or ethylenediamine tetraacetate. The width of the marker in thin transverse sections (less than 40μ thick) is less than 8μ for tetracycline doses of 33 mgm./kgm. intravenously, provided that the growing surface was reason-

ably perpendicular to the plane of section. This resolution exceeds that of calcium-45 (ref. 6) and radium (ref. 7), but not the optimum possible with plutonium-239 (ref. 8). The resolution and non-toxicity make this method preferable to lead[9].

A high-pressure mercury vapour lamp, collecting lens and Wratten 18*A* filter provide a good source of ultra-violet light. Most ordinary bright-field microscopic equipment is satisfactory for this type of ultra-violet work. A Wratten 23*A* filter in the eyepiece reduces transmission of the blue auto-fluorescence of non-labelled bone and permits satisfactory black-and-white photography. More details on the ultra-violet microscopy are given in a paper by Kuper and May[10].

Chlortetracycline, tetracycline and demethylchlortetracycline were supplied by Lederle Laboratories Division of Cyanamid of Great Britain, Ltd., under the trade names 'Aureomycin', 'Achromycin' and 'Ledermycin', respectively. Oxytetracycline was supplied by Pfizer, Ltd., under the trade name 'Terramycin'.

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PATHOLOGY

Cytochemistry of Nucleic Acids in Murine Lymphoma Cells infected with Polyoma Virus *in vitro*

INFECTION of cultures of milk-adapted $P388D_1$ murine lymphoma cells with polyoma virus produces an alteration in the ribonucleoprotein (RNP) of the nucleoplasm, enlargement of the nucleolus, and intranuclear vacuoles containing abnormal RNP[1]. Cytochemical studies of the late stages of infection of lymphoma cells *in vitro* with polyoma virus failed to reveal Feulgen-positive inclusion material[1]. Since the infectivity of nucleic acid preparations from cells infected with polyoma virus appears to reside in the deoxyribonucleic acid (DNA) fraction[2], further attempts have been made to demonstrate abnormal DNA and to elucidate the relationship between changes in DNA and RNA or RNP metabolism in polyoma virus infection.

Three day-old cultures of milk-adapted $P388D_1$ lymphoma cells were infected with a 10^{-1} dilution of the fourteenth serial passage of polyoma virus as previously described[1]. The cells were examined at intervals of 24, 48, 52, 72 and 96 hr. after infection. Some modifications of the previous cytochemical staining procedures[1] were introduced. The intensity of staining was increased by a brief saline rinse before fixation. Hydrolysis of the Feulgen preparations for 30 min. gave more intense staining than the usual 10-min. hydrolysis. Cultures were also stained with acridine orange after fixation in absolute ethanol[3].

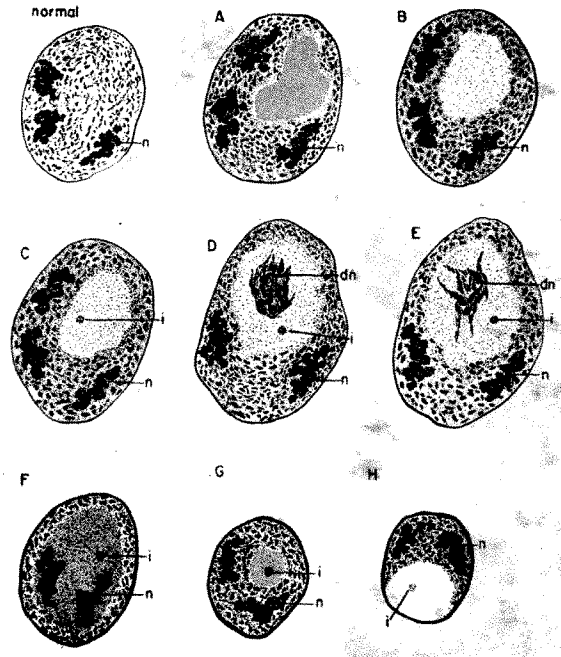

Fig. 1. Nuclei of $P388D_1$ lymphoma cells stained with toluidine blue-molybdate (stage III). *A*—*H* represent stages in the evolution of the lesions. *n*, Nucleolus; *i*, inclusion; *dn*, degenerating nucleolus

Definite lesions were recognized 48 hr. after infection. The pathogenesis was assessed mainly from the time sequence of the changes, but in part by analysis of the increasing disorganization of nuclear structure (Fig. 1). Enlargement of the nucleus and nucleolus was the earliest change and this was accompanied by the appearance of homogeneous intranuclear zones or vacuoles filled with Feulgen-positive DNA (Figs. 1*A* and 2). These Feulgen-positive areas were also stained by toluidine blue-molybdate (TBM), stage III (ref. 4), after ribonuclease digestion. Later, an increasing number of cells with unstained vacuoles or ill-defined clear zones were noted (Figs. 1*B* and 2). Small round homogeneous inclusions then appeared in the vacuoles (Fig. 1*C*). The inclusions stained less strongly than the chromatin but were definitely

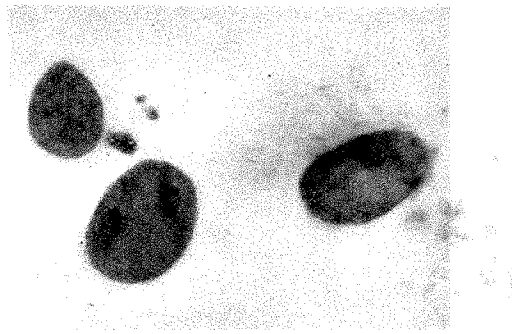

Fig. 2. One normal (top left) and two infected $P388D_1$ lymphoma cells, one of which (left) has an intranuclear vacuole filled with DNA, cf. Fig. 1, normal, *A* and *B*. Feulgen stain. (× 1,400)

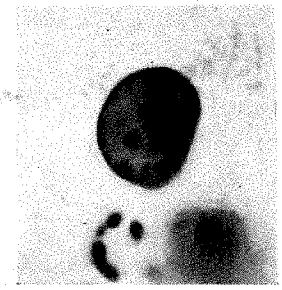

Fig. 3. Intranuclear inclusion body. Feulgen stain. (× 1,400)

Feulgen-positive (Fig. 3). Since the intensity of staining of the inclusions by TBM (stage III) was unaffected by ribonuclease digestion they did not contain any detectable RNA at this stage. Afterwards one or more of the enlarged nucleoli stained less intensely and became more diffuse (Fig. 1*D*). This nucleolar material formed one or more ill-defined masses (Fig. 1*E*) and eventually filled the clear spaces or vacuoles (Fig. 1*F*). The intensity of staining of the inclusions by the Feulgen procedure decreased during this period and the inclusions were more strongly coloured by TBM (stage III). Staining by TBM (stage III) was greatly reduced, but not abolished, by pre-treatment with ribonuclease, indicating that the inclusions contained RNA as well as DNA. Further nuclear disorganization was caused by shrinkage (Fig. 1*G*) and in many shrunken cells RNP could no longer be detected in the vacuoles (Fig. 1*H*). At this stage the inclusions were stained dark green by TBM (stage III) with or without previous ribonuclease digestion and were clearly Feulgen-negative (compare ref. 1, Fig. 9). The inclusions, therefore, no longer contained the nucleolar type of RNP which stains purple in stage III TBM preparations[4]. After very brief fixation (2 min.) in formol sublimate at 37° C., the inclusions stained intensely purple with TBM. In such preparations the inclusions were stained dark green after ribonuclease digestion and not at all after ribonuclease and crystallized deoxyribonuclease (Mann Labs. Inc.) digestion. All staining by TBM was prevented by extraction of nucleic acids with hot trichloracetic acid. The inclusions could not be distinguished from other masses of chromatin in the acridine orange or in the pyronin methyl green preparations. Protein-bound amino and other groups were demonstrated in the inclusions by the ninhydrin–Schiff procedure[1]. In the final stage of nuclear degeneration the thin circumferential wall of the vacuole ruptured and the inclusions could be seen in the adjacent cytoplasm.

The course of polyoma virus infection is interpreted as follows. The normal DNA of the chromatin breaks down to form amorphous Feulgen-positive DNA. DNA is not detectable in the next stage of infection, although it may exist as low molecular weight material which is not preserved by fixation. Inclusions containing DNA then appear and are surrounded by and incorporate RNA of nucleolar origin. As the RNA, and presumably the protein, of the inclusions increases they become less Feulgen-positive. Finally, nucleolar RNP can no longer be detected in the inclusions and they contain another form of RNA, DNA and protein. The failure to stain by the Feulgen procedure is probably caused by physical rather than chemical interference with the staining reaction by viral protein. A similar phenomenon has been observed during the formation of vaccinia virus (Love, R., and Salzman, N. P., unpublished work); the cytoplasmic inclusion is strongly Feulgen-positive in the early stages of infection and becomes less so as the viral particles are formed.

We wish to thank Frances Y. Legallais and Roscoe H. Liles for valuable technical assistance and Joyce L. Sills for the drawings.

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Leptospira pomona Infection in an Eastern Red Fox (*Vulpes fulva fulva*)

THE presence of leptospirosis in Pennsylvania cattle has been well established[1–3]. An epizootiological investigation to determine the relationship between bovine and sylvan leptospirosis is at present being undertaken in south-eastern Pennsylvania. Infected cattle herds are identified and their premises intensively trapped for wild-life. Trapped animals are examined for infection by serological and cultural techniques. Isolations of leptospires have been made from the following animals: woodchuck[4], opossum, skunk, racoon and Norwegian rat. This communication is believed to be the first to report the isolation of *Leptospira pomona* from an eastern red fox (*Vulpes fulva fulva*)[5]. The fox was trapped on the premises of a known infected cattle herd. Prior to the start of trapping, *Leptospira pomona* had been isolated from cattle and from surface waters on this farm.

The fox was caught in a No. 2 coil-spring trap, removed from the trap and delivered to the Leptospirosis Laboratory, School of Veterinary Medicine, University of Pennsylvania. On delivery, the fox was euthanized in a carbon monoxide chamber. A blood specimen was obtained by severing the jugular vein and collecting the flow. One kidney was removed aseptically.

The kidney was ground with pestle and mortar and diluted to approximately a 10 per cent suspension with Stuart's base liquid medium ('Difco'). Two tubes of each of the following media were inoculated with 2–3 drops of kidney suspension: Fletcher's semi-solid medium containing 15 per cent horse serum; Chang's semi-solid medium[6] (Hamilton, Montana, modification[7]) containing 10 per cent rabbit serum; Chang's semi-solid medium containing 15 per cent horse serum; and Stuart's semi-solid medium[8] containing 10 per cent rabbit serum. Tubes were incubated at 29° C. and examined at 10–14 day intervals by dark-field microscopy.

Serum from the blood specimen was examined for antibody content by the microscopic agglutination test[9], employing an antigen bank of eleven serotypes: *L. bataviae*, *L. pomona*, *L. autumnalis*, *L. ballum*, *L. canicola*, *L. icterohemorrhagiae*, *L. alexi*, *L. grippotyphosa*, *L. australis A*, *L. sejroe* and *L. hyos*.

Growth of leptospires was detected on day 34 post-inoculation. Organisms were present in one tube of each of the following media: Fletcher's semi-solid

medium containing 10 per cent rabbit serum, Fletcher's semi-solid medium containing 15 per cent horse serum, and Chang's semi-solid medium containing 15 per cent horse serum. Transfers were made into Fletcher's semi-solid medium containing 10 per cent rabbit serum and into Stuart's liquid base medium containing 10 per cent rabbit serum. Subcultures made at 10–20 day intervals were sent to the Leptospirosis Unit, Animal Disease Eradication Diagnostic Laboratory, United States Department of Agriculture, Ames, Iowa, for typing. They were identified as *Leptospira pomona*.

The microscopic agglutination test titres were: *L. pomona*—1 : 100; *L. autumnalis*—1 : 1,600.

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BIOLOGY

Juvenile Hormone Activity in Micro-organisms and Plants

THE juvenile hormone of insects promotes larval development but prevents metamorphosis. Its presence in an immature insect ensures that when the larva molts it will retain its larval characters and not differentiate into an adult[1]. Extracts with juvenile hormone activity were first prepared from the abdomens of male *Cecropia* moths by Williams[2]. Afterwards active extracts were prepared from adult males and females of 6 families of Lepidoptera as well as from eggs, larvæ and newly moulted pupæ[3,4], from representatives of 6 other orders of insects including Dictyoptera, Orthoptera, Hemiptera, Coleoptera, Diptera and Hymenoptera[4–7] and from various insect products, for example, royal jelly[7], insect fæces[8]. Investigation of other groups uncovered substances with juvenile hormone activity in extracts of the adrenals of cattle[9] and in many tissues of numerous invertebrates in 13 classes, including Hydrozoa, Anthozoa, Anopla (Nemertinea), Cheilostomata and Ctenostomata (Ectoprocta), Pelycepoda, Gastropoda, Polychaeta, Oligochaeta, Malacostraca, Arachnida, Holothuroidea and Balanoglossida[6,7]. The most active invertebrate sources were the eyestalks of crustaceans (*Homarus* and *Carcinides*)[6,7], and the heads of polychaetes (*Nereis*)[7]. Juvenile hormone activity was later demonstrated in many vertebrate tissues besides the adrenals including pituitary, kidney and thymus[10] and lymphatic, parathyroid, thyroid, mammary and gastric mucin (Schneiderman, H. A., and Gilbert, L. I., unpublished observations).

All these active extracts prevented certain tissues of young insects from assuming their adult aspect, but did not interfere with growth itself. In pupæ of Lepidoptera, Hemiptera and Coleoptera, local application of active extracts caused the pupal epidermal cells to lay down a second pupal cuticle while untreated cells nearby deposited normal adult cuticle[2,3,5,6,11].

The present communication reports the occurrence of juvenile hormone activity in extracts of several micro-organisms. Ether or chloroform extracts were prepared from whole ferments (that is, cells plus media) as well as from washed organisms. In those cases where non-synthetic media were used, the uninoculated medium itself was also extracted and tested after autoclaving. Extracts of more than 60 organisms were prepared and assayed for their juvenile hormone activity by the 'Polyphemus' wax test[6] and by other procedures[5,11]. The 'Polyphemus' wax test can detect juvenile hormone activity in extracts with 1/2,000th to 1/10,000th as much activity per gm. as oil extracted from male *Cecropia* moths, whereas the other tests are less sensitive. Extracts of 6 species of micro-organisms had juvenile hormone activity in both the 'Polyphemus' wax test and in at least one other test for juvenile hormone activity[5,11]. These included a ciliate, a flagellate, two bacteria and two yeasts. A representative sampling of the results is recorded in Table 1.

Table 1. JUVENILE HORMONE ACTIVITY OF MICRO-ORGANISMS

Name	Type of extract	Percentage of positive tests	Activity
Ochromonas malhamensis	ether	45	++
Tetrahymena pyriformis	ether	18	+
Euglena gracilis	ether	0	0
Chilomonas paramecium	ether	0	0
Baker's yeast (fresh)	ether	25	+
Brewer's yeast (dried)	ether	100	++
Saccharomyces (eight other species or strains)	chloroform	0	0
Schizosaccharomyces (2 species)	chloroform	0	0
Hansenula anomala	chloroform	0	0
Dipodascus uninucleatus	chloroform	0	0
Debaryomyces disporus	chloroform	0	0
Trichosporon pullulans	chloroform	0	0
Nadsonia elongata	chloroform	0	0
Endomycopsis fibuliger	chloroform	0	0
Lipomyces lipofer	chloroform	0	0
Micromonospora sp. (mycelium)	chloroform	65	+
Streptomyces (seven species or strains)	chloroform	0	0
Escherichia coli (washed cells)	ether	0	0
Escherichia coli (cell-free broth)	ether	75	+++
Proteus spp. (whole broth)	ether	75	+++

In the course of assaying various bacteriological media it was discovered that ether extracts of soy bean meal had juvenile hormone activity, indicating that juvenile hormone activity is not only found in lower plants but in higher plants as well.

Despite some efforts, no activity could be obtained from well-chilled diapausing pupæ or from allatectomized male adults of *Cecropia*. Nor was activity found in lipid extracts of sponges and of numerous familiar animals such as the sea anemone *Metridium dianthus*, the long-necked clam *Mya arenaria*, the horseshoe crab *Limulus polyphemus* and many others. Activity also appeared to be absent from various vegetable oils such as castor oil, wheat germ oil, palm oil, coconut oil, peanut oil, corn oil, olive oil, linseed

oil and cotton seed oil as well as from bees wax, carnauba wax, paraffin wax and ceresine wax. It was also absent from most of the micro-organisms examined. This lack of activity did not seem to be due to the presence of inhibitors in the inactive preparations, for in most cases addition of inactive extracts to active extracts did not cause a loss of activity.

These results indicate that we are dealing with a group of substances which are widespread in Nature, but are probably not universal. Indeed, one would scarcely imagine insects adapting a universal and indispensable molecule as a hormone. It is nevertheless intriguing that substances that can mimic an insect growth hormone occur in protozoa, fungi and mammals. These findings support the opinion offered earlier[6,12], that in many cases the development of humoral mechanisms involves not so much evolution of hormones as such, but more the evolution of target mechanisms which acquire a sensitivity to specific small molecules that may have been present from earliest times, and the development of systems that can ensure the timely production of appropriate amounts of these specific molecules. As Hisaw puts it, often "... it is not hormones which have evolved but the uses to which they are put. . . ."[13].

We wish to express our thanks to Prof. George Holz of Syracuse University, who provided us with Protozoa for extraction.

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A Possible Function of Phycoerythrin in Intertidal Red Algae

THE transmission of light in coastal waters is such that penetration is greatest in the blue-green and least in the red region of the visible spectrum[1]. This has led to the view that the phycobilins, accessory pigments that give rise to the characteristic colour of red algae, are responsible for photosynthesis by these plants because, unlike chlorophyll, the pigments readily absorb blue-green light[2]. Evidence in favour of this theory of complementary chromatic adaptation has been obtained by Haxo and Blinks from experiments in which the action spectra of several marine red algae were found to show a fair correlation with the absorption curves of phycoerythrin and phycocyanin[3].

Continuing recent work on the factors affecting the ecological distribution of certain red algae[4], we have become interested in the way light influences the growth of sporelings of these plants, and have made some preliminary experiments using *Plumaria elegans* (Bonnem.) Schm., a shade-loving species which inhabits the lower mid-littoral zone. We have extracted the red pigment from this plant and find that it has an absorption curve characteristic of phycoerythrin (peaks at 500 and 550 mμ). It is, therefore, well able to absorb blue-green light, and if the theory of complementary chromatic adaptation holds in the case of *Plumaria* sporelings, they would use this light for photosynthesis. To test this we grew sporelings in filtered sea water enriched with Erd-Schreiber medium[5], contained in glass vessels screened from the light source by weak solutions of phycoerythrin, prepared freshly each day. We measured the rate of growth of the plants by counting the number of cells produced by a crop of approximately 200 sporelings during a ten-day period, the method used being one already described[6]. Contrary to expectation, sporelings screened in this way grew at more than twice the rate of the control material.

Because of the instability of solutions of phycoerythrin, we carried out subsequent experiments using a screen 2 cm. thick of a weak sea water solution (0·2 p.p.m.) of the dye eosin yellow, which also has an absorption peak in the blue-green region (515 mμ). Over the very wide range of light intensities used, including some below and some above optimum value (315 lux), it was found that the screened sporelings had a much more marked rate of growth (see Fig. 1).

At first it seemed possible that the dye was protecting the sporelings by removing ultra-violet light inhibitory to their growth. However, this possibility can be excluded because the distribution of spectral energy of the source used, an 'Ekco Daylight' fluores-

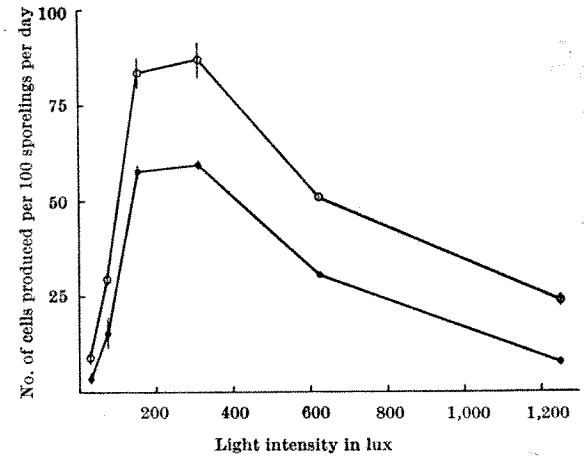

Fig. 1. Cell production by *Plumaria* sporelings grown under an 'Ekco Daylight' fluorescent lamp at different light intensities: ●—●, unscreened; ○—○, screened with a sea-water solution of eosin yellow (0·2 p.p.m.) 2 cm. thick

cent lamp, showed very little energy in the ultra-violet region, and even this small quantity was further reduced by the glass vessels used in the experiment. Moreover, the very weak screening solution of eosin yellow had no measurable effect on the small amount that remained.

The possibility that the dye solution was enhancing growth simply by shading the sporelings is also excluded. For at sub-optimal light intensities, shading would obviously inhibit growth, whereas it was found that the screened sporelings grew faster at a light intensity as low as 30 lux. Furthermore, even at the highest light intensity used (1,250 lux) shading would influence growth to an insignificant extent because the very weak solutions of the dye only absorbed 2·2 per cent of the total light energy in the wave-band 390–700 mμ, and it can be estimated from Fig. 1 that more than 15 times this amount would have to be removed to account for the difference in growth between screened and control sporelings.

It therefore appears that both eosin yellow and phycoerythrin, as used under our experimental conditions, promoted the growth of the sporelings by protecting them from the inhibitory effects of blue-green light emitted by the fluorescent tube, a light source with a spectral energy distribution closely resembling that of daylight. Accordingly, it seems that the theory of complementary chromatic adaptation does not apply in the case of *Plumaria*.

It is hoped to publish a fuller account of this work in the *Journal of the Marine Biological Association*. We thank Dr. E. J. Denton for many valuable discussions.

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Growth Movements of the Radicle of *Striga*

The directional growth of the radical (haustorium) of the root parasite *Striga asiatica* (= *S. lutea*) is normally controlled by a chemotropic factor diffusing from the host plant root[1]. The parasite seeds may be germinated by treatment with a solution in which the host roots (*Sorghum vulgare*, etc.) have been growing. In this case the radicle undergoes a fixed growth movement which is roughly spiral. A basically spiral movement is seen in about 40 per cent of seedlings. More usually the movement is reduced to a strong curvature in one plane followed by a period of more or less straight growth, or by apparently anomalous curvatures in any direction. By growing the seedlings in agar cultures, it was shown that the movements were not influenced by the orientation of the seedlings to gravity or by rotation on a klinostat, at least during the initial curvature, although with

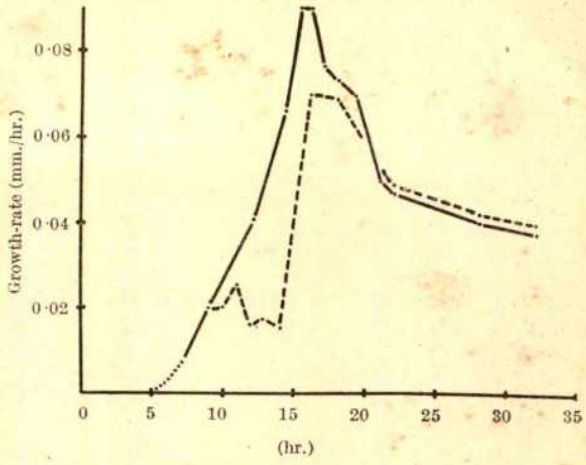

Fig. 1. Average growth-rates (11 seedlings) of the fast-growing (·——·) and slow-growing (·– – –·) sides of the *Striga* radicle during curvature and subsequent straight growth

forces greater than gravity (up to 10*g*) a positive movement was superimposed on the fixed growth movement.

The initial curvature in one plane was used in studying quantitative aspects of the movement. For this purpose seedlings were grown in Petri dishes, growth and curvature being recorded throughout development using a camera lucida in combination with a low-power microscope. The culture dishes were housed on the microscope stage in a light-proof box fitted with removable flaps to permit observation.

An analysis of curvature revealed that this was always associated with an inhibition of cell extension on one side of the radicle, which gave rise to a divergence from a normal sigmoid pattern of growth which characterized the growth of the opposite side (Figs. 1 and 2*A*). The initial period, during which the growth-rates of the two sides was equal, represents a phase of general swelling of the embryo and the commencement of meristematic activity.

In attempting to determine the nature of the factor causing this inhibition, the effects of various anti-auxins on growth and curvature were tested. The anti-auxin 2 : 3 : 5-tri-iodobenzoic acid had a striking effect in reducing curvature, by eliminating the differential inhibition of cell growth on the inner side of the curve (Fig. 2). At a level of 1 p.p.m., 2 : 3 : 5-tri-iodobenzoic acid strongly reduced curvature while

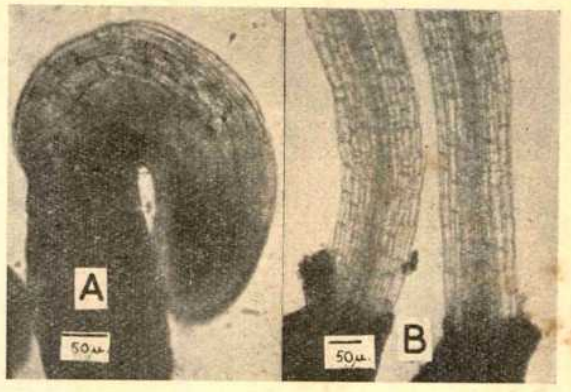

Fig. 2. *A*, *Striga* seedling showing initial curvature of the radicle; *B*, effect of 2 : 3 : 5-tri-iodobenzoic acid (1 p.p.m.) on curvature

linear growth was only reduced by about 20 per cent. Jones *et al.*[2] record that 2 : 3 : 5-tri-iodobenzoic acid reduced geotropic response in rape and rye-grass, but this only occurred at a level which was markedly inhibitory to linear growth. At higher concentrations of auxin; the anti-auxins 2 : 4 : 6-trichlorophenoxy- showed lateral expansion of cells and considerable reduction of linear growth.

Although the effect of 2 : 3 : 5-tri-iodobenzoic acid suggests that the curvature factor may be some form of auxin, the anti-auxins 2 : 4 : 6-trichlorophenoxy-acetic acid and 2 : 4-dichloroanisole, which are supposed to act competitively with auxin at the growth centres, did not selectively reduce curvature. This indicates that the curvature factor, if some form of auxin, must be protected from the competitive action of these anti-auxins. One possible explanation is that the factor may be transferred selectively from a bound form (which could be some auxin/protein association) to the receptive centres for the growth reaction, or that certain places in the growth system are reserved for the curvature factor. The comparative immobility of the curvature factor (that is, not being ordinarily influenced by gravity or rotation on a klinostat) would indicate an association with structural or immobile constituents of the cell. 2 : 3 : 5-tri-iodobenzoic acid, on the other hand, could act at some site before the growth centres, which would be in agreement with Lineweaver–Burk data on the action of 2 : 3 : 5-tri-iodobenzoic acid.

Growth curvatures in other roots are known to be associated with a marked inhibition of extension growth[3,4], and various considerations have led to the view that curvature does not result from a redistribution of polar auxin, but from the production of a specific growth inhibitor on one side of the root. Audus and Brownbridge[3] tested the effect of indoleacetic acid on the geotropic curvature of pea roots (which are stimulated by low concentrations of auxin) and found that both the lower and upper sides of the roots were stimulated to grow faster by low concentrations of indoleacetic acid (that is, the inhibited lower side, in which the auxin-level would presumably be supra-optimal if this substance is the curvature hormone, was also stimulated). This indicates that the curvature hormone in pea roots is not indoleacetic acid, or differs in some way from externally applied indoleacetic acid. The action of the anti-auxin α-(1-naphthyl-methylsulphide) propionic acid in reducing curvature in these roots (Audus and Brownbridge[5]) is attributed to the action of this substance on some endogenous inhibitor which is not indoleacetic acid, and the general promotion of growth of pea roots by this anti-auxin, to its action on residual inhibitors in the cells. The fact that indoleacetic acid and this anti-auxin show mutual antagonism[6] is now explained by competition at a site outside the growth centre.

Audus and Thresh[7], using paper partition chromatography, found that 2 : 3 : 5-tri-iodobenzoic acid reduced in a striking way the level of alcohol-soluble indoleacetic acid in pea seedling tissues, and at the same time induced a negative geotropic response in the side roots of the seedlings; although the possibility that this substance may not actually be indoleacetic acid is indicated by the work of Bennet-Clark *et al.*[4] on the isolation of plant growth substances using starch column chromatography. This shows that a substance distinct from, but appearing like, indoleacetic acid in paper partition chromatography is present in root tissues.

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Variations in Scopoletin in Leaves in Relation to Chloride Treatment of Tobacco

HIGH concentrations of sodium chloride in the soil have an adverse effect on the growth of the tobacco plant. Stunted plants, with thickened leaves containing large quantities of starch, have been reported, and the leaf colour also is affected[1]. Thickening of the secondary xylem elements[2] is also attributed to the effect of high chloride concentrations.

Scopoletin, as well as being a normal constituent of tobacco leaves, has been found to increase markedly in the case of attack by the tomato spotted wilt virus[3] and to be present in higher concentration in differentiating than in non-differentiating tobacco tissue[4]. Scopoletin also acts as an inhibitor of the enzymic destruction of indoleacetic acid and could thus itself act as a growth inhibitor by causing indoleacetic acid to accumulate beyond the stimulatory range[5].

Using fluorescence under ultra-violet light, paper chromatographic studies[6,7] of aqueous and methanolic extracts of oven-dried green tobacco leaves from plants, variety Hicks, grown in sand in the glass-

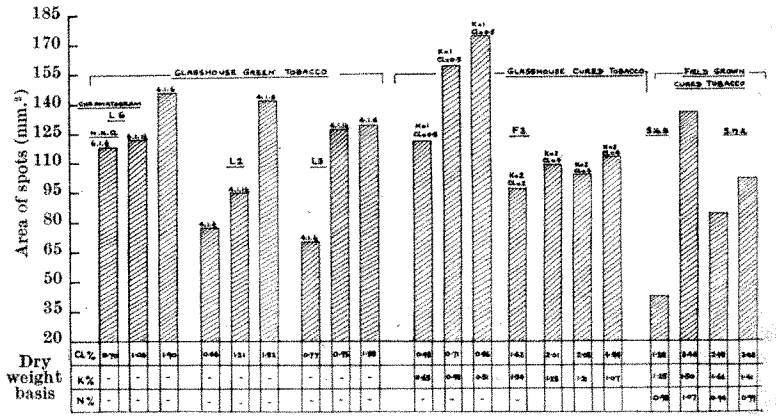

Fig. 1. Scopoletin in tobacco leaves in relation to chloride

house with concentrations of sodium chloride ranging from 0·5 to 6·0 milli-equivalents per litre in the applied nutrient solution, have shown that increased chloride in leaves of the same physiological age is associated with increased scopoletin (Fig. 1). Glass-house-cured tobacco leaves and field-grown cured leaf also show similar relationships in scopoletin and chloride content, and calculations based on the assumption that the spot area is proportional to the logarithm of spot content[6] give concentrations of scopoletin varying approximately from less than two to one hundred and seventy times greater in the leaf with high-chloride than in one containing a low-chloride concentration.

The increase in scopoletin associated with a higher chloride content in the leaf may account for the typical morphological and anatomical effects produced both in the leaf and generally in the plant: the stunting (also noticeable in virus attack[3]) being due to the effect on the indoleacetic acid metabolism, and the thickening of the secondary xylem to increased concentrations of scopoletin at the site of the differentiating tissue. Scopoletin concentrations in the root and stem of tobacco plants under varying chloride treatments are being examined.

As scopoletin passes unchanged into the main-stream smoke on combustion of the tobacco[8], it may be an important factor in tobacco quality as influenced by sodium chloride in the soil. Other factors which affect the nutrient balance, such as low potash content, also appear to favour the accumulation of scopoletin.

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Function of the Osphradium in *Bullia* (Gastropoda)

Krijgsman and Brown[1] have recently described a technique for operating on fully extended and immobilized marine Gastropoda. We have now used this 'water-rigour' method on 124 individuals of *Bullia laevissima* (Gmelin) preparatory to severing their osphradial nerves in order to discover the function of the osphradium. The osphradium in Gastropoda is generally thought to be an organ of chemo-reception, though the evidence in support of this theory is far from satisfactory. Experiments such as those of Copeland[2] are not convincing in view of the crude techniques used. A few workers, notably Hulbert and Yonge[3], have suggested that the osphradium may be concerned with the perception of turbidity; but no experimental data have been presented in support of this view, the only evidence being circumstantial. Detailed histological studies of the osphradium, such as those undertaken by Stork[4], add little to the argument.

Of the 124 snails on which we operated, 52 did not recover and post-mortem examination revealed damage to the pallium and/or the dorsal pallial artery which passes just below the osphradium. When the remaining 72 snails were killed and dissected after the completion of our experiments, it was found that in some cases the osphradial nerve had not been completely severed, while in others nerves other than the osphradial nerve had been cut or damaged accidentally. The results of experiments on these snails were therefore disregarded. In only 13 cases was the operation completely successful, the osphradial nerve being entirely severed without damage to other structures. Of these 13 snails, 12 lived for more than a week in the laboratory and were offered food on each successive day.

Bullia laevissima normally lies half buried in the sand, under water, only the upper part of the shell and the siphon being visible. It can be caused to emerge actively from the sand if suitable food be placed in or near the water. (A detailed account of this behaviour is given elsewhere by Brown[5].) However, individuals which have had the osphradial nerve severed fail to emerge, even when presented with their favourite food—the tunicate *Pyura*. Nevertheless such individuals will feed when placed on the food or touching it, indicating that failure to emerge is not resultant on a disinclination to feed, but rather indicates a deficiency in chemo-perception from a distance. We are therefore of the opinion that chemo-reception is at least the major function of the osphradium in this species.

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CYTOLOGY

Number of Chromosomes in the Human Cell

CURRENT work with human chromosomes in many laboratories has resulted in the publication of numerous photographs of chromosomes of human cells both normal and abnormal. Almost all these have been obtained from cells which are selected at least to the extent that they are cells capable of undergoing mitosis one or more times *in vitro*. These cells are often subjected to physical conditions which might conceivably influence the process of mitosis, that is, temporary chilling, change of *p*H, etc. Further, in most cases the mitotic process has been disturbed intentionally by the use of colchicine.

Because of the possible significance of these factors, we feel that the accompanying photograph (Fig. 1) will be of interest. It shows an unstained, uncolchicinized bone marrow mitosis obtained within minutes after aspiration from a 59-year-old female. There is clear representation of 46 chromosomes. The correspondence of this and other morphological details with those obtained using colchicine and tissue culture methods is to be noted. We feel this is

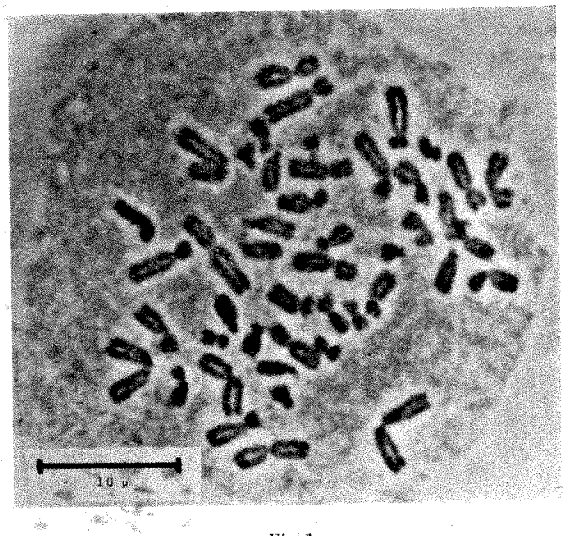

Fig. 1

important in that it demonstrates a lack of dependence of these characteristics on the use of tissue culture and colchicine.

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Growth of the Gametes of *Amoeba spumosa* Grüber

IN a previous paper[1] the biological cycle of *Amoeba spumosa* Grüber, the amoeba most often found in fresh water in Lombardy, was described and the cytological aspects of the gametes of this amoeba were studied by means of the electron microscope.

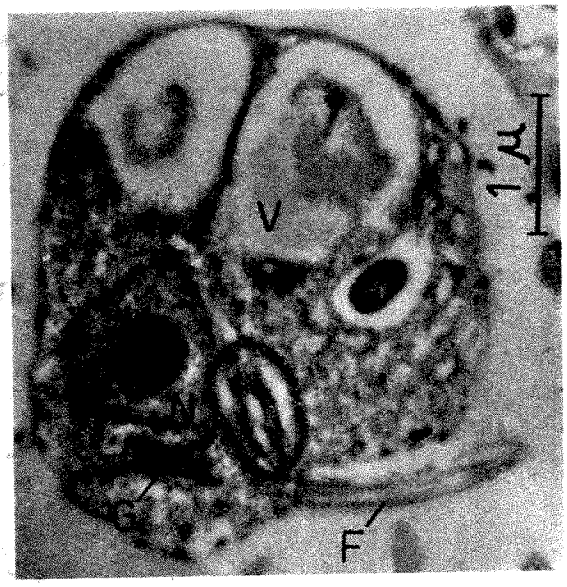

Fig. 1. Electron microscopical picture of a section of an *Amoeba spumosa* gamete. *F*, flagellum; *G*, Golgi apparatus; *N*, nucleus; *V*, vacuoles at the top end

These gametes (Fig. 1) are spherical cells, which move around by means of a flagellum, like those of *Amoeba proteus*: this observation confirms the forgotten observation of Jones[2]. The flagellum has a structure common to the flagella of other organisms: that is, it contains nine peripheral filaments and two central filaments.

The present work was carried out to study these gametes statistically, in order to ascertain their developmental biology.

Amoebæ in gametogenesis, cultured under daylight (at 19° C.), release (Fig. 2) their gametes: in the following days it is possible to study the development of the released gametes. It is better to follow the growth of isolated gametes. In order to obtain quantitative data, we have studied isolated gametes, fixed with vapour, of a 2 per cent solution of osmium tetroxide for 5 min. and stained with Giemsa fluid, diluted 1 : 20 with distilled water.

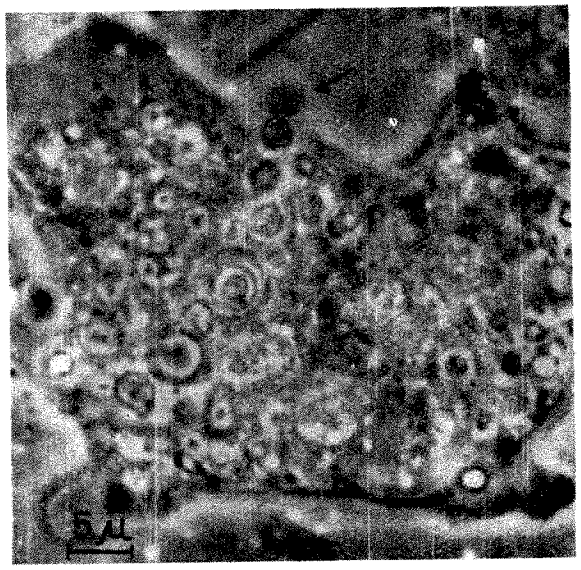

Fig. 2. Gametogenesis in *Amoeba spumosa*; the arrow shows a gamete that is escaping

The size of the gametes ranges between 2·6μ, which is the diameter of a gamete escaping from the mother amoeba, and 11μ: it takes about a fortnight for the gametes to reach this size. The gametes about five days old measure 6·8μ and at this time they copulate. The copulating gametes have the same size; therefore they appear to be isogametes and the zygote, as soon as it is formed, shows bilateral symmetry. A systematic study to see whether there are phenomena of relative sexuality is in progress.

Larger gametes, more than 7μ in diameter, correspond to a senescent stage. These large gametes, which did not copulate and will never copulate, undergo a slow degeneration. These large flagellate forms are, in fact, less stainable and show such a delicate protoplasmic structure that even a dilute staining solution may dissolve them.

The diagram (Fig. 3) illustrates the increase of four different gamete cultures at the stage before copulation. After the discovery of this increase we tried to study it from a cytological point of view. An increase in the size of the vacuoles, which are

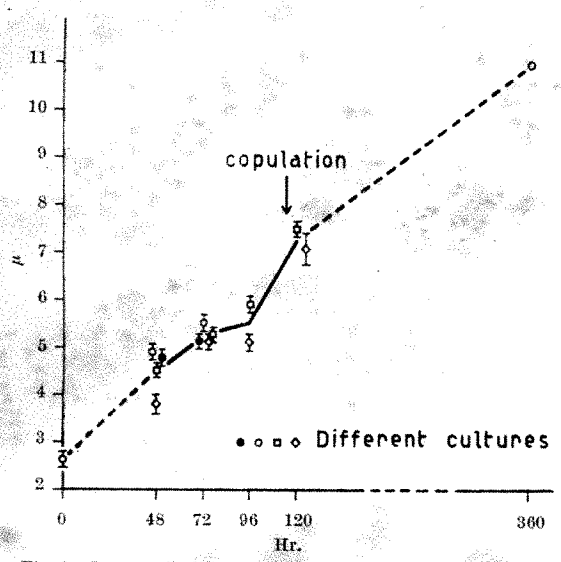

Fig. 3. Increase in diameter of the gametes of *Amoeba spumosa* after their release

placed at the gamete's anterior end, starts during the gamete growth. Some of these vacuoles contain small bodies intensely stained red by Giemsa fluid: they seem to be bacteria living in the culture medium. The conclusion, drawn from the study by the electron microscope[1], that a gamete ingests some bacteria and digests them in its vacuoles, is therefore confirmed. It seems, therefore, that gamete growth depends on true nutrition and not merely on an imbibition process by taking up water.

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VIROLOGY

Concentration of Poliovirus by an Aqueous Polymer Two-Phase System

WITH the technique for polio vaccine production used at present, the end-point titres often are in the neighbourhood of 10^6/ml., which is recommended as the lowest limit. Different methods have been tested to find a simple way for concentration of the virus. The physical and chemical methods proposed so far are rather complicated and give a comparatively low yield of virus[1]. Variations in the technique for cultivation of the virus have also been suggested as a means of increasing the virus titres[2].

In the experiments to be described here, a physico-chemical method for separation and concentration of macromolecules was used[3-8]. The method is based on the almost completely one-sided distribution of macromolecules which may be obtained when these are distributed in an aqueous two-phase system containing two different polymers. For concentration purposes, a phase system is constructed in such a way that the phase in which the virus particles are collected has a small volume compared with the original virus suspension. The virus is partially separated from other cellular constituents since these are distributed in a different manner[6,7,9].

In the present experiments, sodium dextran sulphate (prepared from a dextran fraction with a limiting viscosity number of 70 ml./gm.; sulphur content, 17 per cent; Pharmacia, Uppsala, Sweden) and polyethylene glycol ('Carbowax 6000'; Carbide and Carbon Chemicals Co., New York) were used for concentrations of poliovirus. Experiments with the same system have recently been made on *ECHO* virus[9]. The results of the application of the system to poliovirus, however, are considered worth while reporting, with regard to the possible use in vaccine production.

The polymers were added to harvested tissue culture fluid from *CHAT*-infected monkey kidney cultures until the final concentration was 0·2 per cent (w/w) dextran sulphate and 6·45 per cent polyethylene glycol. The virus suspension had previously been clarified by centrifugation for 10 min. at 2,000 r.p.m. In addition, a 5 *M* sodium chloride solution was added until the salinity of the total mixture was 0·3 *M*. After careful mixing, the system was allowed to separate for 24–48 hr. at + 4° C. Samples were then withdrawn from the top and the bottom phase and from the layer between these two—the interface. The titrations of the virus were carried out in monkey kidney tissue culture tubes, and logarithmic end-point titres were calculated.

A typical experiment gave the results shown in Table 1.

Table 1

	Virus titre/ 0·1 ml.	Volume (ml.)	Total amount of virus (*ID*50)
Original material	6·5	100	$3·2 \times 10^9$
Bottom phase (phase rich in dextran sulphate)	8·4	1·2	$3·0 \times 10^9$
Interface	7·7	—	—
Top phase (phase rich in polyethylene glycol)	4·6	134	$5·2 \times 10^7$

The bottom phase obtained represents about 1/100th of the total volume of the system. The virus, which accumulates in the bottom phase, is therefore concentrated 90–100 times. In controls, none of the polymers showed harmful effect on the virus. At the interface some proteins, probably cell debris, were precipitated. No change in the immunogenic capacity of the final preparation, measured in guinea pigs[10], was found.

The bottom phase contains 17 per cent dextran sulphate and is rather viscous; therefore it would be inconvenient as a vaccine preparation. The following methods were tested to remove the dextran sulphate:

(1) Precipitation by adding either 0·69 ml. 3 *M* potassium chloride or 0·3 ml. 1 *M* barium chloride per gm. bottom phase. All the virus activity remained in solution.

(2) Addition of 5 *M* sodium chloride to the collected bottom phase until the concentration of the sodium chloride became 1 *M*. By this procedure a new phase system was obtained. The volumes of the phases and the distribution of the virus in this system are shown by the results of the experiment recorded in Table 2.

In this secondary system almost all the dextran sulphate is in the bottom phase. Because of the changed molarity, more than 99 per cent of the virus is accumulated in the top phase. This contains only

Table 2

	Volume (ml.)	Titres/ 0·1 ml.	Amount of virus ($ID50$)
Original virus suspension	200	7·1	$2·6 \times 10^{10}$
Primary system : bottom phase	2·0	9·3	$4·0 \times 10^{10}$
Secondary system : top phase	0·5	9·8	$3·2 \times 10^{10}$
bottom phase	1·9	6·7	$9·5 \times 10^{7}$

dextran sulphate of the order of 0·1 per cent and in addition about 1 per cent polyethylene glycol. These small amounts of dextran sulphate may be eliminated by the chemicals suggested in (1). Since the volume of the top phase is about one-fifth of the total volume of the secondary system, a further concentration of virus is obtained.

The procedures described with poliovirus in the system dextran sulphate – polyethylene glycol leads to purification and a 100–500 times concentration of the virus. The product shows an antigenic capacity, which corresponds to the infectious titre measured by the cytopathogenic effect in tissue culture. Residual concentration of polymers in the concentrate is of the order of 0·1–1 per cent.

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SOIL SCIENCE

Diffusion of Ions in Soils

A KNOWLEDGE of the speeds at which ions diffuse in soils is of both basic and agronomic importance, but the development of accurate methods for the measurement of diffusion coefficients has received little attention. During an investigation of the factors controlling the rate of diffusion, the following method has been evolved.

The value of the coefficient of diffusion (D) from Fick's law can be obtained for the system shown in Fig. 1, where at the time when the two sections of soil are placed in contact the amount of the ion under investigation is equal in the two halves, but in one a proportion consists of a radioactive isotope. The quantity of material Q which is diffused across the boundary CD in time t can be calculated from the relationship :

$$\frac{Q}{Q_\infty} = 1 - \frac{8}{\pi^2}\left[e^{-At} + \frac{e^{-9At}}{9} + \frac{e^{-25At}}{25} + \text{etc.}\right] \quad (1)$$

where $A = \frac{D\pi^2}{4L^2}$, L is the distance represented by AC and Q_∞ is the quantity which would cross the boundary in infinite time. When the value of $\frac{Q}{Q_\infty}$ is less than 0·5 this equation may be replaced by :

$$\frac{Q}{Q_\infty} = \frac{2}{L}\sqrt{\frac{Dt}{\pi}} \quad (2)$$

That either equation (1) or equation (2) may be employed according to the value of $\frac{Q}{Q_\infty}$ is illustrated by results for comparable experiments on the diffusion of rubidium (rubidium-86) in a Greensand soil. Using equation (1) for $\frac{Q}{Q_\infty} = 0·96$ a value of $6·19 \times 10^{-8}$ cm.^{2}/sec. was obtained for D, while the value from equation (2) when $\frac{Q}{Q_\infty} = 0·417$ was $6·13 \times 10^{-8}$.

By plotting graphically the theoretical relationship between $\frac{Q}{Q_\infty}$ and At of equation (1), a curve of the type shown in Fig. 2 is obtained. From this curve a value of A may readily be obtained given the experimental determination of $\frac{Q}{Q_\infty}$ for a known time t. D is then calculated from A. This simplified method has been found to give sufficient accuracy.

For experiments with soil, the conditions of the model shown in Fig. 1 are difficult to reproduce, since it is difficult to place two sections of soil in contact so that the boundary is sharp, and the subsequent separation and analysis are accurate. If the system is made so large that errors at the boundary are negligible, then experiments take an unduly long time to complete, for the root mean square displacement of the ions is proportional to $\sqrt{t}$. This problem of experimental procedure has been solved in the following way. It may be seen from Fig. 1 that

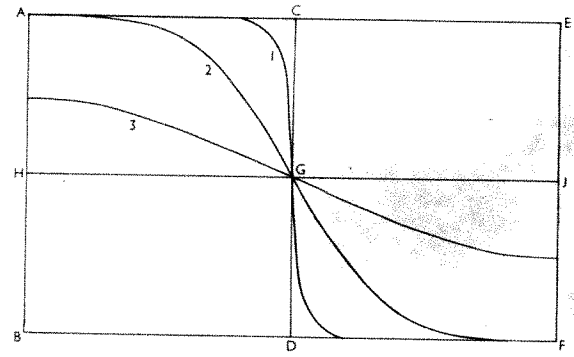

Fig. 1. Two layers of soil with an equivalent content of the ion under investigation are placed in contact and in one a proportion of the ions is present as the radioisotope. At the moment of contact the radioactive ions in section $ABDC$ are uniformly distributed and the height AB represents the value of the original concentration. As a result of the diffusion process radioactive material will move across the boundary CD into the section $CDFE$. As this process continues, the form of the distribution will change with time, as shown by the curves 1, 2 and 3. The line HGJ represents the final distribution after an infinite time

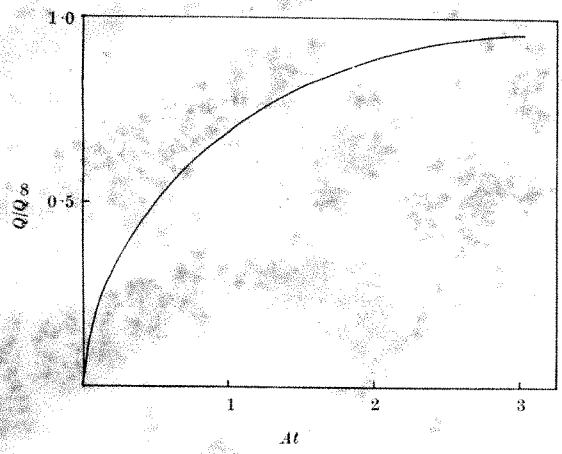

Fig. 2. The relationship of Q/Q_∞ and At as calculated from equation (1)

immediately the ions cross CD, the concentration at this boundary falls to a value represented by DG ($= \frac{1}{2}AB$) and afterwards remains at this level. If a thin sheet of a permeable ion-exchange material containing the diffusing ions at a concentration in equilibrium with DG is inserted between the two sections, the rate and pattern of movement in the soil will be affected to a negligible extent, provided first that the rate of diffusion in the exchange material is fast enough relative to that in the soil, and secondly, that the exchange capacity of the material is considerably higher than that of the soil. It has been found that 'Permaplex' ion-exchange membrane is suitable for this purpose. Calculations for the system indicate that the maximum error introduced by the resin is equivalent to less than 1 per cent of the length of the soil sections (AC of Fig. 1).

The method of experimentation is as follows. Two disks of the ion-exchange membrane are shaken individually in identical solutions containing equal aliquots of a given soil, but in one solution a radioactive isotope of the ion under investigation is incorporated. After equilibration with the soil the two disks are removed and held in contact for about 24 hr. until the radioactive ions have become uniformly distributed as a result of diffusion. One disk is then used to separate the equilibrated radioactive and inactive layers of the selected soil in a small closed cylinder the diameter of which is the same as that of the disk, that is, 1 in. The other disk may be kept to check that the disk in the cylinder does not gain or lose radioactivity during the experiment. The two layers of soil are later removed after a known time and extracted so that the quantities of radioactive material diffusing from one layer to the other may be measured. The value of the diffusion coefficients can then be calculated.

Diffusion coefficients vary with concentration, but the use of radioactive tracers makes it possible to measure differential coefficients of diffusion at exact concentrations under conditions where the total concentration is constant throughout the system but where a gradient of radioactive ions exists. Moreover, the tracer method also eliminates the complexities associated with the displacement of other adsorbed cations.

Using this technique it is possible to work with layers of soil only 2·5 mm. thick. The results so far obtained indicate that the diffusion coefficient may be as high as $1{\cdot}2 \times 10^{-7}$ cm.^{2}/sec. (corresponding to a root mean square displacement of 1·4 mm. in a day). Detailed experiments on one Greensand soil have so far shown that the rate of diffusion is considerably affected by compaction, being maximal at about 1·5 gm./ml. The effects of both temperature and the concentration of the soil solution suggest that a considerable part of the movement takes place when the cations are held in the exchange complex.

The research is now being extended to cover diffusion of several cations and anions in a variety of soils, together with a further analysis of the effects of the water content of the soil, the concentration of the soil solution, and temperature.

We wish to acknowledge our indebtedness to the Agricultural Research Council for a grant in support of this investigation.

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University of Oxford.
July 22.

Aluminium Ions in Aluminium Hydroxide, Phosphate and Soil-Water Systems

IN recent years attention has been given to the solubility of aluminium phosphates in soils. Of the synthetic preparations examined, variscite, $Al(OH)_2H_2PO_4$, has been most extensively investigated and criteria for its existence in soils evaluated[1]. It has been assumed that the solubility product of variscite can be determined from the activities of the ionic species in the expression $K_{sp} = (Al^{3+})(OH^-)^2(H_2PO_4^-)$ and predictions of the phosphate content of soils have been made on this basis[2].

A recent investigation on the ionic species of aluminium in equilibrium with various forms of aluminium oxy-hydroxide and hydroxide has shown that for conditions usually found in soils, $AlOH^{2+}$, $Al(OH)_2^+$ or less-highly charged forms such as $Al_3(OH)_7^{2+}$ (strictly $[Al_3(OH)_7^{2+}]_n$, where n is an integer, but we assume the monomer, although the dimer is perhaps preferable) may be present in appreciable amounts. This means that these species may also determine K_{sp}.

For pH less acid than 4 in the presence of newly formed aluminium hydroxide (commonly called amorphous) and in an unbuffered system of very low ionic strength, the curve obtained on plotting the negative logarithm of the number of moles of aluminium per litre of solution [$p\mathrm{Al}_M$] against the pH had a slope of 2, indicating that $[AlOH^{2+}][OH^-]^2$ = constant (curve C in Fig. 1). This curve agrees with the other workers' results for solubility and hydrolysis. In the presence of buffers, when the system was required to adapt itself to a demand for hydrogen ions by the buffer, more hydrolysis occurred and a curve (D) was obtained with a slope 2/3, which means that $[Al_3(OH)_7^{2+}][OH^-]^2$ = constant. When gibbsite was present, curve B resulted, which agrees with data in the literature on aged aluminium hydroxide. Experiments with diaspore showed that it was less soluble than the previous two forms and gave a curve (A) of slope 1 for pH less acid than 4·6, indicating that here $[Al(OH)_2^+][OH^-]$ = constant. Curve A also agreed with results from the literature for corundum and $Al(OH)_2^+$.

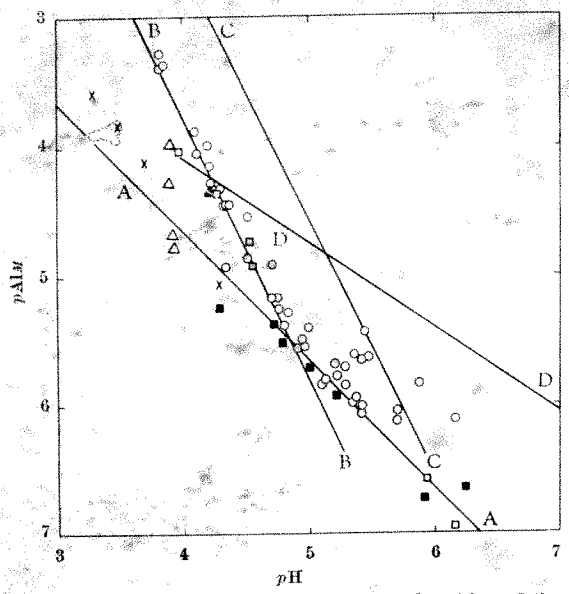

Fig. 1. Relationships between the negative logarithm of the number of moles of aluminium per litre of solution and the pH. Curve A as found for diaspore (■) and predicted for corundum dissolving as $Al(OH)_2^+$; curve B as found for gibbsite (□) and as predicted for aged aluminium hydroxide dissolving as $Al(OH)^{2+}$; curve D as found for fresh aluminium hydroxide in buffered systems (see text). Data for variscite (×), variscite–kaolinite (▲) and phosphated and unphosphated sodium and aluminium kaolinites (△) and for three soils (○) on treatment with 0·01 M calcium chloride are also given. The dotted points falling in a group on the upper left of the figure are for soils treated with 0·001 M hydrochloric acid and 0·01 M calcium chloride

It is of interest to superimpose on Fig. 1 results obtained by other workers for solutions in equilibrium with variscite, clays and soils.

The data for a variscite–kaolinite system[3] (represented by a single point in Fig. 1 where equilibrium has been reached after 56 days), for variscite[3] and for aluminium and sodium kaolinites phosphated and unphosphated[4], fall largely between lines A and B. The data for soils presented in Fig. 1 are for 0·01 M calcium chloride extracts of Hagerstown *s.l.*, Greenville *f.s.l.* and Mardin *s.l.* (refs. 1, 5) (no activity corrections have been applied). The phosphate found in these solutions does not influence the position of the points in any uniform manner, although the range of variation of phosphate is greater than a hundredfold. This indicates that in these systems the important relationship is between pAl_M and pH (ref. 6). Not all soils would be expected to follow lines A and B. The data of earlier workers[7] on more acid soils lie for the greater part against line C, showing that $Al(OH)^{2+}$ was present and indicating that some Al^{3+} may be present under more acid conditions than pH 4·3. Again, the phosphate-level did not exert a systematic influence on the position of the points. These results show that the various aluminium hydroxides examined, amorphous, gibbsite and diaspore, may well represent stable phases in these soils. If variscite coexists as a discrete solid, its solubility does not appear to be fully exerted. On the other hand, it has long been advocated that the phosphate is bound to aluminium hydroxide to form a sorption compound.

The possible existence of variscite in some soils cannot, however, be discarded lightly, because soil–water systems have been observed to show reactions very similar to those of variscite, including the minimum phosphate solubility near pH 4 (ref. 8).

While the reactions giving rise to the solubility of variscite in more acid regions are reasonably clear, little is known of what occurs under more alkaline conditions. A possible reaction which would give rise to an increased solubility of variscite with increasing pH is:

$$H_2O + 3Al(OH)_2H_2PO_4 = Al_3(OH)_7^{2+} + 3H_2PO_4^- + H^+$$

This would give a slope of the pH and logarithm of the soluble phosphate curve which would be of the correct order for variscite and laboratory equilibria for a lateritic soil[8]. It would mean that the point of minimum solubility should be in the pH range 4·2–5·2 (that is, the intersection of curves B and D or C and D) as found in practice. If the kind of aluminium hydroxide present in a 'variscite' system is varied the value of the solubility product will vary so that care must be taken in extrapolating predictions from one situation to another even when it has been shown that the solubility of variscite is a controlling factor. It is clear that, for a detailed knowledge of reactions occurring in soil phosphate systems, it is necessary to study the ionic species present in the soil solution. The next step is to endeavour to determine which are the key reactions in the intricate interplay of processes taking place in the soil solution.

I hope to publish a full account of this work in due course.

M. RAUPACH

Division of Soils,
Commonwealth Scientific and
Industrial Research Organization,
Adelaide,
South Australia.

[1] Lindsay, W. L., Peech, M., and Clark, J. S., *Soil Sci. Soc. Amer. Proc.*, **23**, 357 (1959).
[2] Hsu, P. H., and Jackson, M. L., *Soil Sci.*, **90**, 16 (1960).
[3] Kittrick, J. A., and Jackson, M. L., *Soil Sci. Soc. Amer. Proc.*, **19**, 455 (1955).
[4] Hemwall, J. B., *Soil Sci.*, **83**, 101 (1957).
[5] Wright, B. C., and Peech, M., *Soil Sci.*, **90**, 32 (1960).
[6] Cf. Wright, B. C., Diss. Abstr., **20**, 2991 (1960).
[7] Pohlman, G. G., *Soil Sci.*, **36**, 47 (1933).
[8] Raupach, M., and Piper, C. S., *Austral. J. Agric. Res.*, **10**, 818 (1959).

ARCHÆOLOGY

Recent Discoveries at Olduvai Gorge

As a result of the discovery in 1959 of the skull of *Zinjanthropus boisei*[1], in association with an Oldowan living floor at site *F.L.K.* I Olduvai, funds for a much more extensive programme at the end of 1959 and during 1960 were generously made available by the Wenner Gren Foundation, the Wilkie Foundation and the National Geographic Society of Washington, to all of which I express my deep gratitude.

After some preliminary work in December 1959 and January 1960, major excavations were started at site *F.L.K.* I (where the skull came from) in the middle of February 1960. These excavations are progressing very satisfactorily. An extensive and rich living floor of approximately 1–2 in. in thickness has been uncovered. It rests on a bentonitic deep-water clay and is immediately overlain by a consolidated deposit of water-laid volcanic sand. This living floor lies some 20 ft. below the uppermost deposit of Bed I.

Neither the underlying clay nor the overlying consolidated volcanic sand contains any large bones, nor any coarse material of any kind, and every large object lying on the living floor must have been brought there. All the larger animal bones have been broken open to obtain the marrow; all jaws and skulls of animals are smashed. A high proportion of the bones represent immature animals. Many more stone tools of the Oldowan culture have also been found.

Our hope of obtaining the mandible which belongs to the original *Zinjanthropus* skull has not, so far, been realized, but we now have a nearly complete tibia and fibula (Fig. 1), as well as what is probably a small piece of the pelvic girdle, together with some additional teeth and parts of the skull of a second individual, all from this original site.

The quantity of stone tools and flakes now available from this living floor will make it possible to assess the components of an industry of the Oldowan culture in great detail.

In addition to the excavations at this main site, a second site has been located, not far away, at what appears to be a slightly lower level of Bed I. This site is called *F.L.K.N.N.* I and, so far, it has yielded an amazing wealth of fossils—but only a very few artefacts.

The hominid fossils from this second site include fragments of a skull and some teeth, two clavicles (Fig. 2), a large part of a left foot (Fig. 3), six finger bones and two ribs. The animal fossils consist of a remarkable assemblage of genera and species, many of them new to Olduvai, and some unquestionably new to science.

Perhaps the most remarkable object from this second site (*F.L.K.N.N.* I) is a genuine bone tool (Fig. 4). This would appear to be some sort of a 'lissoir' for working leather. It postulates a more evolved way of life for the makers of the Oldowan culture than most of us would have expected.

Yet another site in Bed I (known as *F.L.K.N.* I) has been located during the past few weeks. This lies at a level some 20 ft. above the other two floors and immediately below the topmost deposit of Bed I. This third site consists of a very rich living floor with quantities of broken-up animal bones and many stone tools and flakes. Work on it has only just started.

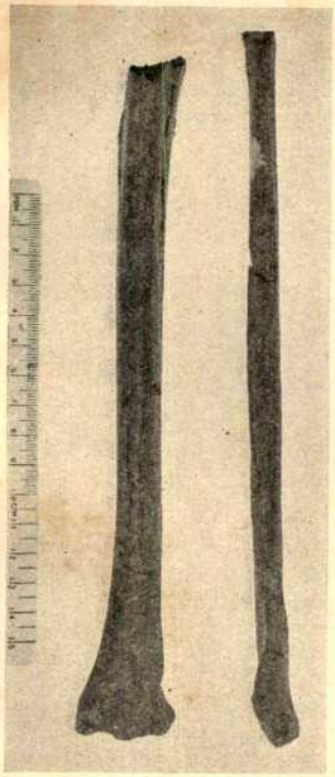

Fig. 1. The tibia and fibula from site *F.L.K.* I

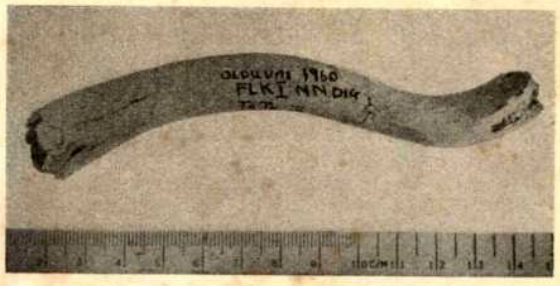

Fig. 2. One of the two clavicles from site *F.L.K.N.N.*

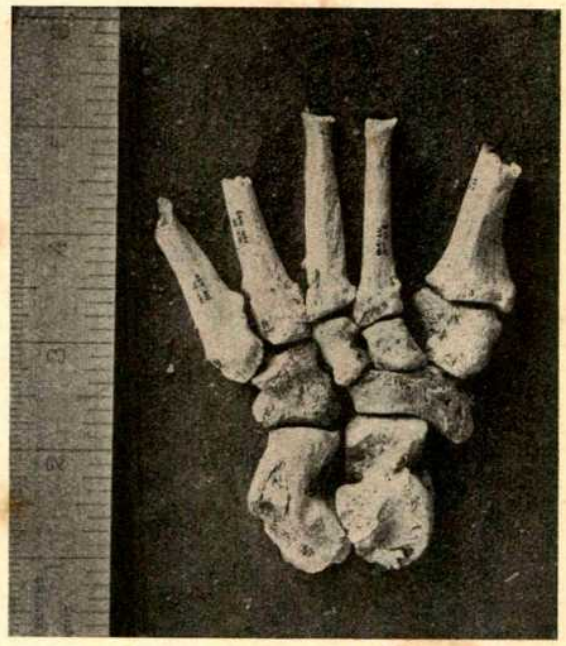

Fig. 3. Some of the bones of the left foot. The calcaneum is damaged

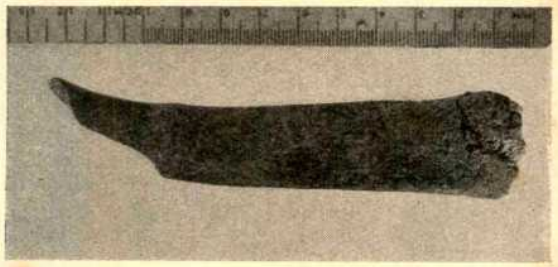

Fig. 4. Bone tool from site *F.L.K.N.N.* I

Excavations have also been conducted at a site known as *F.L.K.* II, which is stratigraphically well above the main *F.L.K.* I site, and this, as was expected, has yielded a fauna comparable to that of Olduvai sites *B.K.* II and *S.H.K.* II. The fauna is in direct association with an assemblage of artefacts of Stage 3 of the East African Chellean sequence.

The discovery of parts of hand and foot are of very special importance, for hitherto we have had no knowledge of these parts of the skeleton in early hominids.

This year's work has very strongly confirmed the statement which I made last year that Bed I is very distinct (both from the point of view of its fossil fauna and its culture) from Beds II, III, IV. Bed I is of Lower Pleistocene, or Villafranchian age; whereas Beds II, III and IV belong to the Middle Pleistocene.

As a result of the work carried out so far this year, the National Geographic Society has kindly made available a further grant to continue work for four or five more months.

L. S. B. LEAKEY

The Coryndon Museum,
Box 658, Nairobi,
Kenya.
Sept. 16.

[1] *Nature*, **184**, 491 (1959).

MISCELLANY

"Education of Scientists"

IN his account of the British Association meeting on the education of scientists in *Nature*, October 22, p. 270, Prof. M. W. Thring reports that students who have obtained a General Certificate of Education examination in six subjects, of which three are at the Advanced Level, have reached the minimum requirements for entry to a university. These attainments are, in fact, much higher than are specified by the majority of British universities for entrance purposes.

In my own lecture, I was commenting on the high calibre of students joining the Diploma in Technology courses and expressing my satisfaction that, of the 700 students already accepted for these courses at the Northampton College of Advanced Technology, London, more than 300 had passed in three subjects at the Advanced Level in addition to the Ordinary Level requirements.

One other matter in the report needs clarification. In setting up the diploma in technology, the National Council for Technological Awards had clearly in mind that students who obtained first-class honours should be every bit as good as the first-class honours university graduate, and there is every reason to believe that these aims are being attained. The recommendation of the Committee of Vice-Chancellors and Principals to the Universities, that holders of the diploma in technology should be considered on the same footing as university graduates for registration for higher degrees, was an acceptance of this belief, and it is good to know that the recommendations have already been put into effect. In fact, one young man whose qualification is a diploma in technology has joined the academic staff of a provincial university.

JAMES S. TAIT

Northampton College of Advanced Technology,
St. John Street, London, E.C.1.

Cost of Scientific Periodical Publications

I REFER to the figures showing the cost of scientific journals which have been given and discussed in recent issues of *Nature*. The figures quoted by Mr. K. W. Humphreys and Mr. H. D. Barry[1] give the comparable costs per page to libraries for various journals. (Incidentally, the cost of the *Biochemical Journal* is £4 per volume of approximately 620 pages, that is, 1·5*d.* per page, not 0·75*d.* as quoted.)

Captain Maxwell's table[2], however, compares the price charged to libraries for the *Journal of the Chemical Society* and some other journals with the price charged to individuals for the publications of Pergamon Press. Since fellowship of the Chemical Society is open to all approved persons throughout the world interested in the science, and one of the Society's main purposes is to disseminate chemical knowledge as widely and as cheaply as possible among scientists, it is proper to compare the price to Fellows with that of Pergamon journals to individuals. For the *Journal of the Chemical Society* the Fellows' price is approximately 0·5*d.* per page against a price to libraries of 1·0*d.* per page.

Captain Maxwell also states that a journal which has the backing of a scientific society has the advantage of a guaranteed circulation to its members, and, in most cases, a subsidy. These statements are incorrect if intended to apply to the Chemical Society, the only British publishing society mentioned in his table. The *Journal* is available only to those Fellows who choose to pay for it, and at the present time only some 16 per cent of Fellows exercise this option. Moreover, the Society does not receive any subsidy or outside grant for its publications, which are currently produced at a modest profit. I submit, however, that the prices quoted by your contributors show that this profit is not achieved by means of an unduly high price to libraries.

M. W. PERRIN

The Chemical Society,
Burlington House, W.1.

[1] *Nature*, **186**, 124 (1960).
[2] *Nature*, **187**, 1052 (1960).

CAPT. MAXWELL'S reply[1] to the paragraph concerning publication costs[2] is disingenuous; to show how cheap his publications are he compares his reduced price to private individuals with the top price of others to corporate subscribers. It is necessary in a fair comparison to compare 'like things with like'. Thus if, for example, *Tetrahedron* to the private individual costs 0·7*d.* per page, *Chemical Abstracts* to the private member subscriber costs 0·15*d.* per page, which brings our journal to the top of the list at a price and value which is second to none.

To say that journals backed by scientific societies have guaranteed circulation is unrealistic in most cases; it certainly is not true with *Chemical Abstracts*. Member subscribers to *Chemical Abstracts* are subsidized in an effort "to ensure maximum dissemination", but *Chemical Abstracts* has been on a self-supporting basis since 1956.

D. B. BAKER

The Chemical Abstracts Service,
Ohio State University,
Columbus 10, Ohio.

[1] *Nature*, **187**, 1052 (1960).
[2] *Nature*, **186**, 124 (1960).

FORTHCOMING EVENTS

Monday, December 19

INSTITUTION OF MECHANICAL ENGINEERS, STEAM GROUP (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Discussion on "Safety on Construction Sites".

Tuesday, December 20

INSTITUTION OF ELECTRICAL ENGINEERS, MEASUREMENT AND CONTROL SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Discussion on "Digital Transducers", opened by Mr. L. Airey.

Wednesday, December 21

INSTITUTION OF ELECTRICAL ENGINEERS, ELECTRONICS AND COMMUNICATION SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. L. J. Ward: "Microminiaturization".

SOCIETY OF CHEMICAL INDUSTRY, CORROSION GROUP (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Discussion on "Practical Problems in Corrosion".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned.

ASSISTANT (graduate in mathematics, mathematical statistics or statistics, and preferably experience with punched cards and electronic computers) IN RESEARCH IN THE DEPARTMENT OF HUMAN ECOLOGY, to engage in the planning and the analysis of medical research projects—The Secretary of the Faculty Board of Medicine, The Medical School, The University, Tennis Court Road, Cambridge (December 31).

JUNIOR ASSISTANT LIBRARIAN (university graduate, preferably with some experience and/or professional qualifications in classification and cataloguing)—The Librarian, University College of North Staffordshire, Keele, Staffs (December 31).

LECTURER (with a degree in bacteriology or equivalent qualification) IN BACTERIOLOGY—The Secretary, West of Scotland Agricultural College, 6 Blythswood Square, Glasgow, C.2 (December 31).

POSTDOCTORAL RESEARCH FELLOW IN PHYSICAL CHEMISTRY, to study the properties of solids by mass spectrometry—The Registrar, The University, Edgbaston, Birmingham 15 (December 31).

SENIOR LECTURER IN ORGANIC CHEMISTRY; and a LECTURER IN ZOOLOGY, WITH SOME PHYSIOLOGY—The Registrar, Hatfield Technical College, Hatfield, Herts (December 31).

COMPUTATIONAL ASSISTANT (with a degree in mathematics or engineering or similar qualification, and preferably experience of the use of an electronic computer) IN THE DEPARTMENT OF MECHANICAL ENGINEERING, to use the university digital computer for work concerning the lubrication research which is going on within the Department—The Registrar, The University, Leeds 2 (January 6).

LECTURER (with qualifications in any of the branches of zoology, and preferably an interest in physiology, genetics or some other branch of experimental zoology) IN ZOOLOGY at the University of Tasmania, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, January 6).

SCIENTIFIC OFFICER or SENIOR SCIENTIFIC OFFICER (honours graduate in biochemistry and/or physiology, with appropriate research experience), to undertake research on hill sheep nutrition—The Secretary, Hill Farming Research Organization, 48 Palmerston Place, Edinburgh 12 (January 7).

CHADWICK CHAIR OF CIVIL ENGINEERING tenable at University College—The Academic Registrar, University of London, Senate House, London, W.C.1 (January 9).

FORESTERS (recently qualified university forestry graduates) in the New Zealand Forestry Service—The High Commissioner for New Zealand, 415 Strand, London, W.C.2, quoting Ref. B.11/9/8 (January 9).

HORTICULTURAL ADVISORY OFFICERS (with a degree in horticulture, preferably with practical experience in the production of horticultural crops, and in field advisory and experimental work) in the Agriculture Department, New Zealand, to advise growers on the production of horticultural crops, chiefly fruit and vegetables, undertake field experiments, and conduct surveys and special investigations—The High Commissioner for New Zealand, 415 Strand, London, W.C.2, quoting Ref. B.11/2/28 and Vacancy No. 3474 (January 9).

INSPECTORS OF EXPLOSIVES (2) (men or women at least 30 on November 1, 1960, with a degree (preferably first- or second-class) in chemistry or chemical technology, or equivalent qualification) with the Home Office, for duties involving travel to all parts of the country, and include advising on safety precautions for the manufacture, storage and conveyance of explosives; inspecting premises licensed for manufacture and storage; and advising on safety precautions for the storage and conveyance of petroleum and other dangerous substances—The Civil Service Commission, 17 North Audley Street, London, W.1, quoting S/5284/61 (January 10).

CHAIR OF CIVIL ENGINEERING—The Registrar, University College, Singleton Park, Swansea (January 14)

FISHERY INVESTIGATING OFFICERS (male, physically fit, with an honours degree in zoology, and prepared to spend considerable time in the field) in the Marine Department, New Zealand, to undertake local investigations and advise on biological aspects of freshwater fisheries management and development problems in all parts of New Zealand, with headquarters in Wellington—The High Commissioner for New Zealand, 415 Strand, London, W.C.2, quoting Ref. B.11/15/6 and Vacancy No. 3271 (January 16).

SOIL SURVEYORS (2) (graduates in botany, chemistry, geography, geology or agriculture and preferably with previous experience in soil survey, particularly in the tropics) in the Regional Research Centre for the West Indies, Faculty of Agriculture, University College of the West Indies, Trinidad—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (January 20).

LECTURER (part time), to investigate respiratory functions in childhood—The Secretary, Institute of Child Health (University of London), Great Ormond Street, London, W.C.1 (January 21).

ASSOCIATE PROFESSOR OF MEDICAL BIOCHEMISTRY IN THE DEPARTMENTS OF MEDICINE AND BIOCHEMISTRY, University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, January 23).

CHAIR OF PARASITOLOGY in the University of Malaya, Singapore—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (January 31).

LECTURER or ASSISTANT LECTURER IN ELECTRICAL ENGINEERING—The Registrar, The University, Southampton (January 31).

SENIOR LECTURER IN CIVIL ENGINEERING (STRUCTURES) at the University of Western Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, January 31).

EXPERIMENTAL OFFICERS (preferably with a pass degree or H.N.C., and a knowledge of electrical and electronic methods of measuring displacement, velocity, acceleration, strain and temperature under vibration conditions and experience in the design of electronic circuitry would be an advantage) to set up and operate instrumentation for an interesting programme of environmental testing. Duties will include the design of special electronic instruments to meet particular requirements—The Senior Recruitment Officer, U.K.A.E.A., A.W.R.E., Aldermaston, Berks, quoting Ref. A.2684/84.

HEAD (man or woman, with a good honours degree and experience) OF THE MATHEMATICS DEPARTMENT—The Headmistress, Queen Anne's School, Caversham, Reading.

NATIONAL RESEARCH COUNCIL AND OTHER POSTDOCTORAL FELLOWSHIPS IN THE DEPARTMENT OF PHYSICS—Prof. H. E. Duckworth, Chairman, Department of Physics, McMaster University, Hamilton, Ontario, Canada.

PHYSIOLOGIST or ZOOLOGIST (with a good degree in physiology or zoology, preferably with Ph.D., and interests and experience in the field of mammalian reproduction) in a small unit investigating the biochemical and physiological properties of cervical secretions, with particular reference to fertility—The Secretary, National Institute for Research in Dairying (University of Reading), Shinfield, Reading, Berks, quoting Ref. 60/17.

READER (able to show evidence of research ability in the academic and industrial fields, and preferably with experience in the food industry) IN FOOD PROCESSING AND FOOD ENGINEERING—The Principal, National College of Food Technology, St George's Avenue, Weybridge, Surrey.

RESEARCH ASSISTANT (preferably with an honours degree in physical and inorganic chemistry) IN THE DEPARTMENT OF MINERALOGY AND PETROLOGY, for a programme of research concerning fundamental solid-state problems in the field of cement chemistry—Dr. J. D. C. McConnell, Department of Mineralogy and Petrology, Downing Place, Cambridge.

RESEARCH ENGINEER (with an honours degree in chemical engineering and proved research ability) IN THE DEPARTMENT OF CHEMICAL ENGINEERING, to work under Prof. Edgeworth Johnstone on the dimensional scaling-up of a particular type of process plant—The Registrar, The University, Nottingham.

SENIOR TECHNICIAN II (with special experience in bacteriology) to take charge of a laboratory—The Secretary, Forest Group Hospital Management Committee, Langthorne Road, Leytonstone, London, E.11.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Ciba (A.R.L.), Limited. Technical Notes No. 212 (August, 1960). The "Bluebird" C.N.7. Pp. 8. (Duxford: Ciba (A.R.L.), Limited, 1960.) [149

British Welding Research Association. Fifteenth Annual Report, 1959–60. Pp. 64. (London: British Welding Research Association, 1960.) [149

Hopkin and Williams, Ltd. Organic Chemical Reagents. Monograph No. 40. 2.9-Dimethyl-1.10-Phenanthroline ("Neocuproine") Reagent for Copper. By E. J. Newman and G. Peters. Pp. 6. (Chadwell Heath, Essex: Hopkin and Williams, Ltd., 1960.) [149

Henry Wiggin and Co., Ltd. Incoloy DS: Heat-Resisting Nickel-Chromium-Iron Alloy. Pp. 7. (London: Henry Wiggin and Co. Ltd., 1960.) [149

A Bibliography of Farm Buildings Research, 1945–1958. Part 3. Buildings for Poultry. Pp. 84. (London: Agricultural Research Council, 1960.) 4s. 6d. [149

Television and the Family. (A Report on an Enquiry designed and directed by Dr. W. A. Belson, and carried out by the Audience Research Department of the B.B.C. under the supervision of Professors A. R. Knight, M. G. Kendall, P. E. Vernon, and Barbara Wootton.) Pp. xx+151. (London: British Broadcasting Corporation, 1959.) [149

New Check List of British Agarics and Boleti. By R. W. G. Dennis, P. D. Orton, and F. B. Hora. (Supplement to *Transactions of the British Mycological Society*, June 1960.) Pp. 225. (London: Cambridge University Press, 1960.) 15s. net; 2.50 dollars. [149

Department of Scientific and Industrial Research, and Fire Offices' Committee Joint Fire Research Organization. Fire Research 1959: Report of the Fire Research Board with the Report of the Director of Fire Research. Pp. viii+63+8 plates. (London: H.M. Stationery Office, 1960.) 5s. [149

Science Masters' Association. Provision and Maintenance of Laboratories in Grammar Schools (1959). (Results of a Questionnaire issued in 1959 by the Science Masters' Association, Association of

Women Science Teachers, National Union of Teachers, and Joint Four Secondary Association.) Pp. 16. (London: John Murray, 1960. Published for the Science Masters' Association.) 1s. net. [149

National Union of Teachers. Treasure Chest for Teachers: Services available to Teachers and Schools from Societies and Associations which have some bearing on various aspects of the School Curriculum. Pp. 94. 3s. Mathematics in the Primary School. By R. A. Swallow. (Curriculum Studies, No. 1.) Pp. ii+44. 2s. 6d. Science in the Primary School. By Cedric Griggs. (Curriculum Studies, No. 2.) Pp. 35. 2s. (London: The Schoolmaster Publishing Co., Ltd., 1960.) [149

Department of Scientific and Industrial Research: Building Research Station. Factory Building Studies, No. 7: Structural Frameworks for Single-Storey Factory Buildings. By H. V. Apcar. Pp. v+34. (London: H.M. Stationery Office, 1960.) 4s. net. [149

Price's (Bromborough) Limited. Technical Publication No. 7: Water Conservation—Bibliography of References in the Published Literature including some of the chief references to the literature in Allied Fields. Pp. 70. (Bromborough Pool, New Ferry, near Birkenhead: Price's (Bromborough), Ltd., 1960.) [149

Annual Report on the Meteorological Office for the year April 1, 1959 to March 31, 1960. Pp. 55+4 plates. (M.O. 683.) (London: H.M. Stationery Office, 1960.) 4s. net. [149

The North of Scotland College of Agriculture. Calendar, 1960–61. Pp. 138. (Aberdeen: North of Scotland College of Agriculture, 1960.) [149

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INDUSTRIAL RESEARCH AND DEVELOPMENT

IN the Sir David Russell Memorial Lecture delivered last March on the perils of leadership in science, Sir Lindor Brown said there are three major decisions of strategy to take in scientific work: what to start, when to stop, and where to go, in that rather peculiar order. Although Sir Harold Hartley's address* on the choice of subjects for research and development at the autumn research meeting of the Institution of Gas Engineers in November was concerned primarily with technology, his address recalled a good deal that Sir Lindor Brown said, as did indeed the debate opened by Lord Shackleton in the House of Lords on November 9 on the report of the Advisory Council on Scientific Policy. Lord Hailsham's important speech in that debate in particular indicated how largely the right balance of effort in the technological, as in the scientific, fields depends on wise decisions of exactly the type that Sir Lindor Brown emphasized. The prime requisite is always sound judgment.

Sir Harold Hartley, after quoting Prof. J. Jewkes's aphorism that science is directed towards understanding and technology towards use, and admitting that the economic aspects of research and development must always be governing criteria of policy, emphasized that the ultimate decision is always a matter of such judgment trained by experience. Moreover, like Lord Stamp, Sir Harold Hartley is well aware of the importance of suiting the tool to the job; Lord Stamp's observation that, while in writing a paper for the Royal Society 100 per cent accuracy is the objective, in industrial research a 60 per cent accuracy is a good achievement, is in line with Prof. T. L. Cottrell's recent criticism of the graduate's failure to apply theory or to approach a problem critically and consider the purpose to be served before choosing the means. Clearly what Sir Harold Hartley has in mind is the ability to seize an opportunity, and to make sound decisions as to what real openings may be offered by some interruption of a research programme through the demands of what he describes as first aid or an emergency call for immediate help.

Sir Harold is obviously prepared to accept a certain amount of such work as a legitimate function for a research department, provided that a careful watch is kept for such opportunities of new developments. Apart from this, it may lead to the acquisition of experience on which sound judgment can be based; this is not less true of work directed at the improvement of existing practices and products. Here he recognizes that the selection of research projects and the guidance of their progress are matters of national importance, and that it is not easy to determine the division of effort between the development of existing practices and exploring the possibilities of entirely new departures. One function of research in regard to the former is the provision of accurate and simple means for assessing efficiency; but this can tell us nothing about entering entirely new fields. On the other hand, the considerations and criteria that could be applied in assigning priorities to possible research projects, which Sir Harold described in this section of his paper, seem to be responsible for the continued demand manifested both in the House of Lords and in the House of Commons for the release of more information on such topics as the reports on shipbuilding research and on the machine-tool industry in Britain. It should also be added that in his reference to operational research into maintenance costs and research into instrumentation and automatic control, Sir Harold touched on a field which it is recognized offers increasing opportunities for co-operation between firms and groups of firms, both nationally and on an international scale.

In discussing his third category of research and development projects, namely, those aimed at the invention and development of new techniques, new materials and new appliances, Sir Harold Hartley relies rather too closely on Prof. J. Jewkes's study in "The Sources of Invention", and does little to clarify the distinction between research and invention or the factors that contribute to inventiveness, or even the criteria that may guide the choice of projects for research and development. Indeed, he accepts it as axiomatic that the bulk of the work of most industrial research laboratories will be concerned with what he describes as first aid, and with the improvement and development of existing processes in the light of advances in scientific knowledge. The choice of the latter projects must rest on cost analysis, on market research, and judgment of their scientific and engineering possibilities, though to suggest that they must also rest on the research effort available is to contradict a remark Sir Harold made in opening his address: there is surely a time at which a project calls for an expansion in research staff to seize an opportunity. That at least is obvious from some of the case-histories of Prof. Jewkes which Sir Harold quotes.

Sir Harold's argument here seems essentially to stress the importance of such an inquiry as that undertaken by the Advisory Council on Scientific Policy at the request of the Minister for Science; but he rightly emphasizes the need to adjust a research programme from time to time in accordance with its progress and other circumstances, and the importance in the direction and administration of research of an intimate day-to-day contact with the individuals concerned so as to avoid frustration or the destruction of confidence. He also makes one important constructive suggestion. The most successful system he has seen involved detaching a group of able people

* Institution of Gas Engineers. Publication No. 578: The Choice of Subjects for Research and Development. By Sir Harold Hartley. Pp. 9. (London: Institution of Gas Engineers, 1960.)

from all responsibility for specific projects, so that they could follow the progress of the different projects and keep in close touch with both the makers and the users of the products of the laboratory. The group was thus in a position to adjust the research programme to meet changing circumstances, and it was on its advice that projects were strengthened if they showed promise and were needed, or slowed down, or stopped. Sir Harold recognizes that such a system requires delicate handling, but he said that it had worked well and prevented projects being continued long after they were likely to pay a dividend. It does not, however, appear to be a system that is easily applied to fundamental scientific research; but it is easily recognized as the embryo of the Advisory Council on Scientific Policy, as distinct from the research councils themselves. Lord Shackleton, who opened the debate in the House of Lords on November 9, appeared to recognize this, though he was not altogether willing to accept the division of function and responsibility between a research council and the Advisory Council for Scientific Policy. He seemed to lean too readily to the view that massive support of research is all that is required and to ignore the demands which the selection of projects makes for judgment. It is true that in discussing the magnitude of the research and development effort in Britain he recognized the need for further investigation, and particularly into comparative figures for expenditure in terms of the gross national product, but he was concerned as to whether the right balance was being maintained between research and development.

That balance was not really considered in the Advisory Council's recent report, which Lord Shackleton was discussing, but he did not suggest that the balance was necessarily wrong. He admitted that the distinction is difficult to draw in practice, and it could well be maintained that any survey of the scientific effort in Britain as a whole, such as the Advisory Council initiated, could not fail to bring to light any weaknesses, in either pure or applied science; indeed, the recent report directs attention to gaps quite impartially in the scientific and the technological field. Some of those gaps, as Lord Shackleton himself acknowledged, have been emphasized by Lord Hailsham, and two in particular received some emphasis in the debate. Both these were noted by Lord Shackleton, and Lord Hailsham, who followed him, referred to them in some detail. He began by stressing the importance which he and the Council attach to the reports of the Economic Section of the Council for Scientific and Industrial Research into the machine tools industry and into the shipbuilding industry. The purpose of these reports, which were concerned solely with the scientific and research aspects of these industries, was to keep the Advisory Council informed on the economic aspects of their scientific research and on their particular research programmes, so as to enable the Council to advise industry on what they may regard as their research requirements. In other words, the Economic Section is in large measure assisting the Advisory Council to fulfil one of the essential functions to which Sir Harold Hartley directed attention in his address to the Institution of Gas Engineers.

Lord Hailsham said that the report on the machine tools industry was compiled with the full co-operation of the industry and contained so much confidential information from individual firms that an undertaking had to be given that it would not be published without the consent of the industry itself. He believes that the report has already yielded important results. For example, it appeared that the pattern for training engineers in universities and colleges is not well suited to the needs of the machine tool industry, and in consequence of the report new courses are likely to be available. Also, it had established forcibly the need for a research association and one is already being formed. The need for development on certain lines had also been brought to light, and Lord Hailsham also referred to a forthcoming report from a committee under the chairmanship of Sir Stewart Mitchell appointed to consider Prof. Seymour Melman's report on the Western European machine tool industry presented to the European Productivity Agency last year.

This report was published on November 10, and afterwards the Department of Scientific and Industrial Research and the Machine Tools Trades Association issued a statement giving details of what is being done by way of schools of research, higher training in machine tool technology, scholarships and special courses, to meet the challenge to the British industry. Subsequent speakers in the debate again pressed Lord Hailsham on the publication of these two reports; but although he indicated that he had always favoured publication of such documents, he firmly defended the decision not to publish on the ground that a promise had been given in good faith that private information should be kept private. Nevertheless, it was clear that Lord Hailsham was much less happy about the report on the shipbuilding industry, and did not exclude the possibility of publication of that report or some modified version of it, or some programme of research which would embody part of the report. He stated originally that the information was not obtained on quite the same confidential basis as that in the report on the machine tool industry, and he did not regard the Department of Scientific and Industrial Research as having given an undertaking that the information should not be published. The decision whether or not the report should be published must rest with the Council for Scientific and Industrial Research; all that he urged was that the confidential discussions on which he was engaged with the industry should not be prejudiced by publication. On December 1, Sir David Eccles, as representing the Minister for Science, stated in the House of Commons that the industry and the Department had that morning agreed on publication as early as possible.

Two other comments made by Lord Shackleton drew important statements from the Minister for

Science. Lord Shackleton referred to the organization of Government research and the work of the Zuckerman Committee, and in reply Lord Hailsham outlined very clearly his conception of his own responsibilities. He proposed to use the Advisory Council on Scientific Policy as was indicated in its current annual report; but while the Government is responsible for seeing that gaps in our scientific activities are filled and the work is done, the responsibility for doing the work rests elsewhere—with the Research Councils, Government departments, the universities and industry. He is considering with the officers of the Royal Society how an even closer liaison could be achieved between that Society and the various bodies for which he is responsible.

In reply to Lord Shackleton's comment that some of the recommendations in the Advisory Council's report are too general, Lord Hailsham suggested that his function was to some extent discharged, in any event in the first degree, when he caused these questions to be asked; and that the right inference to be drawn was that the proposals are actively under discussion in independent fields as a result of the inquiry. Specifically, he agreed that the arrangement of the rapidly increasing work within the scope of the Research Councils requires further consideration; but as regards Lord Shackleton's request that he should entrust the responsibility for natural resources to the Nature Conservancy, he said that the Advisory Council on Scientific Policy would probably be asked to consider in the near future the detailed pattern of our effort in regard to natural resources.

On receiving the recent report, Lord Hailsham said he had directed the attention of the various responsible bodies to findings which he thought particularly concerned them. He was confident that the universities and the University Grants Committee would take the report into account, and though he fully recognized the force of the objection to earmarked grants, Lord Hailsham indicated that he would not hesitate to deal with the difficulty if need arose. He is particularly concerned at present, he said, both with the shortage of qualified engineers and with the insufficiency of engineering research, both in the universities and in industry. Both these factors are major weaknesses in Britain at present, and will not be removed until this field attracts a due proportion of the best intellects in the country.

Here Lord Hailsham suggested a decisive factor is the status which engineering enjoys in the universities, and this is a matter which only the universities can remedy. Lord Hailsham did hesitate to proclaim his own view that engineering should enjoy a far higher status in the universities than it has hitherto been allowed to do, and his profound respect for university autonomy should not be construed as inhibiting action if due regard is not paid to Britain's interests. Obviously, he prefers to work through the accepted channels, but the whole tenor of his speech implied readiness for resolute and even drastic action here and elsewhere if the need were established.

One other topic on which Lord Hailsham touched is the matter of development contracts. In 1952 the Advisory Council on Scientific Policy recommended that the use of development contracts in civil industry should be urgently explored, and afterwards the function of the National Research Development Corporation was extended to cover the promotion of research likely to lead to some important invention. The Department of Scientific and Industrial Research has been authorized to act as focus for the idea of civil development contracts; but so far results, apart from the activities of the Atomic Energy Authority and the National Research Development Corporation, have been meagre.

The Advisory Council takes the view that the problem of the development contract is not insoluble, though it is very difficult when Government is not the direct customer and has not laid down in detail the specifications and objectives; but a solution should substantially improve the development of the results of scientific research. It is not, however, in the Council's view, a problem to be solved by centralized action alone, but one in which industry must take a leading part. Essentially it is a matter of research-mindedness and a tradition of using the results of scientific and technological advance.

Lord Hailsham expressed the hope that this situation would soon be altered. He referred to proposals for development contracts in the field of machine tools likely to be put forward through the National Research Development Corporation or the Department of Scientific and Industrial Research, and to proposals under discussion for computers. It is possible that a new technique may be developed; but if this does not happen, it is clear that Lord Hailsham is prepared to examine the whole problem afresh, and in replying on the whole debate he made pointed and reassuring reference to the place of the research associations.

Neither the Advisory Council nor the Minister for Science is under any illusion that support of a research association is any substitute for research-mindedness and an active research policy within an individual firm; but both his speeches in this debate indicated that the Minister for Science, like the Advisory Council, has a firm grasp of essentials and of the conditions in which creative activity is most fruitful. Lord Hailsham revealed himself as determined to stimulate those conditions; but equally he was resolute to avoid generating unnecessary opposition or causing friction which might waste effort or defeat the objective. His final remarks that these matters should be kept clear of party politics so far as possible deserves to be widely noted. Emphatically, Lord Hailsham is right to hold that the relation between science and Government and between science and industry must be appropriate to the type of industrial and social organization a country possesses. All that should be added is that those relations should change as the organization may change, and without undue time lag. The provision of a Parliamentary Secretary to the Minister should assist the Minister for Science to pursue his inquiries into these and other matters

more readily and in greater detail. No scientist or technologist could well ask of a Minister for Science a more forward-looking mind than Lord Hailsham revealed in the debate, or clearer indication of readiness to act where necessary, while respecting the practices and traditions which have proved their value in scientific and academic work. He obviously looks to the research associations to play an important educational function in industry apart from any actual contribution to research, and the debate should dispose of any uneasiness as to the future of the research associations as a whole. Specifically, in reference to an instance mentioned by Lord Pethick-Lawrence, of a scientist who had left Britain for America because he was unable to obtain the equipment he needed here, Lord Hailsham undertook to examine any similar instance in which some particular aspect of science was not properly cared for by the provision of apparatus if the matter were brought to his notice. The keen awareness of the importance of scientific and technical education at all levels, and perhaps especially of that designed to provide the supporting technicians needed in the universities, as well as in industry and Government departments and institutions, was a most encouraging feature of a notable debate.

THE NEWER COSMOLOGY

The Nature of the Universe

By Prof. Fred Hoyle. New and extensively revised edition. Pp. vii+103+6 plates. (Oxford: Basil Blackwell, 1960.) 8*s*. 6d. net.

THIS is a revised edition of the well-known book of some ten years ago in which Prof. Hoyle recorded his very popular broadcast talks on what he described as "The New Cosmology". The order of presentation and general style are unchanged, but there are, of course, revisions of certain details. Chief interest, however, will centre on the substantial changes, and these are considerable.

The estimated density of interstellar matter has been reduced a thousandfold, thus annihilating important effects formerly ascribed to the 'tunneling' of stars through this medium. The number of planetary systems in a galaxy is now at least 1,000 and perhaps 100,000 times greater than before, while the age of our Galaxy, previously given as "quite definite and precise" is now increased fourfold and has become "reasonably definite and precise".

The greatest change, however, concerns the origin of the planets. In the earlier book it was shown that the idea that these originated from solar material "must be wrong", "hopelessly wrong", and that the planets "must have" originated in the explosion of a companion of the Sun. Now, however, it appears that the planets did originate from solar material, the companion having been non-existent. "There is no idle speculation here." Prof. Hoyle's faith that the cosmology of 500 years hence will appreciably resemble the particular cosmology of to-day which he now favours remains unshaken.

It is very remarkable that such fertile imagination and mathematical skill can accompany such credulity and lack of critical power in one person. The general reader may decide what weight to attach to the astronomical conjectures from the "personal view" at the end concerning "continued existence after death", for here he is not menaced by the fear of incommunicable mathematics in the background which elsewhere confounds his judgment. "My own answer would be that mind is an intricate organization of matter. In so far as the organization can be remembered and reproduced there is no such thing as death. If ordinary atoms of carbon, oxygen, hydrogen, nitrogen, etc., could be fitted together into exactly the structural organization of Homer, or of Titus Oates, then these individuals would come alive again exactly as they were originally. The whole issue therefore turns on whether our particular organization is remembered in some fashion. If it is, there is no death. If it is not, there is complete oblivion."

Suppose Prof. Hoyle were regrettably to die tomorrow, and someone fitted the atoms into the necessary structure: which view of the origin of planets would the resurrected mind, "as it was originally", take? If the structure changes from moment to moment while we live, to take account of growing experience, is it not strange that it never by accident gets shaken into a configuration that knows the future, and that so many otherwise quite diverse organizations all happen to be aware of the Suez crisis, say—now that it has occurred, of course? But perhaps, after all, our knowledge of these matters, as of some others, is not yet quite definite and precise.

HERBERT DINGLE

SPACE RESEARCH

The Exploration of Space

A Symposium on Space Physics, April 29–30, 1959. Edited by Robert Jastrow. (Sponsored by the National Academy of Sciences, the National Aeronautics and Space Administration, and the American Physical Society.) Pp. v+160. (New York and London: The Macmillan Company, New York, 1960.) 5.50 dollars; 38*s*. 6*d*.

THIS book is the record of the papers presented at the symposium on "Space Physics" held at Washington during April 1959, and of the 'round-table discussions' which concluded each session. The first three papers show how much has still to be learnt about interplanetary space, or the 'Sun's outer atmosphere' as it is now sometimes called. F. L. Whipple surveys our present knowledge of solid particles in the solar system, remarking that "the general subject of meteoritics is in a sorry plight". T. Gold deals with the ionized particles and magnetic fields, and stresses the importance of electromagnetic effects. E. Parker, looking at the same region with a different bias, emphasizes the hydrodynamic expansion of the solar corona, as it streams into space at speeds of around 500 km./sec. Next, the radiation zones are described by their discoverer, J. A. Van Allen, and the *Argus* experiment by its proposer, N. C. Christofilos. H. E. Newell reviews the United States plans for future space-vehicles, G. de Vaucouleurs summarizes what is known about Mars and Venus, and G. P. Kuiper discusses the Moon, contending that the craters are caused both by volcanic action and by meteoritic impacts. H. C. Urey, in a paper entitled "Primary and Secondary Objects", suggests that

stony meteorites originated in a primary object of roughly lunar size formed about 4,000 million years ago. There are two contributions concerned mainly with space-research techniques: H. Friedman on the rocket astronomy he has done so much to promote, and L. Goldberg on astronomy from satellites. Finally, J. W. Townsend outlines a programme for future space research, and R. Jastrow describes the Earth's outer atmosphere.

The book can be thoroughly recommended, and fully justifies the publishers' claim that it is a "comprehensive survey of the most recent developments in space science", though the developments are now not quite so recent as they were, since the increased pace of scientific progress has not been matched by any corresponding acceleration in printing, proof-reading —or reviewing. All but one of the papers given at the symposium were first printed in the November 1959 issue of the *Journal of Geophysical Research*, and the book is a faithful reproduction of the pages from the *Journal*, including all the misprints. The book illustrates a growing and deplorable tendency to reprint unchanged, in book form, scientific articles which are known to have misprints. If publishers wish to adopt this practice for economy, they should surely include a list of errata: for this book, such a list could well be headed by the value for the age of the Moon on page 143, which is in error by a factor of 10^{18}.

D. G. KING-HELE

INVARIANCE PROPERTIES OF PARTICLES AND FIELDS

Theory of Elementary Particles

By Paul Roman. (Series in Physics.) Pp. xii+575. (Amsterdam: North-Holland Publishing Company; New York: Interscience Publishers, Inc., 1960.) 100*s*.

THE progress that has been made in establishing a basic theory of the elementary particles and their interactions has depended to a large extent on the use of invariance properties under transformations. These range from the obvious Lorentz transformations to rotations and reflexions in isobaric space. They give rise to conservation laws, selection rules and relationships between reactions, all of which can be tested by experiment. Their deduction does not necessitate the solution of the field equations, which has so far not proved to be generally possible for the strong interactions. For the weak interactions almost complete understanding has been achieved as a result of the comparatively recent discovery of the non-conservation of P and C.

Dr. Roman's book is particularly concerned with the invariance properties and their influence on the structure of the quantum field theory used to describe the elementary particles and their interactions. The treatment is outstandingly good. It is inevitably mathematical and requires an effort on the part of the reader (particularly the experimental variety), as is recognized by the author in his preface. He has most successfully sugared the pill by setting out the mathematics in considerable detail and carefully discussing its implications and limitations. The experimental implications are kept constantly in view and it is made clear how experimental results have determined the structure of the theory at every stage.

The first 100 pages are devoted to the theory of the four-dimensional orthogonal group and its representations. In the next 114 pages the quantum field theory is developed, starting with a classical treatment of the field equations to establish their form for the different fields. Quantization of the fields is then introduced, leading to the commutation rules and the use of creation and annihilation operators. The remainder of the book is devoted to the invariance properties. In particular, P, C, T transformations and the relation between them are considered in detail and a section is devoted to the effects of the non-conservation of P and C in weak interactions. Transformations in isobaric space are then introduced, leading to the Gell-Mann Nishijima classification of the elementary particles. There are interesting discussions of the $|\Delta t| = \frac{1}{2}$ selection rule and of the properties of neutral K mesons. Finally, more complete mathematical models of the elementary particles are considered, including the Prentki-d'Espagnat theory of isospace. It should perhaps be mentioned that no attempt is made to include the methods (such as dispersion relations) that are being tried for dealing with the strong interactions.

This book can be recommended unhesitatingly to those who wish to become familiar with the basic theory of the elementary particles and their interactions. It will also be a vital source of reference for those who are only intermittently concerned with the basic aspects of the theory.

A. ASHMORE

CHEMICALS AND INSECTS

Methods of Testing Chemicals on Insects, Vol. 2.

Edited by Harold H. Shepard. Pp. iii+248. (Minneapolis, Minn.: Burgess Publishing Company; London: Mayflower Publishing Co., Ltd., 1960.) 40*s*.

THIS volume is the second in a series projected by the former Chemical-Biological Co-ordination Center, having as its object the publication of "a manual of test methods dealing with the effects of chemicals on insects".

The first volume has already been reviewed in *Nature* (183, 352; 1959). The second volume begins with a group of three papers: "Pre-test Conditions which affect Insect Reaction to Insecticides", "Factors affecting Insects during Exposure to Insecticides", and "Post-exposure Conditions and Determination of End Point". This division looks orderly on paper, but it is difficult to maintain, and a single chapter would probably have been preferable. Much of the second chapter would be more correctly entitled "Factors affecting Insecticides during the Exposure of Insects"—which is quite a different subject.

The remaining chapters deal with testing methods for insecticides used for specific purposes. Chapter 4, "Exposure to Treated Food Medium", and Chapter 5, "Screening Space Sprays against Flies and Cockroaches", give good straightforward outlines of the methods used, but some comments on the fundamental factors concerned would have assisted the intelligent use of these methods. Chapter 6 deals with "Soil Insecticides". Chapter 7, "Testing Resistance of Chemically Treated Textiles", unlike Chapter 5, gives full details for carrying out the tests, and it may be said again that it seems regrettable that the

various contributions are not standardized in this respect. Chapter 8, "Screening Chemical Repellents", describes various methods, and instructively relates the fundamentals of the subject to the testing procedure. Chapter 9 deals with "Insect Proofing of Food Packing Materials". Chapter 10, "Screening Chemical Attractants", gives a rather unorganized account of this difficult subject. It includes a method for assessing 'contact attractance' which is out of place, and much material about the use of attractants in conjunction with insecticides which has no relevance to screening.

Chapter 11, "Testing Acaricides", is one of the best in the book, and supplies the information that anyone embarking on this work would require. Chapter 12, a short one, entitled "Animal Sprays, Dusts, Dips and Dressings", gives an account of field test methods. Chapter 13, "Techniques for the Evaluation of Systemic Insecticides against Livestock Sprays", is a clear introduction to this subject. However, some of the methods used sound unpleasant for the animals, and one wonders if alternatives could not be devised.

This is a useful reference work and the best chapters give excellent introductions to the subjects discussed. Unfortunately test-insects are not listed in the index.

W. A. L. DAVID

CONTROL OF PLANT GROWTH

Crop Production and Environment

By Dr. R. O. Whyte. New edition. Pp. 392+31 plates. (London: Faber and Faber, Ltd., 1960.) 63*s*. net.

THE title of this book is not a reliable guide to the contents. Some of the subjects discussed, for example, the morphology of stem apices, the biochemistry of reproduction and the effects of growth substances, extend into much wider fields than the relation between crops and their environment. On the other hand, the most important practical aspect of this relation—the dependence of crop yield on climate, seasonal weather and soil factors—is barely mentioned.

The purpose of the book is to summarize results of research on the physiology of plant growth and development published since 1946, when the first edition appeared, and to show their application in agriculture and horticulture. As in the first edition, the chief topic is control of morphological development, particularly flowering, by temperature and day-length, that is, vernalization and photoperiodism, but there is also some discussion of quantitative growth of field crops, and of the significance of leaf area as a determinant of yield. An account of equipment for growing plants in controlled environments ranges from commercial glasshouses to phytotrons. Twelve chapters deal with the physiology of growth of different crop species, and the "agricultural botanists, agronomists, crop ecologists, plant breeders and general biologists" for whom the book is intended will probably find this the more interesting and useful part.

The author's aim has been to give as much factual information as possible within the prescribed space; he has not attempted to write a critical review, nor to deduce general relationships from the mass of experimental data. The resulting narrative has no clear pattern and few connecting threads, so it is difficult to read and still more difficult to absorb. Much of the text consists of quotations from the original papers, and their variation in style contributes to the lack of unity and cohesion. The figures and plates are used to squeeze in still more information in a compact form; often they are not mentioned in the text, and sometimes the descriptions in the legends are inadequate.

Although, as the author himself says more than once, this book is superficial and not comprehensive, it will be a valuable reference work, for there is no other that attempts to cover the same ground. It is thoroughly documented, and has a bibliography of about four hundred references.

D. J. WATSON

EARLY THOUGHTS ON PROGRESS AND PROFITS

Progress and Profits in British Economic Thought, 1650–1850.

By G. S. L. Tucker. (Cambridge Studies in Economic History.) Pp. vii+206. (Cambridge: At the University Press, 1960.) 27*s*. 6*d*. net.

MR. TUCKER provides a scholarly analysis of the course of the debate in Britain about the relationship between the return on investment and economic progress. It should be of great interest to those who ponder the attempts of societies to understand themselves.

It is a little curious that it is during the beginning of the story, in the second half of the seventeenth century, that the debate is closest to the kind of emphasis applied nowadays. For then men argued, more or less instinctively, about the ability of rulers to affect the course of events by manipulating an indicator, which might also be a determinant. Josiah Child and his kind were all for pushing down interest rates, to attain by synthetic means what the course of commerce had produced in Holland, with the idea that this would create the most favourable conditions for British commerce. But with Adam Smith, and especially Ricardo, the emphasis changed; the debate became more concerned with distribution than with growth. The author throws much light on how this occurred, though perhaps he does not sufficiently emphasize the restrictive nature of the full Ricardian theory, making the whole outcome depend on diminishing returns to agricultural effort. The only policy measure left to Ricardo and his school for the furthering of growth was the plea for free trade, so that the margin of cultivation could be thrown back to the New World. But with the next generation, though much Ricardian influence is still present, the problem of excessive capital formation has become pressing. Britain had arrived at a situation similar to that of the Dutch much earlier, but instead of plenty of capital guaranteeing progress, the fear that it might be excessive gains ground, as the stresses mount in Britain in the late 1830's and the 40's. Thus J. S. Mill, Wakefield, Torrens and others begin to think in terms of the export both of capital and men, so that both may find better opportunities abroad, and may, in conjunction, reduce the cost of imported primary products to Britain. Here, at the mid-nineteenth century, Dr. Tucker's story ends; he might well continue it.

S. G. CHECKLAND

Electrolytic Conductance

By Prof. Raymond M. Fuoss and Prof. Filippo Accascina. Pp. ix+279. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1959.) 59*s*.

THIS book deals with the theory of electrolytic conduction as developed on the basis of the Onsager equation by Fuoss and Kraus and later workers of their school. Briefly, their treatment was to introduce the Bjerrum hypothesis of the formation of ion pairs into the theory of Debye and Huckel, and to extend the treatment so as to cover non-aqueous solutions. In 1955, Fuoss and Onsager solved the theoretical problem for a model in which the ions were represented by charged spheres instead of point charges. The resulting equation involved two arbitrary constants, the limiting conductivity of the Onsager equation and the ion size. Fuoss later extended the treatment to electrolytes in which the ions are associated into ion pairs, but the equation is limited to very dilute solutions. The authors say in the preface that they do not think there is any hope of extending the theory to higher concentrations, where they think the treatment must start from fused salts, which are supposed to be diluted with non-electrolytic material.

The theory is developed in the book, the necessary mathematics being first summarized in short chapters on such matters as vectors and tensors (restricted to Gibbs's dyadics), hydrodynamics, and statistical mechanics. The static phenomena such as activity coefficients are fairly simply disposed of. The difficulty begins when conductivities are considered. The relaxation field is extended to higher terms, then binary and higher associations of ions are brought in. In general, the mathematical treatment is clearly set out, but it would be a help to the reader if it were stated at the beginning of each chapter just what was to be done in it. The book is restricted to the particular theory stated, but it contains material useful in the study of the alternative theories, which are not considered.

J. R. PARTINGTON

The Physics of Electricity and Magnetism

By Prof. William Taussig Scott. Pp. xvi+635. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1959.) 70*s*. net.

ONE is conscious at the present time of the feedback from research and discovery to the matter and methods of elementary instruction, or, more accurately perhaps, of the need for such a cycle. Physicists, for example, while complaining that the younger generation is ill-versed in the principles developed in the seventeenth and eighteenth centuries, also take exception to syllabuses and treatments that date from somewhere about the middle of the nineteenth. But it is not easy to see how to improve matters by any process of mere addition of information; substitution would be even less effective. The problem is one of integration, and the volume under review, though not elementary in standard, adopts this very refreshing approach with success.

Prof. Scott, after explaining the general ideas of charge, field, and potential in the first chapter goes on to the physics of the metallic state in the second and the behaviour of dielectrics in the third. By chapter seven, he is introducing the idea of the magnetic field in terms of the Lorentz law of force on a moving charge. The mathematical development, which is in itself ageless, is as firmly implanted in the pattern of modern physical thought as Maxwell's was in the physics of his day. The author claims that the book gives a sound logical basis for understanding the physics of electricity and magnetism, and this claim is justified. The level is about that of the honours degree.

G. R. NOAKES

A Degree Physics

By Dr. C. J. Smith. Part 5: Electricity and Magnetism. Second edition. Pp. vii+743. (London: Edward Arnold (Publishers), Ltd., 1959.) 45*s*. net.

THIS book contains what the author describes as the fundamentals of electricity and magnetism for general degree students. It can be recommended without reservation. Throughout, it shows the mark of the experienced teacher, who knows where stress should be laid and where difficulties lie for students. He pays proper tribute to the pioneers—Faraday, Curie, and so on—so that students can see how the various branches of the subject have arisen.

The M.K.S. system is not used because the author claims that it has no academic (as distinct from utilitarian) value. This is probably true; nevertheless, it is a pity that he has also rejected the idea of differentiating between the dimensions of B and H and of D and E, an offshoot of the M.K.S. approach. Thus, in discussing dimensions he has to say, for example, "if we suppress the dimensions of κ" (p. 700) and that the equation $\mu = \mu_0 + 4\pi\chi$ is better than $\mu = 1 + 4\pi\chi$.

But this is a minor criticism in an otherwise admirable book. It is a pity that, on the grounds of expense, a chapter on electromagnetic waves could not be included; a treatment of this subject in the same vein as the rest of the book would have been invaluable.

H. LIPSON

Valency

Classical and Modern. By Dr. W. G. Palmer. Second edition. Pp. xi+244. (Cambridge: At the University Press, 1959.) 30s. net.

THE first edition of this book was published in 1944. It became deservedly popular as a good down-to-earth account of valency, with a pleasant historical flavour, and closely related to observable chemical behaviour. No less than three reprints were called for. Now Dr. Palmer has brought forward a new edition. It must be said at once that this new version preserves the admirable qualities of the older one; and the author has taken the opportunity to correct a few of the slips that had crept in. But, without extending the size of the book, he has added more information about the transition elements, the ubiquitous hydrogen bond and electron-deficient compounds. This additional material enhances the value of the book.

The author is at his best when describing, and collating, experimental results, and many of his tables of numerical data will be exceedingly valuable. But he is less confident with the more theoretical side of the field. Thus a false account of the energies of the molecular orbitals in oxygen still survives, the words 'ligand-field-theory' do not appear in the index, nor (I believe) in the text, and very little explanation is offered for the hydrogen bond. But these are minor blemishes in a useful and sensible account.

C. A. COULSON

TUNGSTEN-185 FROM NUCLEAR BOMB TESTS AS A TRACER FOR STRATOSPHERIC METEOROLOGY

By Dr. HERBERT W. FEELY and Prof. JEROME SPAR*

Isotopes, Inc., Westwood, New Jersey

THE introduction of artificial radionuclides into the atmosphere by nuclear bomb tests has provided meteorologists with new tracers for the study of atmospheric circulation and mixing processes. In particular, the high-yield weapons that were detonated between 1952 and 1958, and which injected large quantities of radioactive dust into the stratosphere, have presented atmospheric science with several useful tracers for the study of stratospheric meteorology.

To account for the low water vapour content of the stratosphere, Brewer[1] had suggested the existence of an organized meridional circulation with air moving upward through the equatorial tropopause, then horizontally poleward at high levels, and sinking back into the troposphere in the polar regions. A similar circulation was later accepted by Dobson[2] to explain the ozone distribution in the atmosphere. Dobson, to account for the seasonal variation of ozone, suggested that cold air from high altitudes over the winter pole sinks to lower levels in the late winter or early spring, bringing high ozone concentrations with it. The 'Brewer–Dobson' circulation model was adopted by Stewart *et al.*[3] as a reasonable explanation of the observed variations of radioactive fall-out with latitude and time. Machta[4] and others[5–8] have also found the predictions of the 'Brewer–Dobson' theory compatible with measurements of fall-out at ground-level. Hagemann *et al.*[9] used the 'Brewer–Dobson' model to explain the observed stratospheric concentrations of carbon-14 from bomb tests, and Burton and Stewart[10] employed it in their explanation of the stratospheric concentrations of the radon daughter products.

An alternative theory of the effective transfer processes in the stratosphere was proposed by Spar[11], who suggested that large-scale horizontal mixing (turbulent diffusion, 'Austausch') plays a dominant part in the dispersion of radioactive debris in the stratosphere. In the lateral mixing theory the 'gap' between the tropical and polar tropopauses is considered to play a significant part in the transfer, by horizontal motion, of debris from the stratosphere to the troposphere.

Data recently obtained by the High Altitude Sampling Program on the dispersion in the stratosphere of debris from the United States 'Hardtack' nuclear weapons tests of 1958 appears to be in contradiction to the 'Brewer–Dobson' model, but are apparently consistent with the hypothesis of lateral mixing as the most effective exchange agency. The data on which this conclusion is based are the measurements of the unique tracer tungsten-185, which was produced in several of these equatorial shots.

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The sampling programme[11–13] has involved the collection of filter samples of stratospheric air in a meridional-vertical plane in the western hemisphere extending from the North Pole to 57 degrees south. The samples are collected by Lockheed *U*-2 aircraft, and are analysed for fission products including strontium-90 as well as other artificial and natural radionuclides such as plutonium, tungsten-185, rhodium-102 and beryllium-7. The data on the distribution of tungsten-185 in the stratosphere are especially relevant to the attempts to describe stratospheric transfer processes.

About 95 Mc. of tungsten-185 were injected into the stratosphere during the 1958 'Hardtack' tests[12] near latitude 12° N. between May and July of that year. Tungsten-185 decays with a half-life of 74 days, so that it is necessary for the geophysical analysis of tungsten data to correct for the radioactive decay rate. All the tungsten data referred to here have been corrected for radioactive decay to a common date of August 15, 1958.

So far as is known, tungsten-185 was only produced in significant quantities by the few 'Hardtack' weapons. It is therefore a unique tracer, having been injected at one place only, the Bikini–Eniwetok area at about 12° N., and within a limited time-interval, unlike strontium-90 which has been injected over a period of six years at high and low latitudes. The tungsten data therefore offer an excellent opportunity to study the dispersion of a cloud of radioactive particles injected into the tropical stratosphere.

The debris from the 'Hardtack' tests spread rather quickly through the stratosphere. By late 1958 tungsten-185 was included in the stratospheric debris which was falling out in north temperate latitudes[14]. Tungsten-185 was detected in most filter samples of stratospheric dust collected by the High Altitude Sampling Program on and after May 24, 1958.

Vertical profiles of tungsten-185 and strontium-90 (expressed in disintegrations per min. per 1,000 standard cu. ft. of air: abbr. d.p.m./1,000 s.c.f.) are shown in Fig. 1 for four ten-degree latitude belts for the period November–December 1959. The distribution of tungsten-185 at this time was similar to that which had existed as early as September 1958, except for the fact that the peak concentration and the vertical and horizontal gradients have diminished. During this entire period the maximum tungsten-185 activity has been located between 10° N. and S. and close to the 70,000-ft. level. (During July–August 1959 the maximum lay clearly below 70,000 ft. in the equatorial zone.) At higher latitudes the level of maximum tungsten activity is found at lower

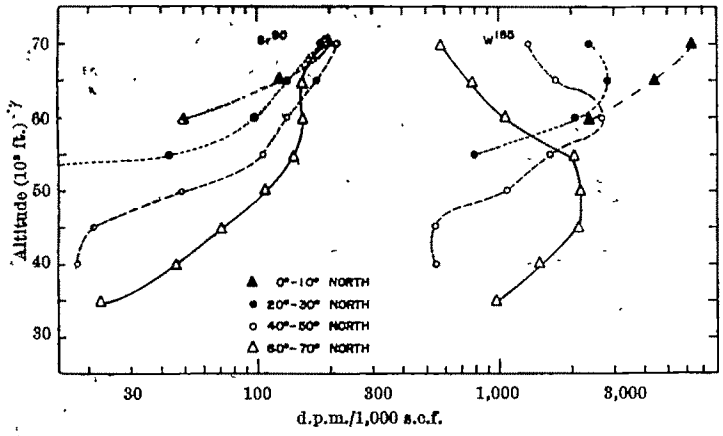

Fig 1. Vertical profiles of strontium-90 and tungsten-185 (corrected for decay to August 15, 1958) in the lower stratosphere during November–December 1959

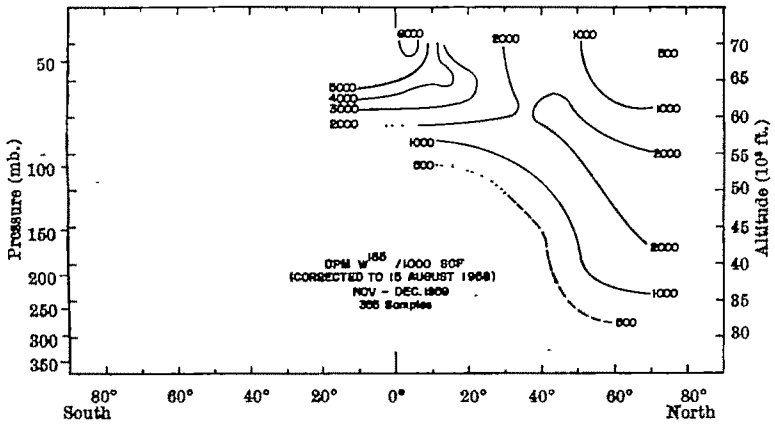

Fig. 2. Mean distribution of tungsten-185, November–December 1959

altitudes, diminishing in height toward the Pole. Data for the southern hemisphere were obtained only up to August 1959. Up to that time the distribution of tungsten-185 was roughly symmetrical about the equator, but with somewhat lower activity in the southern hemisphere. This pattern differs from that of the strontium-90 shown in Fig. 1, which, at all latitudes, shows maximum activity at the maximum sampling altitude of the aircraft.

The tungsten-185 distribution is shown more clearly in the meridional-vertical cross-section for November–December 1959 (Fig. 2). Here can be seen the virtually stationary 'core' of the tungsten cloud over the equator, and the layer of maximum tungsten activity sloping downward toward the North Pole. The slope of this zone of maximum tungsten, it may be noted, does not parallel the isentropic (potential temperature) surfaces in this region of the atmosphere, for the latter are nearly horizontal. Fig. 3 is a schematic cross-section showing the relation between the layer of maximum tungsten-185 and the tropopause structure.

According to the 'Brewer–Dobson' model, tungsten-185 should have reached the lower polar stratosphere by moving upward into the high tropical stratosphere, migrating poleward at high altitudes, and then descending into the lower polar stratosphere. However, since 1958, and at least until April 1960, the highest tungsten concentrations have been found in the equatorial stratosphere at 65,000–70,000 ft., indicating no significant upward motion of the debris in that region. Furthermore, high concentrations of tungsten have never been found at the 65,000–70,000-ft. sampling altitudes in the polar stratosphere, indicating that the movement of this nuclide into the lower polar stratosphere, where the higher concentrations are found in these latitudes, has not been due to subsidence of air and debris from the high polar stratosphere.

The observed distributions of tungsten-185 suggest a lateral spreading by turbulent 'Austausch' from the latitude of injection, at about 12° N., into both the northern and southern polar stratosphere, as indicated by the arrows in Fig. 3. The lateral mixing appears to have occurred within a sloping layer which decreases in height toward the poles. The fact that the 'mixing surface' slopes more steeply than the isentropic surfaces may indicate the existence of a systematic sinking of the radioactive debris relative to the air as it mixes poleward, possibly by gravitational settling or some other mechanism, or a systematic subsidence of the air itself as it mixes into the polar regions. There is no indication, however, of a large-scale subsidence of polar stratospheric air from very high levels.

The profiles of strontium-90 shown in Fig. 1 are consistent with the concept of lateral mixing, if there exists a zone of maximum strontium-90 con-

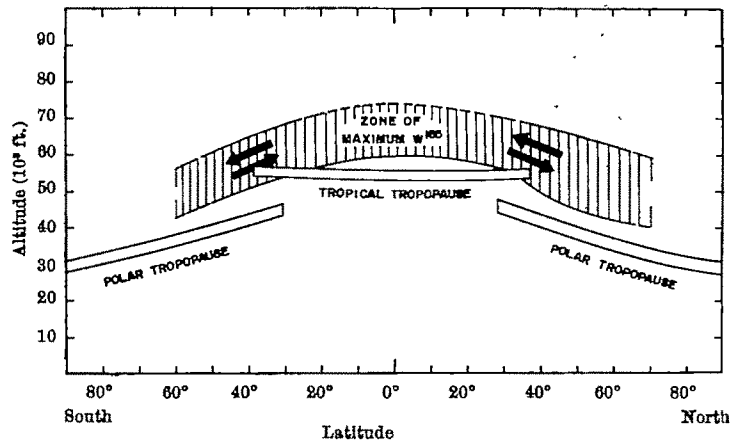

Fig. 3. Zone of maximum tungsten-185 concentration

centration which is broader and at a higher altitude than the zone of maximum tungsten-185 but roughly parallel to it. Such a distribution of strontium-90 was probably produced by the high-yield 'Hardtack' weapons in the summer of 1958. The high concentrations of strontium-90 found at high altitudes in the polar stratosphere may then be explained as the result of lateral spreading of this debris. Prior to the 'Hardtack' tests, our data indicated a distribution of strontium-90 similar to the present distribution of tungsten-185. Of course, the strontium-90 data are not as easily interpreted as the tungsten-185 data due to the presence of some strontium-90 from Soviet high-latitude tests.

The distribution of ozone in the stratosphere, which was accounted for by the 'Brewer–Dobson' model, may also be interpreted in terms of the mixing model presented here. Ozone is produced in high concentrations in the tropical stratosphere below 100,000 ft., the same region that received injections of strontium-90 from high-yield 'Hardtack' tests. According to Paetzold[15], the relatively high ozone concentration found below 65,000 ft. in the polar stratosphere and the deficit of ozone found below 89,000 ft. in the tropical stratosphere, as well as the seasonal variations in ozone, suggest the existence of a meridional transport of ozone toward the poles in the layer from 50,000 to 80,000 ft. Such a transport may certainly be effected by lateral 'Austausch'.

The increase in the rate of fall-out of nuclear debris in the north temperate zone, which has been observed during the early spring of each year, is attributable, in part, to a rise in the concentration of nuclear debris in the lower polar stratosphere during the winter as a result of the influx of debris from lower latitudes. This influx occurs in response to increased rates of turbulent mixing within the winter stratosphere. During the late winter and early spring this material is released to the troposphere by turbulent mixing through the tropopause and through the tropopause gap, and by the raising of the tropopause with the onset of warmer weather. The early spring increases in fall-out rate in 1956, 1957, 1958 and 1959 were augmented, as Martell[16] has suggested, by debris injected into the polar stratosphere during the latter half of the preceding year. As Walton[14] has pointed out, however, fall-out in the north temperate latitudes during the first six months of 1959 appeared to come from a well-mixed source, presumably an area of the lower polar stratosphere, which contained debris injected into the lower tropical stratosphere by United States tests in the summer of 1958 as well as debris injected into the lower polar stratosphere by Soviet tests during the autumn of 1958. Such a stratospheric source could have resulted only from extensive turbulent mixing between bodies of polar and tropical air during the winter of 1958–59.

It would appear that the data on the distribution of most natural and artificial tracers in the stratosphere (and data on the surface distribution of fall-out of stratospheric origin) can be explained as well by a stratospheric mixing and transfer model which invokes turbulent mixing as the most effective process as by one which invokes an organized meridional circulation. However, data on the distribution of tungsten-185 in the stratosphere can be interpreted much more easily in terms of the former model, although the exact configuration of the apparent mixing surfaces has not yet been adequately explained.

The High Altitude Sampling Program has been supported by the United States Defense Atomic Support Agency.

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ORIGIN OF THE PACIFIC BASIN: A METEORITE IMPACT HYPOTHESIS

By E. R. HARRISON

Atomic Energy Research Establishment, Harwell, Berkshire

VERY little is known about the processes that have fashioned the major features of the Earth's surface. Of the many problems unsolved, perhaps one of the most intriguing of all is that of the origin of the Pacific Basin.

It is known that the lighter crustal layers, which form the continental land masses to a depth of 20–40 km., are relatively thin on the ocean floors and in the particular case of the Pacific Basin are almost entirely absent[1–3]. The Pacific Ocean itself has a mean depth of 5 km. and occupies almost half the Earth's surface; the greater density of its underlying rocks is consistent with the absence in the gravitational potential of any first harmonic terms about the axis of rotation[4]. It was pointed out by Suess in 1888 that an outstanding characteristic of the Pacific

is that it is surrounded by a variety of features which lie parallel to its coastlines. Among these features are the island festoons and the multiple arcs of deep-focus earthquakes, gravity anomalies, and ocean deeps. A further impressive characteristic is the seismic passivity of the Pacific Basin itself, which is in direct contrast with the continual tectonic activity in the surrounding regions where dissimilar crustal structures are in close contact and the land masses are folded as if by thrust against the denser and stronger mass of the Pacific Basin.

To explain such major surface characteristics it is proposed that the Pacific Basin was the seat of an immense explosion in the primitive Earth, and that the explosion was possibly due to a collision with a planetesimal or a satellite of approximately 100 km. radius. An attempt will be made to show that the explosion excavated a large crater of several thousand kilometres in radius and some hundreds of kilometres in depth. The great masses of material that were swept back and dropped at the rim of the crater formed the discontinuities of crustal structure and composition which survive to the present day and are responsible for the peripheral features of the Pacific Basin. Following the recovery of hydrostatic equilibrium there remained a shallow and permanent crater depression (because of the absence of the lighter surface layers) which is the present Pacific Basin.

There are very few theories which attempt to account for the absence of the lighter crustal rocks on the ocean floors and in the Pacific Basin. A well-known theory is that due to Fisher, who, in 1889, elaborated on the idea that the Moon originated from the Earth with the suggestion that the Pacific is the scar left by this event. The idea that the Moon originated from the Earth was further developed by G. H. Darwin with the tidal resonance hypothesis. However, detailed analyses, particularly by Jeffreys, have cast doubt on the whole idea that the Moon originally was in some way wrenched from the Earth. A particularly strong argument against such ideas is that, failing the coincidence of a third body in the immediate neighbourhood, the ejected Moon would most likely fall back and in any event could not become a satellite of the Earth.

In an alternative theory, Hills[4] has more recently proposed that the lighter crustal rocks such as granite were concentrated into continental rafts by the convection currents that occurred while the Earth was solidifying from a molten state. A comparison is made with boiling jam in which the convection currents sweep the scum on the surface from the centre to the sides. There are a number of difficulties with any theory of this kind, among which are Urey's[5] arguments in favour of formation of the Earth while in a relatively cold state. However, if the Earth was at some time in a molten state the present surface rocks, which are likened to the scum formed on jam, were not necessarily the first materials to solidify, but in all probability were the last. Most materials have a greater density in the solid than in the liquid phase; also, the melting points of silicates increase considerably with depth; hence it is highly unlikely that a solid crust of substantial thickness would first form and then float on a liquid or even a semi-liquid mantle. It would seem that the major event which led to the destruction of the surface symmetry happened while the Earth was in a solid state.

In any discussion of this kind the Moon's surface is of prime interest. The processes which formed the lunar surface may also have been active on the terrestrial surface in the past. But unlike the Earth's surface the salient features of the Moon have not been effaced by erosion. There is little doubt that the majority of the large craters on the Moon were formed by explosions and it is now agreed by most[5–8] (who have argued quantitatively in this field) that the most plausible explanation is that the craters were produced by the explosive impact of incident bodies of various sizes, compositions, and relative velocities, falling singly or in groups. Covering large areas of the Moon are the maria, which may be either lava floods or compacted fragmentary material presenting a similar appearance[9,10]. The processes which produced the craters and the maria appear to have operated simultaneously; the numerous craters continually erupted and tended to obliterate the maria, and the maria less-frequently swept out and covered the existing craters. There is no reason for believing that there were not several cycles or even a continuous history of mutual obliteration in which at any instant, including the terminal period of the process, the Moon had in principle the same kind of surface features as it has now.

In 1893, Gilbert[11] argued strongly against a volcanic origin of the maria and was the first to point out that the evidence is consistent with the idea that the maria were also formed by collisions. He directed attention to the fact that Mare Imbrium, the largest of the maria, with a diameter of about 1,000 km., was surrounded by belts of mountains and radially directed furrows and splashed surfaces as if a great explosion had blasted material in all directions. Baldwin has given considerable support to this view and states that ploughed and splashed surfaces can be detected radiating from some of the other maria. Urey and Kuiper have developed the idea further, and the former ascribes the origin of Mare Imbrium to the oblique impact of a large meteorite of 100 km. radius.

Whether or not the explosive upheavals which formed the maria were plutonic or meteoritic in origin, the main suggestion is that the Pacific Basin was formed by a similar but even larger explosion. No known plutonic mechanisms appear to be adequate, and we shall therefore leave aside the question of a plutonic origin and proceed with the assumption that the Pacific Basin was formed by an explosive impact.

The multiple objects that were incident on the Earth and Moon some 10^9 years ago or more were not improbably the remnants of the birth processes peculiar to the Earth–Moon system. Either the objects were satellites of this system, or they were planetesimals which were swept up in some tens of millions of years[12]; or possibly a combination of both. In the first case the energy εE released per unit mass of a satellite on impact with the Earth is given by $\frac{1}{3} \leqslant \varepsilon < 1$, where E is the escape energy of 6×10^{11} ergs gm.$^{-1}$ from the Earth; in the second case, the energy released per unit mass of a planetesimal in most cases is given by $\varepsilon > 1$ and depends on the form of the orbit. If the object had a mean density of 3, roughly equal to that of the Moon, the total energy released by the collision was $10^{24}\alpha^3\varepsilon$ ergs, where α is the radius of the satellite (or planetesimal) measured in units of 100 km.

The physics of crater formation by explosive impact are complex, and are still in an initial state of development. In the case of large craters the following rather crude arguments give results which are possibly sufficiently accurate for the present purpose. It happens that for $\varepsilon > \frac{1}{2}$ the meteorite has a relative velocity v which in many instances is greater than the propagation velocity of longitudinal waves in the Earth's outer layers, and a one-dimensional fluid treatment is adequate for the first stages of the impact. (This is not necessarily true for the Moon, and it seems likely that the maria are not true explosion craters, but are mainly compacted and sintered beds of the fragmented impacting body.) During the collision, shock fronts advance into the Earth and the meteorite, and behind the shock fronts a compacted region of high pressure and temperature builds up and moves into the Earth with a velocity of $\frac{1}{2}v$ (assuming that the meteorite and the outer layers of the Earth have the same density). When the shock front reaches the rear end of the meteorite, rarefaction waves develop and the explosion commences. From the conservation of momentum and energy one finds that at the instant the explosion commences the compacted region has a total mass twice that of the original meteorite, and a kinetic energy half that of the original meteorite; the remaining half of the kinetic energy has been converted into heat and other forms of internal energy in the compacted region. Following this instant, the one-dimensional model progressively breaks down as the compacted mass bores down into the Earth. However, we have that at least half the original kinetic energy of the meteorite is available for the explosion and is converted entirely into heat as the compacted region expands into a gas (the ionization energy of the intermediate plasma state is also eventually available as heat), and at the most only half the original kinetic energy is propagated into the Earth and uphurls large areas of the surface and sets the Earth into large-amplitude oscillations.

Gilvarry and Hill[13] have calculated the temperature and pressure in the compacted region using an equation of state based on the statistical Thomas-Fermi model of the atom. However, it is essential to remember that the moment expansion commences their results no longer apply, and one finds that the temperature tends towards that of an ideal gas of 24,000 ε °K. for an average atomic weight of 20. From Gilvarry and Hill's calculations it is found that for $\varepsilon \simeq 1$ the density in the compacted region prior to the explosion has been increased by 8/5, and therefore the shock fronts have velocities of $4v/3$ (downwards) and $-v/3$ (upwards), and the meteorite plunges into the Earth a distance equal to 3/4 of its diameter before the explosion begins; or for $\varepsilon \simeq 3$, the density is increased by 2, the shock velocities are v, 0, and the meteorite penetrates a distance of 1 diameter.

The complexity of the phenomena involved makes it extremely difficult to estimate the dimensions of the crater formed by an explosion. In general, the crater is large in comparison with the size of an exploding missile. The extrapolation of known data on crater dimensions by the empirical scaling rules used in nuclear explosions[14] means that for very large craters the energy released approaches, and can even be less than, the necessary work done against the gravitational field. If W is the energy released, it is usual to assume that the crater radius varies as $W^{1/3}$ and the depth as $W^{1/4}$. It follows that the work done against the gravitational field is proportional to volume × depth, or $W^{7/6}$. Since the work done must be less than W there is a limit beyond which these scaling rules cannot be applied. This limit occurs for very large craters where the gravitational field plays the dominant part in determining their size. Baldwin's empirical formulæ, which are quadratic in logarithms and therefore yield indices which are functions of the crater size, also encounter, so it appears, a similar difficulty, particularly when it is remembered that the final depth of a large crater may be very much less than its initial depth. It is also important to remember that in the case of very large craters the final depth (which is the parameter used in the scaling rules and the empirical relations), after the recovery of hydrostatic equilibrium, cannot depend solely on W but must also depend on the density gradient at the surface of the Earth; if there is no density gradient the final depth is zero and is independent of the value of W.

It would seem plausible, therefore, to assume that for an explosion of the magnitude and nature that we are discussing the initial crater dimensions are determined primarily by work done against the gravitational field. Thus, if all the kinetic energy $(4/3)\pi a_s^3 \rho_s \varepsilon E$ of the meteorite is expended in excavating a crater of radius R, the minimum work done against the gravitational field for a conically shaped crater (that is, the depth relative to the Earth's curved surface changes linearly) of maximum depth d is $\pi R^2 d^2 \rho_e g/12$. If we now suppose that the maximum depth is approximately the radius of the satellite, or $d \simeq a_s$, then it follows that:

$$R^2 \simeq 16\,\varepsilon a_s a_e \rho_s \rho_e^{-1} \qquad (1)$$

since $E = g a_e$. This estimate represents an upper limit to which crater radii tend for very large explosions. It neglects the effect of the curvature of the Earth's surface, and also the possibility that material escapes from the Earth. We have seen that the internal energy density of the compacted region is $\frac{1}{4}\varepsilon E$, and for $\varepsilon > 2$ there is the possibility that a fraction of the ejected material encircles the Earth and is deposited as rays similar to those observed radiating, for example, from Tycho; also for $\varepsilon > 4$ it is not unlikely that some of the ejectamenta escape from the Earth. In any event, the existing proto-atmosphere would be blown away either completely or partly from the Earth; this would expend only a negligible amount of the available energy if the total mass of the proto-atmosphere was of the same order of magnitude as the mass of the present atmosphere. From the abnormally low abundances of the inert gases it is known[15] that at some stage the Earth must have lost its original atmospheric envelope, and that the present atmosphere is of secondary origin and was formed by chemical and photosynthetic processes acting on juvenile gases from the Earth.

Assuming that $\varepsilon \simeq 1$, and $\rho_e \simeq \rho_s$ for the surface layers of the Earth, we find that for meteorites of radii 100 km. and 500 km. the crater radii are approximately 3,000 km. and 7,000 km., respectively. It is remarkable that Baldwin's empirical formula, which is constructed from the known data of comparatively small explosions, gives crater radii of approximately 2,500 km. and 7,000 km. A crater of radius 3,000 km. is possibly adequate to account for the size of the Pacific Basin. The hypothesis therefore is

that a satellite or planetesimal with a radius of approximately 100 km., and $\varepsilon \simeq 1$, penetrated a distance of 100–200 km. and exploded; the expanding gases released an energy of the order of 10^{24} ergs and swept back the surface layers to form a crater, at the edge of which large quantities of material were dropped; almost simultaneously there was hydrodynamic flow in the Earth caused by the subsiding rim and the rising crater floor, and the gravitational energy released caused considerable melting over a wide area; finally, there remained only a relatively shallow depression surrounded by a slightly elevated 'land mass' of lower density and dissimilar composition.

Perhaps it should be emphasized that an explosion of this magnitude bears no comparison with any known terrestrial event. In terms of present-day nuclear weapons the total energy released was of the order of 10^{11} five-megaton hydrogen bombs, and over an area of 3,000 km. radius this amounted to a mean energy density of approximately 1 atom-bomb (20 kiloton) per square metre. Using Einstein's mass-energy relation, it is found that the total energy released is equivalent to a loss of mass of 10^{13} gm., or a mass weighing approximately 10^7 tons.

Of all the assumptions that one might make the simplest is that the collision was made by a planetesimal, such as one of the large asteroids. In the past there may have been many such bodies with orbits close to that of the Earth. This point of view raises the possibility that there may have been multiple encounters with the Earth of the particular kind that we have considered with $\varepsilon > 1$. It is then logical that one should go even further than has been implied so far in this discussion, and ask: Is it conceivable that all the ocean basins, underlaid by rocks denser than the surrounding land masses, are crater depressions produced by explosive impacts and have in common the same origin as the maria on the Moon?

As an alternative approach it is not improbable that the Earth once possessed more than one natural satellite, and that the particular collision we have considered was made by a satellite that was deflected from its normal orbit by a third body such as the Moon, or was sufficiently close to lose angular momentum by tidal friction. In the case of several satellites a close examination of the mechanics involved is necessary to establish whether the idea of multiple collisions with the Earth is at all valid. The possibility that the early Earth possessed two 'moons', which moved apparently in opposite directions across the sky in very much the same way as Phobos and Deimos appear to move from Mars, is sufficiently intriguing, however, to consider briefly some conditions for a collision caused by tidal friction.

Quite what the conditions were like for tidal friction is not known; but according to Jeffreys's calculations the Moon was at approximately 0·6 of its present distance some 4×10^9 years ago. For a satellite to spiral inwards it must be close enough to rotate faster than the Earth's surface, or since the day was then only 7 hr. long, this requires that the satellite's distance r_s satisfied $r_s < 3a_e$. If the conditions for tidal friction were the same then as now, the time taken by a satellite of 100 km. radius to reach the Earth would not exceed 10^6 years and would be considerably less in the event of tidal resonance. But also any satellite at the present moment at a distance of approximately $r_s < 7a_e$ spirals inwards because of tidal friction. It follows that if initially the satellite was at a distance $3a_e < r_s < 7a_e$, and if the tides raised by the Moon were larger than those raised by the satellite, then the satellite would first have spiralled outwards and when the Earth's surface rotated faster would then have spiralled inwards. The condition that the Moon raised the larger tides is that $a_s/r_s < a_m/r_m$, or the sufficient condition is that the satellite had a radius of less than 130 km. At distances less than the Roche limit of 2–3 Earth radii a fluid satellite has no equilibrium configuration, and therefore it breaks up. But in the case of a solid satellite one finds that the maximum differential force due to the Earth's gravitational field is less than the internal strength (assuming a critical stress difference of 10^9 dynes cm.$^{-2}$) for radii of less than 120 km.; therefore a solid satellite with a radius smaller than 120 km. does not break up. A more detailed analysis by Jeffreys[16] gives substantially the same result. It seems therefore that a satellite of approximately 100 km. radius at an initial distance of less than approximately 7 Earth radii would at some time in the past have struck the Earth, would also have remained a coherent body without fracture as it approached the Earth, and in the final collision could have released perhaps just sufficient energy to account for the Pacific Basin. It must be emphasized that this rudimentary picture is totally inadequate if one adopts the point of view that there has been more than one large collision with the Earth. As we have seen, a single such collision is sufficient to affect profoundly the fluid envelopes in which the tidal friction occurs; without a closer examination of the problem one might say that this reason alone weakens the idea that several collisions were due to tidal friction.

Baldwin has made the suggestion that there should be geological evidence in the pre-Cambrian rock strata of repeated meteoritic impacts with the Earth. In this discussion I have taken the suggestion one stage further. On making the reasonable assumption that at least one body has collided with the Earth comparable in size with that responsible for producing Mare Imbrium, it follows that the evidence for such a collision should be immediately apparent even nowadays if it is looked for on a sufficiently large scale. It is proposed that the Pacific Basin has many characteristics that strongly suggest an origin of this nature.

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EXPERIMENTS WITH DIVING SEALS*

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ALL mammals can withstand complete submersion in water for a little while; but some forms are able to remain submerged at considerable depths for remarkable periods of time. It will be obvious that there are few accurate observations on the maximum length of time for which any mammal can remain under water: it would mean diving the animal to extinction. The following is a list of record durations of dives that have been taken from Scholander[1], Scheffer[2] and Harrison and Tomlinson[3]:

Pigeon	1 min.	Ringed seal	20 min.
Hen	3 min.	Common seal	28 min.
Duck	17 min.	Porpoise	12 min.
Penguin	7 min.	Blue whale	50 min.
Water rat	2 min. 17 sec.	Sperm whale	75 min.
Rabbit	3 min.	Bottle-nosed whale	120 min.
Dog	4 min. 25 sec.	Man (pearl and sponge divers)	2 min. 30 sec.
Muskrat	12 min.		
Grey seal	20 min.		

The maximum depth reached by a diving animal is as difficult to determine as the duration of a dive. The literature is full of anecdotes of fouling of cables, hooks and nets by seals and whales at immense depths; but there is no evidence that the animals were not dying before they became entangled or whether they would have survived had they returned to the surface. The following are a few recorded deep dives (see references for duration):

Penguin	at least 12 m.	Experimental dives
Weddell seal	92 m.	Diving below ice
Common seal	92 m.	Experimental dives
Grey seal	146 m.	Caught on hook
Harp seal	278 m.	Caught on hook
Porpoise	20 m.	Line attached
Fin whale	355 m.	Line attached
Sperm whale	900 m.	Entangled in cable
Man	165 m.	Flexible suit with special breathing mixture

All evidence indicates that young seals and whales cannot equal the performance of adults. Scholander[1] records that a 4-month-old grey seal pup on its first swim in deep water dived to 22 m. for a total time of 1 min. A 6-month-old hooded seal dived spontaneously to 75 m. and remained submerged for more than 4 min. A young hooded seal, which had been submerged the previous day for 18 min., was weighted by Scholander and submerged to a depth of more than 300 m. in 3 min. It was drawn to the surface immediately after reaching that depth over a period of 9 min. The seal was reflexless on return to the surface, its heart beat very weakly, one pupil was widely dilated, one a short slit, the nostrils were firmly closed and it died shortly afterwards. No water was found in the lungs, but there was an abundance of air bubbles in the mesenteric arteries. Death was presumed to be due to air embolism.

Our experiments were carried out on pups, yearlings and adolescent common seals (*Phoca vitulina*) obtained from the Wash, East Anglia, through the kind co-operation of the Eastern Sea Fisheries Joint Committee and the Hydrographic Survey Ship, H.M.S. *Scott* (Commander H. R. Hatfield, R.N., then in command). Diving performance was assessed by immersion in a shallow tank, at sea, and under water or in air in a pressure-chamber capable of simulating a pressure of 300 ft. of water. Seals were secured to a board in a fashion similar to that described by Scholander[1], or in a specially designed lace-up 'Terylene' harness to enable free-swimming to take place at the end of ropes. Leads were connected from axillary electrodes to a portable Elmquist electrocardiogram. When required, animals were anæsthetized with 3–10 ml. of a solution of 1 gm. in 40 ml. sodium thiopentone injected into the extradural vertebral vein as if performing a lumbar puncture. Anæsthesia was afterwards maintained by introducing a Magill endotracheal tube (child's size) and administering nitrous oxide and oxygen.

Investigations of heart- and respiratory-rate were made on pups and young seals out of water, and the heart-rate was recorded during all experimental dives. The animals were secured as loosely as possible to a board or harness and were not anæsthetized during the dives unless specifically stated. No animal was 'dived' again unless the heart-rate and behaviour had returned to conditions prevailing at the beginning of the first dive.

Heart-rate Surfaced

This displays considerable variation, and even irregularity, in all animals whatever their age and whether or not they have recently dived. Young pups have a resting heart-rate of 90–180 beats per min.; in 2–3-year-old adolescents it varies from 75 to 180 beats per min. Proximity to the investigator or indication to the seal that it is about to dive (by submerging it a number of times for a few seconds) does not unduly influence the heart-rate. Any tachycardia that resulted from a struggle to secure the seal to a board, or in its harness, soon subsided and seals often went peacefully to sleep during a pause in a diving programme.

Respiratory-rate out of water is comparatively regular at 18–20 per minute, in both pups and adults. It is less regular when the seal is immersed in a harness with only its nostrils above water. The heart-rate increased from 112 to 144 when a seal was immersed suddenly up to its neck, head still above water, and fell to 120 after 5 min. It occasionally slowed from 120 to 60 for a few seconds following a respiratory pause longer than normal. This slowing of the heart associated with changes in respiratory-rate has been described also by Irving, Solandt, Solandt and Fisher[4] and Irving[5]. Forcible closure of the nostrils and mouth of a seal out of water (so as to prevent respiration) caused a fall in heart-rate from 130 to 80 after 5 sec., to 48 after 22 sec., to 15 after 68 sec., and was followed by violent struggling which prevented further recordings. One yearling common seal was anæsthetized (with thiopentone, intubated, and then nitrous oxide and oxygen mixture used to continue the anæsthesia) and an attempt was made to determine the effect variations in respiratory-rate

* Substance of a Friday Evening Discourse delivered to the Royal Institution on November 11.

would have on heart-rate. Increasing the respiratory-rate artificially to 40 for a period of 2 min. had no appreciable effect on the heart-rate. The respiratory-rate was then lowered to 5; after 1¼ min., when the heart-rate had dropped to 17, the animal collapsed, but was later resuscitated.

Tweaking the vibrissæ caused episodic slowing of the heart-rate to 75 beats per minute for a few seconds; smacking the face raised the rate to 165 beats per minute. Throwing cold water over the face had little effect on the heart-rate.

Shallow Dives

Animals were 'dived', secured on a board, for periods of up to 28 min. In a dive of this length, intermittent struggling started at 15 min. and became extreme during the last minute so the animals were brought to the surface. The diving bradycardia did not develop as rapidly as in *Halichoerus*[1]; the slowest heart-rate (6 beats per minute) occurred between 1 and 3 min. after diving. Thereafter the heart-rate gradually increased as time passed. The degree of bradycardia and the rate at which it developed were not significantly affected by the rate at which the heart was beating before the dive commenced. Repeated diving of the same animal (after a short recovery period of a few minutes) did not influence the rate of onset, degree of bradycardia or recovery behaviour. There was always a recovery tachycardia lasting for 5–10 min. after a dive of more than a few minutes. The slowest and longest lasting bradycardia was observed in older seals: the bradycardia also developed more rapidly.

A two-year-old seal was secured in a harness that left its head, four flippers and tail free; guide ropes and electrocardiograph leads were attached. The animal swam freely in a shallow tank, and dived for periods of several minutes. The heart-rate showed changes similar to those recorded when the seal was secured to a board. It was noticed that the seal exhaled when it broke the surface after a short shallow dive; this observation has been frequently confirmed by us and is also mentioned by Harrison Matthews[6]. Another young seal behaved similarly in a harness when allowed to swim in the sea. It towed a small dinghy containing two men with ease at about walking speed, and afterwards towed a skin-diver for a short distance under water.

A seal secured to a board was prepared for diving in a shallow tank; before diving and throughout the dive it was forcibly prevented from opening its nostrils or mouth. The heart-rate was 144 beats per minute on the surface (nose and mouth closed) and fell to 24 beats per minute after 30 sec. It remained at that rate for 75 sec., after which it struggled so violently to exhale that no further recording was possible.

Deep Dives

Three types of experimental diving were carried out: (*a*) pups a week old were lowered into the sea on a board; (*b*) two-year-old seals were placed in a tank filled with water inside a pressure chamber and the air pressure increased by stages to depths equivalent to up to 80 ft.; (*c*) two-year-old seals similarly secured were taken rapidly to 300 ft. and kept there for periods up to 5 min.

The pups showed an immediate bradycardia to between 10 and 16 beats per minute, but within a few minutes under water the rate began to rise to 30 beats per minute. The older animals displayed an immediate bradycardia to 4–15 beats per minute, which was maintained for 2·0–5·0 min. at depths in the pressure chamber equivalent to up to 200 ft. There was no indication in the older animals of a gradual decrease in the bradycardia as the dive progressed at a constant depth. There was, however, an increase in heart-rate as the animal returned to shallower depths. The pups often showed a marked decrease in bradycardia after quite a short period (1–3 min.) at only 20 ft. There was no noticeable change in the bradycardia of adolescent seals in dives of short duration even at 200 ft. One young seal, taken to about 100 ft., managed to raise its nostrils above the water in the pressure tank on return when at 50 ft. It appeared healthy immediately after the dive, and carried out shallow diving during the ensuing weeks without ill-effect. Three months later the seal became anorexic, lost weight and was killed. Extensive surgical emphysema was seen in the lungs, thoracic wall and vertebral venous system at post-mortem examination. It was concluded that the animal had inhaled air under pressure and ruptured a lung during the return to the surface.

A two-year-old seal was taken rapidly to a depth of 300 ft. in 4 min. 30 sec. It remained at this depth for 1 min. 20 sec. and returned to the surface by stages, pausing for 30 sec. at every 50 ft. to make electrocardiograph recordings. On return to the surface the respiratory-rate was 30 per min.; the animal appeared fit and active, and displayed no signs of 'bends'. The same animal was 'dived' to 300 ft. the next day and kept there for 5 min. Towards the end of this period the cardiac complex on the electrocardiographic recordings indicated some degree of physiological 'defeat'. The animal was returned to the surface, and its heart was beating slowly on removal from water. Its pupils were dilated, muscular movements were weak. The heart stopped a few seconds later, and the animal could not be resuscitated. At post-mortem no evidence of air embolism, lung damage or hæmorrhage could be detected. It is possible that the animal suffered a 'squeeze' at this depth such that the heart could not contract fully and cerebral anoxia followed.

Every seal was observed to exhale air when or just after it was immersed in water, and again later as the pressure increased in the chamber.

Exposure to Increased Air Pressure

It was considered to be of interest to investigate the effect on a seal of simply exposing it to a steady increase of air pressure simulating depths equivalent to those it had 'dived' when under water. Two-year-old seals were placed in a pressure chamber and allowed to breath naturally as the air pressure was increased. The respiratory-rate was assessed by counting the nostril openings over periods of half a minute. Increased air pressure equivalent to a depth below water of 200 ft. caused a bradycardia from 120 to 30. It was not sustained, however, and the heart-rate rose to 150 for periods lasting up to 5 sec. The increase in air pressure caused the respiratory-rate to slow from 24 to 8, and it was noticed that this was correlated with the periods of most marked bradycardia. Increase in air pressure to depths equivalent to 30–80 ft. caused little slowing of the heart-rate and no disturbance of respiration. The seals were in no way embarrassed by exposure to

increased air pressure, but did seem puzzled at the strange sensation. It appeared that only when the seal held its breath was there any heart slowing, again indicating that the bradycardia is linked with interruption of regular respiration.

Stimulation and Section of the Phrenic Nerve

A thick, striated muscle sphincter is present on the posterior vena cava immediately cranial to the diaphragm in all seals we have examined. It is supplied by branches of the right phrenic nerve[6]. To ascertain the effect of closure of the sphincter the posterior vena cava was clamped just caudal to the liver in an anæsthetized pup: this procedure had no effect on the heart-rate in a surfaced animal. The right phrenic nerve was cut in the neck under anæsthesia in several young seals and they were afterwards allowed to recover. The animals were 'dived' a few days later. In all there was an eventual bradycardia similar to that in normal animals, but the onset of the bradycardia was delayed. Stimulation for short periods of one or both phrenic nerves had no effect on the heart-rate in surfaced anæsthetized animals.

Stimulation and Section of the Vagus Nerve

Stimulation of the intact right vagus of an anæsthetized pup resulted in slowing of the heart-rate from 120 to 22, with immediate recovery to 120 on cessation of stimulation. Stimulation of the intact left vagus resulted in disappearance of the ventricular complex on the recording: *P* waves continued to occur at 120 a minute. Stimulation of either vagus in an anæsthetized adult seal completely abolished the heart-beat for the period it was applied.

Section of the right vagus in the neck in anæsthetized pups caused no change in the heart-rate surfaced (180) and a fall to only 100 on diving. The beats were irregular. Section of both vagi in pups caused no change in the heart-rate surfaced: in an adult the rate increased from 60 to 90. In short dives other anæsthetized pups with bilateral vagal section showed no slowing of the heart. Another was anæsthetized and both vagi were exposed; it was then 'dived' and after the heart-rate had fallen to 24, both vagi were sectioned with the seal under water. There was an immediate rise in heart-rate to 156 which persisted for the remainder of the dive and after surfacing.

Discussion of the significance of some of these findings is given by Harrison and Tomlinson[3]; the parts played by various vascular modifications in seals is discussed by Harrison and Tomlinson[7] and Barnett *et al.*[8]. Further observations and discussion will be published shortly.

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OBITUARIES

Dr. Hugh Scott, F.R.S.

DR. HUGH SCOTT, distinguished entomologist and biogeographer, died on November 1 at his home at Henley-on-Thames, at the age of seventy-five. He was born on September 16, 1885, the elder son of William Edward Scott and was educated privately and at Trinity College, Cambridge, where he was an exhibitioner and obtained a first in the Natural Science Tripos, Part I, in 1906. He received his Sc.D. in 1919.

At Cambridge Scott was deeply influenced by the training he received from Dr. David Sharp, whom he succeeded as curator of the Zoological Museum. In 1908 he joined the Second Percy Sladen Trust Expedition to the Indian Ocean and made an extensive collection of insects in the Seychelles. Scott afterwards organized the study of the collection by specialists, and himself undertook a considerable part of the work on the Coleoptera. Rarely, if ever, has a collection been so completely studied. With characteristic tenacity Scott saw the work through to completion and analysed the results in a summary of the faunal relationships of the Seychelles which is a model of clarity.

His experiences with the Seychelles fauna aroused an enduring interest in biogeography which influenced all his subsequent work. His special interest lay in the fauna of that area including East Africa and south-western Arabia where the Palæarctic and Ethiopian faunal elements meet and overlap. To further this work Scott made four long collecting expeditions in the area: to the central highlands of Abyssinia during 1926–27, the Aden Protectorate and Yemen during 1937–38, the Gughé Highlands in southern Abyssinia during 1948–49 and the Simien Mountains in northern Abyssinia in 1952–53. The extensive collections of insects and plants which resulted from these journeys provided information on areas, the fauna and flora of which were previously almost unknown. The expedition to south-western Arabia was, for example, the first in the area since that of Niebuhr in 1762. These expeditions were prepared and carried out with great thoroughness and attention to detail, and great credit is due to Scott for the tenacity with which he sought his objectives in the face of physical disability, chronic ill-health and the political obstacles of those troubled regions.

In 1930 he was appointed assistant keeper in the Department of Entomology, British Museum (Natural History), a position that he held until his retirement in 1948.

In addition to his work on the systematics of Coleoptera, Scott was an authority on the Nycteribiidae, the louse-like, wingless flies which parasitize bats. He was also the author of several works on the fauna associated with the giant lobelias and the tree senecios of the East African highlands, and on the peculiar and extensive fauna of the leaf axils of the Bromeliaceae. He also wrote a number of valuable works of a geographical nature and a book on the

expedition to south-western Arabia entitled "In the High Yemen" (1942). During the Second World War he was the chief author of the naval intelligence "Handbook on Western Arabia and the Red Sea".

He was elected a Fellow of the Royal Society in 1941, an Honorary Fellow of the Royal Entomological Society of London in 1954, and was an original member of the Entomological Research Committee formed by the Colonial Office in 1909, which later developed into the Imperial Bureau (now Commonwealth Institute) of Entomology.

Scott will be remembered by all who knew him as a kindly, courteous and deeply learned man. He was possessed of a deep religious conviction, a fact which influenced his life to a high degree.

In 1913 he married Beatrice Emily Streatfield (who died in 1947) and leaves a son and daughter.

E. B. BRITTON

Dr. A. B. Edwards

AUSTIN BURTON EDWARDS was born in Melbourne in 1909 and educated at the Caulfield Grammar School. He graduated from the University of Melbourne with first-class honours in geology and was awarded the Howitt natural history scholarship in geology and the Bartlett scholarship. After the publication of the first two of the 128 contributions to geological science with which he is identified either as sole or joint author, he was awarded an 1851 Exhibition which enabled him to continue his studies in London at the Imperial College of Science and Technology, where he obtained his Ph.D. in 1934.

He won his university half-blue in football at Melbourne and his colours in athletics at the Imperial College; his athletics background was of great value to him in his geological work, much of which was performed in mountainous terrain.

On returning to Australia he joined the Mineragraphic Section of the Commonwealth Scientific and Industrial Research Organization, which maintains close relationships with the Geological Department of the University of Melbourne. Thus commenced a long association with the officer-in-charge of the Section, Dr. F. L. Stillwell, whom he succeeded in 1953. His early work with the Section produced a series of studies of Australian ores and ore deposits which was extended to the examination of mill products and mill tailings and eventually to smelter products such as mattes, speisses and slags. At the same time he sustained a keen interest in petrological problems and completed various papers begun in London, of which the more important were his studies on the tertiary volcanic rocks of Central Victoria and the differentiation of dolerites of Tasmania. In 1937 he shared with Prof. R. D. Wright the David Syme research prize of the University of Melbourne. He gained his doctorate of science in 1942.

His first independent mineragraphical task was the study of the occurrence of manganese in iron ore of Iron Knob in South Australia, later extended to the iron ores of the Middle Back Ranges. This was the first of a series of studies which culminated in the recognition and discovery of the oolitic iron ores in the Northern Territory and Constance Ranges in Queensland.

As the scope of work of the Mineragraphic Section widened, Dr. Edwards made contributions to sedimentary petrology, geochemistry, meteorites and geomorphology. The sedimentary petrology commenced with a study, jointly with G. Baker, of the Jurassic arkoses in Victoria, later extended to the Mesozoic and Tertiary sediments of the Aure Trough, Purari Valley and the Wahgi Valley in Papua. His interest in geochemistry arose in the past few years from studies of the selenium content in sulphide deposits and the distribution of cadmium, manganese and iron in Broken Hill sphalerites. His descriptions of meteorites were a natural extension of his mineragraphical work, while his interest in geomorphology absorbed him during his vacations.

Lecturing in the University of Melbourne on mining geology between 1941 and 1953, his interest was roused in Victorian coal. Subsequent papers on Wonthaggi and Victorian brown coals elevated him to a position of authority on brown coal and resulted in a request from the State Electricity Commission to act as geological consultant. He allocated his consultant's fees to the purchase of equipment for the Mineragraphic Section.

In 1946 a postgraduate course was provided by the Geological Department of the University of Melbourne for eight Indian graduates. Dr. Edwards contributed to this course a series of lectures on mineragraphy and ore textures. These lectures provided the basis for his book, "Textures of Ore Minerals", which the Australasian Institute of Mining and Metallurgy published in 1947 and which met with such world-wide success that the demand quickly exhausted the first edition. A new and enlarged edition (1954) was exhausted in 1960, and further reprinting was in progress at the time of his death.

In preparation for the Fifth Empire Mining and Metallurgical Congress in Australia in 1953, Dr. Edwards initiated a symposium on the geology of Australian ore deposits. It was organized by a committee appointed by the Australasian Institute of Mining and Metallurgy with Dr. Edwards as chairman. The result was a volume comprising 135 articles contributed by the leading geologists in the Commonwealth, which were edited by Dr. Edwards, with the gaps filled in with his own editorial contribution. He served as assistant editor of the *Proceedings* of the Institute until his departure overseas.

Ore minerals and their textures was the subject chosen by Dr. Edwards for the Clarke Memorial Lecture to the Royal Society of New South Wales in 1952. The last honour received by him was the award of the Society's Clarke Memorial Medal in 1960.

He was a member of the Council of the Australasian Institute of Mining and Metallurgy, Corresponding Fellow of the Edinburgh Geological Society, Foreign Member of the Mineralogical Society of India, and observer for 1958–61 for the Commission on Geochemistry of the International Union of Pure and Applied Chemistry.

In preparation for his overseas tour he acquired a knowledge of spoken Italian. He left with his wife on August 25 but died in Rome.

With his death Australian geological science suffers the loss of a brilliant and energetic scholar whose clear thinking and rapid grasp of a problem was a constant help and guide to all associated with him. This loss, at the height of his career, is most keenly felt, both throughout Australia and overseas.

F. L. STILLWELL

NEWS and VIEWS

Electrical Engineering at Edinburgh: Prof. W. E. J. Farvis

MR. FARVIS, senior lecturer in applied electricity and head of the postgraduate school of electronics and radio in the University of Edinburgh, has been appointed to the newly established chair of electrical engineering. He graduated B.Sc. from the University of Bristol in 1936, with first-class honours in electrical engineering. After junior teaching appointments at Dundee Technical College and University College, Swansea, he joined the Telecommunications Research Establishment in 1940, working first on new decimetric radar. The following year he transferred to counter-measures work for the radio defence of London, and for the remainder of the War led a group developing and using new ground and air interception devices. Immediately before the end of hostilities he was one of a team sent to Europe to investigate German radio and radar war-time research. In 1945 he returned to Swansea as lecturer, and in 1947 took the external B.Sc. degree of the University of London in physics. He was appointed lecturer at the University of Edinburgh in 1948, and afterwards senior lecturer. During his twelve years in the Engineering Department there Mr. Farvis has evolved a new electrical engineering degree curriculum, founded the postgraduate diploma course in electronics and radio (now in its eleventh year) and built up a research school on various types of gas discharge. His personal research has been in high-current arcs and fundamental problems associated with power-circuit interruption, interests which began during his student training at the switchgear works of the British Thomson-Houston Co. He took part in the official British programme for the International Geophysical Year, setting up stations in Shetland and Edinburgh for recording the absorption of galactic radio noise. This work, sponsored by the Royal Society, is still continuing in Edinburgh.

The British Industrial Biological Research Association

IN a written answer in the House of Commons on November 28, Sir David Eccles, as representing the Minister for Science, said that the British Industrial Biological Research Association was not designed to supplement the work of the Department of Scientific and Industrial Research. It had been formed by industry as a co-operative industrial research association, and its new laboratories were to be sited at Leatherhead on land adjacent to existing laboratories of the British Food Manufacturing Industries Research Association to facilitate the sharing of facilities. In answer to further questions on December 1, Sir David said that the laboratories would cost £56,000, and the main purpose of the facilities was to investigate the effect on health of substances used in food, or which may find their way into food from such things as pesticides, packaging materials or utensils. The site had the additional advantage of proximity to the Medical Research Council's Toxicological Research Unit at Carshalton. Questioned about the Minister's proposal to close the Research Station at Greyhope Road, Aberdeen, the Joint Parliamentary Secretary to the Ministry of Agriculture, Fisheries and Food, Mr. W. M. F. Vane, stated that the work proposed at Leatherhead was entirely different from that done at Aberdeen. During the past twelve months the latter had included: the installation and operation of the Mark I commercial prototype accelerated freeze-drying cabinet loaned from Chicago; production of field-trial samples of various foods processed by the accelerated freeze-drying method, and of experimental rations for large-scale trials by the three Armed Services; work on the quality and storage life of dehydrated foods; research into problems of flavour in vegetable products; investigation of enzyme activity in dehydrated raw meats with low-moisture content, and of the reasons for the deterioration of dehydrated raw meat; investigation of the mechanism of oxidative rancidity and of the application of free-radical acceptors to the inhibition of oxidative rancidity induced by radiation. Three other projects had been undertaken with grants provided by the United States Department of Agriculture, including the investigation of new antioxidants, of the freezing and drying of muscle tissues, and of the significance of carotenoid breakdown in the deterioration of fruits and vegetables.

Tax Assessment for Scientific Societies in Britain

CLAUSE 9 of the Rating and Valuation Bill, which received its second reading in the House of Commons on November 30, gives effect to the recommendation of the Pritchard Committee that the total exemption from rates given by the Scientific Societies Act of 1843 to societies established for the purposes of science, literature or the fine arts, exclusively, should be terminated. In moving the second reading of the Bill, the Minister of Housing and Local Government, Mr. H. Brooke, after a tribute to the work of the Pritchard Committee, said that the Government proposed to follow the report in this difficult matter. The definition in the 1843 Act had proved so difficult to apply that he doubted if anyone would advocate its retention unaltered, and under Clause 8 of the Bill, practically every organization which now obtains benefit from the 1843 Act would in future qualify automatically for 50 per cent derating, and the local authority would have discretion to give up to complete exemption if it thought fit. As regards research associations, Mr. Brooke added, in reply to a question, that derating would turn entirely on whether an association could establish that it was a charity.

Mr. Brooke also said that the Pritchard Committee was clearly in some doubt about the position of the universities. While, as stated in the first schedule to the Bill, they were undoubtedly charities, they were also substantially financed by Exchequer grants, and, unlike other charities, many of them held a considerable if not a dominating position in the towns and cities in which they are established. Accordingly, it did not seem to the Government that a sufficient case existed for giving the universities a statutory 50 per cent exemption from local rates, although the Chancellor of the Exchequer was ready to give an

assurance that any additional rates falling on the universities in consequence would be taken into account in determining the amount of their recurrent Exchequer grants. He said also that this arrangement would not apply to the Oxford and Cambridge colleges, which as charitable foundations would receive the 50 per cent mandatory relief.

In the debate, Mr. C. M. Woodhouse challenged this discrimination between the universities and the Oxford and Cambridge colleges as contrary to the recommendation of the Pritchard Committee, although that Committee had explicitly recognized that these colleges stood in a different relation to the Exchequer from university institutions in general in that they received no financial aid directly from the University Grants Committee. Mr. Woodhouse doubted whether the distinction was valid or should be perpetuated, and pointing out that the finances of university and colleges were interlocked, observed that in its memorandum to the Pritchard Committee the Treasury had been disinclined to accept the obligation that Mr. Brooke now said the Exchequer would accept for the universities. He thought it perfectly reasonable that an increased burden on the universities should be met from the national Exchequer rather than from local funds, but that the same argument should apply to the colleges, and pointed out that in view of the decision in a test case brought last year to the Lands Tribunal by three of the colleges the effect of the present Bill would be to give the colleges double relief. A Government contribution, suggested by the colleges in their memorandum to the Pritchard Committee as the proper remedy, would avoid these rating anomalies, and Mr. Woodhouse urged the Minister to exercise his power of addition to the First Schedule and include at least the Oxford colleges.

In replying on behalf of the Government, the Parliamentary Secretary to the Ministry, Sir Keith Joseph, said that in representations before the Pritchard Committee the colleges had made it clear that they regarded the question of value as an entirely separate issue from that of rate relief. In general, the Government viewed the Oxford and Cambridge colleges as closer to educational establishments than grant-aided universities, but promised to study the point raised before the committee stage of the Bill. The question of scientific societies, and particularly the point raised by Lord Adrian in the House of Lords, was not mentioned in this debate.

The Medical Research Council of Canada

THE National Research Council of Canada has established a Medical Research Council with responsibility for all activities formerly conducted by the National Research Council's Division of Medical Research. The new Council will have virtually complete autonomy in its operations and full responsibility for policy concerning the support of medical research, but will function under the general administration of the National Research Council. The Medical Research Council has been set up as an interim measure pending the Government's future consideration of appropriate legislation. The eventual establishment of a completely independent Medical Research Council was implied in a statement in the Canadian Parliament last summer by the Hon. Gordon Churchill, chairman of the Canadian Privy Council Committee on Scientific and Industrial Research.

Officers and members of the new Medical Research Council are: *Chairman*, Prof. R. F. Farquharson, professor emeritus of medicine, University of Toronto, vice-president (medical), National Research Council; *Secretary*, Prof. J. Auer, professor of anatomy and associate dean, University of Ottawa; *Members*, Prof. L. B. Jaques, professor and head of the Department of Physiology and Pharmacology, University of Saskatchewan; Prof. R. W. Reed, professor and head of the Department of Bacteriology, McGill University; Prof. C. B. Stewart, dean of the Faculty of Medicine and head of the Department of Preventive Medicine, Dalhousie University; Prof. M. Brown, professor of medicine, Queen's University; Prof. M. Darrach, professor and head of the Department of Biochemistry, University of British Columbia; Prof. R. Rossiter, professor and head of the Department of Biochemistry, University of Western Ontario; Prof. J. Doupe, professor and head of the Departments of Physiology and Medical Research, University of Manitoba; Prof. A. L. Chute, professor and head of the Department of Pædiatrics, University of Toronto; Prof. R. Gingras, assistant dean of medicine and head of the Department of Biochemistry, Laval University; Prof. W. C. MacKenzie, dean of the Faculty of Medicine and professor of surgery, University of Alberta; Prof. F. C. MacIntosh, professor and head of the Department of Physiology, McGill University; Prof. L. P. Bouthillier, professor and head of the Department of Biochemistry, University of Montreal; Prof. H. E. Taylor, professor and head of the Department of Pathology, University of British Columbia.

Jubilee Celebrations in Berlin

THE Humboldt University of Berlin celebrated its 150th Anniversary together with the Charité Hospital, the 250th Anniversary of which ran concurrently. Symposia, conferences, discussions and exhibitions were offered to participants by the various faculties, including those of Medicine, Philosophy, Mathematics, Physics, Politics, Economics, Pedagogy, and Jurisprudence. The Institute of Anglo-American Literature organized lectures and discussions simultaneously. The proceedings took place during November 6–20 and enabled each faculty to give its guests noteworthy entertainment from the operatic, theatrical and musical riches which the city possesses. University dignitaries, ministerial houses and student bodies opened their doors in a succession of receptions and discussions which encouraged the informal interchange of ideas and ideals. The Faculties of Philosophy and Medicine took three days to discuss together their understanding of humanism and medicine, representational thinking, cybernetics and its role in medicine, the concept of illness and, finally, the theory and practice of medicine. The physiology symposium, spread over three days, was devoted to an exhaustive, many-sided analysis of the red-blood cell structure and function. Energetics, cell stability, and biochemical interrelations received outstanding treatment by workers drawn from many countries.

Wildfowl Conservation Committee

SINCE 1954 the Nature Conservancy has held a regular series of informal meetings with leading wildfowlers and wildfowl conservationists, including representatives of the Wildfowlers' Association of Great Britain and Ireland, the Wildfowl Trust and the

British Field Sports Society. Much experience has been gained as a result of these meetings in bringing together the interests of conservationists and wildfowlers and about the selection and management of wildfowl refuges, such as those already set up on the Humber, at Southport and at the Caerlaverock National Nature Reserve. Wildfowl refuges form a desirable and, in some conditions, an indispensable means of conserving and increasing wildfowl stocks, in which the wildfowlers are no less interested than the protectionists and scientists. It is now intended to develop out of this consultation and agreement a National System of Wildfowl Refuges which will in due course form the main British contribution to the projected international network of European refuges. North America has long since operated such a system with outstanding success. The Conservancy has decided in view of the importance of the work of this informal group that it should now be formally constituted as the Wildfowl Conservation Committee with the status of a special advisory committee of the Conservancy. Mr. E. M. Nicholson, director-general of the Nature Conservancy, will be chairman of the Committee, which will include members of the Wildfowlers' Association of Great Britain and Ireland, namely, Lieut-Cmdr. J. W. Anderton, Mr. J. L. Hirst, Brig. G. D. Holmes, Colonel J. N. Vallance, Mr. E. L. Parish and Dr. G. W. Storey; the Wildfowl Trust, Mr. Peter Scott, Dr. G. V. T. Matthews, Mr. G. L. Atkinson-Willes and Mr. Hugh Boyd; the British Field Sports Society, Major J. G. Morrison, Brigadier A. H. Pepys and Sir Ralph Clarke; and the Nature Conservancy, Dr. J. Berry, Dr. E. B. Worthington and Mr. R. E. Boote. There are also two independent members of the Committee, namely, Colonel H. J. Cator and Major-Gen. C. B. Wainwright.

Country Life

An interesting example of the fine work done by the Council for the Preservation of Rural Wales is described in its annual report for 1958–59 (Pp. 77+5 plates. London: Council for the Preservation of Rural Wales, 1960). In 1958, the late Lord Bledisloe, then president of the Gloucestershire branch of the Council for the Preservation of Rural England, offered to present a cup to be competed for annually for the best kept village in that county. Since then, many other competitions on a county basis have been held throughout England and Wales based on the Gloucestershire pattern. Some of these have been held under the auspices of various branches of these two councils, others under the auspices of other bodies such as women's institutes, county associations of parish councils, and rural community councils. In Wales, the competitions were inaugurated in Glamorgan through the award of the D. C. Jones Challenge Cup for the best kept Village in the Vale, under the joint sponsorship of the Council for the Preservation of Rural Wales, Glamorgan Branch, and the Barry Horse and Horticultural Society. Now there is a competition annually in most of the Welsh counties, and the entries are increasing every year. In the first year's competition, twenty-one villages entered and the prize was awarded to St. Nicholas, which was runner-up jointly with St. Fagans to St. Hilary last year. The report, available from the Secretary, Council for the Preservation of Rural Wales, 4 Hobart Place, London, S.W.1, contains full details of the many-sided activities of the Council in its work. The Council would welcome new members.

Archive for History of Exact Sciences

In spite of the proliferation of scientific periodicals of all kinds, a warm welcome must be extended to the publication of a new journal, *Archive for History of Exact Sciences* (Vol. 1, No. 1. Pp. 106. Five numbers, individually priced, constitute a volume. D.M. 19.60. Berlin: Springer-Verlag, 1960). It should help in what has become almost an international duty, namely, to build those bridges possible between the domains of the sciences and the humanities. To do this is far from easy, but the need is a very real one. A study of the history of science is beneficial in both camps, always provided that it does not become merely a soft option; in other words, that the standards are set high. This, the new journal seems prepared to accept: it has a distinguished editorial board, and it will do well if it lives up to its dedication, "to uphold the tradition of P. Duhem and E. T. Whittaker". The first issue contains two papers—both dealing with important themes—one on rational mechanics in the Age of Reason, and the other on the beginnings of Euclid's axiomatic system. Contributions will be acceptable in the usual European languages, with the addition of Latin. To judge from the publisher's notice and the first of these articles, the English rendering leaves a good deal to be desired; the phrasing is a little clumsy and in one or two cases quite obscure. Improvement here should not be difficult, but it needs taking in hand at once, before this otherwise excellent production becomes suspect and its merits overlooked.

Leather Manufacture

The inaugural lecture by Prof. A. G. Ward, following his appointment as professor of leather industries at the University of Leeds, was concerned with science and art in leather manufacture. Prof. Ward emphasized that, despite sixty years of intensive research, the making of leather still remains mainly an art and will continue to do so until its properties become amenable to measurement. At present there is little unanimity about what those properties are. In a brief historical review, Prof. Ward showed how much the improvement in the qualities of leather has been due to practical tanners who used methods analogous to scientific experiment but who lacked an accepted body of theoretical knowledge (Science and Art in Leather Manufacture: an Inaugural Lecture. Prof. A. G. Ward. Pp. i+20. Leeds: Leeds University Press, 1960. 2*s*. 6*d*.). Many efforts to provide the theoretical background to empirical facts have so far failed to provide an accepted and adequate view of leather-making processes. But the pace of change to-day makes it dangerous to the industry to assume that the art can develop fast enough to meet the challenge from industries based on science. Both the need of the industry and the state of the subject emphasize that an extension of basic science in this field is opportune. It is to be hoped that successful research can enable one more of the great craft industries of Britain to play its part in the modern world.

Some Water-mites from Seepage Water

Collections by T. Gledhill from one locality yielded seven species of water-mites, each from a different family; four species are new to Britain and a fifth has previously been recorded from Ireland. The collections were made in seepage-water and are

outlined in the August issue of the *Journal of the Quekett Microscopical Club* (5, Ser. 4. No. 11. 1960). The locality is about 300 ft. above sea-level and situated on the eastern slopes of Claife Heights in the Lake District. The water appeared from under a large boulder, and made an area of wet woodland debris in some parts of which *Chrysoplenium oppositofolium* was growing. It was only when the surface debris was removed and a small hollow made that water would collect, and is the type of place which continental workers would call a helocrene. The species caught were: *A-Thienemannia schermeri*; *Hygrobates norvegicus*; *Hydrovolzia placophora*; *Panisellus thienemanni*; *Pseudofeltria scourfeldi*; *Bandakia concreta*; *Ljania bipapillata*. The first four were previously unknown in Britain, while *Panisellus thienemanni* is the only known species of its genus.

Heterotrophic Nutrition of *Chlorella*

In studies of the heterotrophic nutrition of *Chlorella vulgaris* (Brannon No. 1 strain) cultured in darkness, D. J. Griffiths, C. L. Thresher and H. E. Street (*Ann. Bot.*, N.S., 24, 1; 1960) have tested the utilization, as carbon sources for growth and respiration, of a range of sugars, sugar alcohols, sugar phosphates, organic acids and monohydric alcohols. Considerably higher rates of growth and respiration were obtained with *d*-glucose than with any other substance tested. Ethanol (at 0·005 *M*) sustained both growth and respiration at *c.* 50 per cent of the level with glucose (0·028 *M* or higher). Evidence was obtained that the organism can become 'adapted' to utilize *d*-galactose and sucrose as effective carbon sources. Sustained growth was not obtained with any of the other substances tested. The glucose monophosphates, methanol and certain organic acids (oxalacetate, α-ketoglutarate, *cis*-aconitate, and pyruvate) clearly stimulated oxygen-uptake, but to a less extent than ethanol. The other substances tested were either inhibitory to respiration or inactive, or of very low activity as substrates. The growth in darkness and in liquid culture of *Chlorella* when supplied with *d*-glucose was insensitive to *p*H over the range 4·5–7·0, and was markedly enhanced by a high level of aeration. Gains in cellular dry weight ranging from 45 to 90 per cent of the weight of *d*-glucose disappearing from the culture medium were recorded in growth experiments; measurements of evolution of carbon dioxide in the Warburg apparatus indicated retention of up to two-thirds of the glucose–carbon in cell material.

Christmas Lectures for Young People

Among the lectures which are to be specially organized for young people during Christmas and the following weeks are: The one hundred and thirty-first course of six Christmas lectures, which is to be given by Dr. V. E. Cosslett on "Seeing the Very Small", at the Royal Institution on December 29, 31, January 3, 5, 7, 10, at 3 p.m. (Further information can be obtained from the Royal Institution.) A lecture on "Plastics and Textiles", to be given by Dr. H. A. Thomas in the Lecture Theatre of the Institution of Electrical Engineers, Savoy Place, London, W.C.2, on January 2, at 2.30 p.m. (Further information can be obtained from the Plastics Institute, 6 Mandeville Place, London, W.1.) A lecture on "Gyroscope and Pendulum—the Modern Travel Agents", to be given by R. J. Lees, head of the Instrument and Photographic Department of the Royal Aircraft Establishment, in the Lecture Theatre, Royal Aeronautical Society, 4 Hamilton Place, London, W.1, on January 5, at 3 p.m. (Further information can be obtained from the Royal Aeronautical Society.)

Announcements

Prof. W. Hume-Rothery, Isaac Wolfson professor of metallurgy in the University of Oxford, has been elected an Honorary Member of the Institute of Metals. Major C. J. P. Ball, Dr. Maurice Cook and Lieut.-Colonel S. C. Guillan have been elected Fellows, in recognition of the services that they have rendered to the Institute. The total number of Honorary Members and Fellows are each restricted to twelve.

Prof. Alan Wood, professor of geology at the University College of Aberystwyth, has been awarded the Silver Medal of the Liverpool Geological Society in recognition of his contributions to geology.

Prof. V. F. Weisskopf has been appointed director-general of CERN, in succession to Dr. J. B. Adams, who will, next year, return to the United Kingdom as director of the Culham Laboratory for Plasma Physics Research. Prof. Weisskopf has been at the Physics Department, Massachusetts Institute of Technology, since 1945.

Brigadier H. E. Hopthrow, assistant secretary to Imperial Chemical Industries, Ltd., has been elected secretary of the Royal Institution, in succession to the late Sir Harold Spencer Jones.

The Television Society has invited Sir Harold Bishop, director of engineering of the British Broadcasting Corporation, to become president in succession to the late Sir George Barnes. Sir Harold Bishop has been with the Corporation since it was the British Broadcasting Company, Ltd., in 1923. He has been director of engineering since 1952.

Biographical material relating to the late Academician A. F. Joffe is being collected by Madame Joffe. Any letters, photographs or personal recollections would be welcomed and should be sent to Madame Joffe at the Institute for Semiconductors, Kutuzova 10, Leningrad *D*-187, U.S.S.R.

A symposium on "Light Metal Industry in India" is to be held in the auditorium of the National Metallurgical Laboratory, Jamshedpur, during February 14–17, 1961. Further information can be obtained from the Director, National Metallurgical Laboratory, Jamshedpur-7.

The fifth international conference on "Ionization Phenomena in Gases" is to be held at Munich during August 28–September 1, 1961. The conference is being organized by the Verband Deutscher Physikalischer Gesellschaften. Further information can be obtained from the Secretariat, Fifth International Conference on Ionization Phenomena in Gases, Oskar-von-Miller-Ring 18, Munich 1 (P.O. 463).

A Supplement (1957–1959) to the Catalogue of Lewis's Medical, Scientific and Technical Lending Library has now been published (Pp. 306. To subscribers to the Library, 5*s*. net. London: H. K. Lewis and Co., Ltd., 1960. 10*s*. 6*d*. net). It is arranged alphabetically by authors, and is provided with a classified subject index which gives the names of authors of books listed in the Supplement which deal with the subjects classified.

CITY OF LIVERPOOL COLLEGE OF TECHNOLOGY

NEW SCIENCE BLOCK

SIR David Eccles, Minister of Education, opened the first instalment of the new City of Liverpool College of Technology on September 30, 1960. The new building provides accommodation for the Departments of Chemistry and Biology, Physics and Mathematics, and Pharmacy. The building (Fig. 1) has been designed and the work carried out under the direction of Dr. Ronald Bradbury, city architect and director of housing. It has been erected by Messrs. Henry Boot and Sons, Ltd., of Bootle, at a cost of £310,500. It is a concrete cased steel-framed structure, faced with rustic brickwork and artificial stone, purpose made bricks and coloured tiles forming patterned infilling panels between the floor-levels on the front elevation. The various floors, formed with precast concrete flooring units, have been finished generally with thermoplastic floor tiling, which in the case of the laboratories is acid resisting. Particular attention has been given to the design of the specialized laboratory furniture and fittings, which incorporate drawer and storage units and which are interchangeable, the whole of the units being finished in acid-resisting lacquer. The various services to the laboratories, which include hot and cold water, gas, electricity, compressed air, vacuum, steam, etc., are concealed in vertical and horizontal ducts, as well as in the suspended ceilings. The latter are formed with rectangular panels of asbestos board, and the patented system of suspension enables each panel to be removed easily when access to the various services is desired. Each floor is served by an automatically electrically operated passenger and service lift, the latter enabling stores and materials to be transported conveniently from the main store on the ground floor to the materials issue stores on the upper floors. The laboratories have been designed, so far as possible, to house the most modern equipment and apparatus for teaching and research work in the departments concerned.

The Department of Chemistry and Biology occupies the ground and first floors, with certain advanced-research laboratories located on the second floor. The remainder of the second floor and the whole of the third floor accommodate the Department of Physics and Mathematics. The Department of Pharmacy is accommodated on the fourth floor, and a range of animal houses and ancillary rooms has been provided on the main roof. Each department has appropriate types of laboratories, rooms for departmental heads and staff, classrooms, lecture theatres and store rooms. The Department of Chemistry and Biology provides full professional training, postgraduate work and research for chemists and biologists, including courses leading to the external B.Sc. degree of the University of London, the diploma in technology in applied chemistry, and graduateship of the Royal Institute of Chemistry.

Fig. 1. New Science Block, City of Liverpool College of Technology

The Physical Chemistry, and Inorganic and Organic Laboratories are well equipped for teaching purposes. The Organic Research Laboratory includes apparatus specially designed by the staff for research work on gas adsorption, gas chromatography and electrochemistry. The equipment provided in the Instrumental Laboratory includes a recording polarograph, emission spectrograph, and an argon chromatograph. Some important and costly pieces of equipment have been installed in the special laboratories on the second floor. These include a Phillips E.M.100 electron microscope giving a resolution of 20-15 Å., and is being used in conjunction with an Edwards '12 E 6' coating unit for the examination of various inorganic gels and precipitates; a 'Raymax 60' X-ray generator, which is being used for X-ray powder photography, and a 'Unicam S.P.100' infra-red spectrometer. A suite of rooms is provided for research work in radiochemistry and radiobiology.

The Department of Pharmacy is responsible for the training of pharmacists who will eventually take their place in hospitals, manufacturing industry and retail work. Students attend the pharmaceutical chemist qualifying course. The Dispensary provides all the facilities required for modern dispensing. The Pharmaceutical Chemistry Laboratory is fully equipped to deal with standard analytical and preparative procedures with a particular bias to semi-micro techniques. Specialized apparatus includes a spectrophotometer, electrophoresis tank, a polarograph and Karl Fischer apparatus. The accommodation includes the Pharmacology and Physiology Laboratory and the Aseptic Laboratory, which enables students to work under conditions designed to exclude bacterial and fungal contamination from the air. The small-scale manufacturing laboratory permits many large-scale processes to be duplicated accurately. The research laboratories (situated on the second floor) are used for investigations covering pharmaceutical subjects, using modern techniques and apparatus.

The Department of Physics and Mathematics provides courses leading to the National Certificate in Applied Physics and to graduateship of the Institute of Physics, and examinations for external degrees of the University of London. The Department is also responsible for the mathematics and physics classes required by other departments for their certificate, diploma, and Diploma in Technology courses. Postgraduate courses are provided, and the Department has organized a number of research projects. The Physics Laboratories are well equipped and include spectrographic apparatus, high-vacuum equipment and an electron-microscope, the latter being a gift from an industrial concern. A large differential analyser has also been presented to the Department by an industrial firm. For the courses in mathematics and statistics there are various calculating machines, and an analogue computer is to be built.

Research projects undertaken by the Departments accommodated include the following: chromatography, electrochemistry, inorganic, polymer, sugar, surface and radiation chemistry, X-ray diffraction, electron microscopy; electron magnetic resonance, examination of cosmic dust, numerical analysis, and pharmaceutical subjects. A considerable amount of research work is carried out in collaboration with various industrial organizations. A number of members of staff have qualified for research grants from the Department of Scientific and Industrial Research.

Departments of the College offering professional courses award College associateships (A.C.T. (Liverpool)) to students who have satisfactorily completed courses approved for this purpose by the Board of Studies. Full-time and 'sandwich'-course students may be awarded an honours associateship, and, in exceptional cases, only students completing approved part-time courses. The College fellowship (F.C.T. (Liverpool)) is awarded for approved research work carried out in the College. S. A. J. PARSONS

CROYDON TECHNICAL COLLEGE

A NEW building, which was opened by H.M. the Queen on November 2, houses Croydon Technical College, Croydon College of Art and the Denning Hall. The premises, which occupy a site of nearly four acres, were projected before the War, but construction had to be deferred, and work was not begun until 1953. Although it has been dealt with in three stages under three separate contracts, building work has been going on continuously from 1953. The total cost of the building is about £1,450,000 and of the equipment housed in it about £375,000. The provision made will be enough for some 500 full-time and 10,000 part-time students. The architects are Messrs. Robert Atkinson and Partners, of Manchester Square, London, W.1.

Croydon Technical College traces its ancestry back to the establishment of classes, mainly in scientific subjects, in 1838, when the Croydon Literary and Scientific Institute was founded. But possibly a more important occasion was the foundation of a scheme for technical classes for artisans by the Rev. Oakley Coles, curate of the Croydon Parish Church, in 1888. Two years later the Croydon Council decided to set up the Polytechnic, based on this modest beginning, and a new building was opened by the then Archbishop of Canterbury, Dr. E. W. Benson, in December 1891. As this was some years before the establishment of the local education authority, the Polytechnic was in fact the first educational institution to be maintained by the Council and is also the oldest technical institution to be maintained by any Council in the Greater London area. Control of the Polytechnic was transferred to the new Education Committee in 1903. The work of the College was extended continuously until, in 1929, H.M. Inspectors reported that the old building was inadequate for the services which the College was providing. Expansion of the work of the College has continued for the past thirty years, and recently the number of student enrolments has been increasing annually by at least 10 per cent. The expansion of the work since 1945 has in fact been greater than during the whole history of the College before that date. Enrolments for the present

session total 450 full-time and 8,000 part-time students.

The six-storey building consists of a centre block housing the administrative offices, refectory, laboratory and gymnasium—facilities shared by both the Technical College and College of Art—and four wings. The two west-wings and the majority of the south-east wing provide accommodation for the Technical College, while the north-east wing is exclusively for the College of Art. Noisy workshops used for mechanical engineering and building have been placed at the lower-ground floor-level, with special construction to keep noise and vibration from affecting the quieter rooms above, while a service road for these workshops runs under the whole length of the building. Lecture rooms, drawing offices and the lighter laboratories and practical rooms for science, electrical engineering, commerce, domestic science and food trades are grouped on the floors above. Lifts and the main staircases situated at the junctions of the two west wings and the two east wings communicate with all teaching floors; other staircases are provided at the extreme ends of the four wings. In the courtyard between the two east wings is situated the Denning Hall, which will seat approximately 750, and is a gift to the town by Mrs. Elizabeth Denning, in memory of her husband, who was Mayor of Croydon during 1913–16. This fine Hall may be used for the purposes of both Colleges and for other public purposes with an educational association.

Space will permit the detailed description of one Department of the College only, and the Department of Science has been chosen. This Department occupies almost all the fourth-storey accommodation of the two west wings and the centre block. The south-west wing provides laboratories for inorganic, organic and physical chemistry together with balance, store, preparation and dark rooms, a lecture theatre and classrooms. Physics is housed in the north-west wing, and is provided with four laboratories, a workshop, dark room, a lecture theatre, classrooms and stores. Also in this wing is the radioisotopes suite with the X-ray room adjacent. In the centre block on this floor are general science and biology laboratories together with further class-rooms. This accommodation serves the following courses of study:

	Students
Full-time	
General Certificate of Education	125
Part-time (day)	
General Certificate of Education	112
B.Sc. (General)	38
Ordinary National Cert. in applied physics	43
Higher National Cert. in applied physics	43
Graduateship of Institute of Physics	9
Ordinary National Cert. in chemistry	57
Higher National Cert. in chemistry	20
Evening	
General Certificate of Education	248
Horticulture	17

In addition, the Science Department acts as a 'service' department by undertaking the teaching of science required by other Departments of the College, for example, Bakery Science.

To provide for unknown expansion in the future, the building is designed on a unit grid with external planning and services as flexible as possible. In the chemistry section, for example, the larger class-rooms on the opposite side of the corridor to the existing laboratories are already provided with floor ducts and connexions to existing services to permit them being converted readily into extra laboratories. This means that, if additional building is needed, it will be principally class-room accommodation and that the dispersal of the various kinds of departmental practical rooms will be avoided.

Many new technical colleges cater for future expansion by building different blocks for different purposes, each of which has a 'growing point' for extensions. This method may be simpler than that described above; but the Croydon plan, with 'growing points' for class-room accommodation available on the inner sides of the existing east wings, is likely to provide the more compact building with shorter lines of communication for its users.

The integral nature of the building and the decision to place two independent Colleges under one roof are perhaps the most distinctive features of what the Queen referred to as "this imaginative experiment" in which young scientists, technicians, craftsmen and artists may "meet and exchange ideas with those trained in other fields of knowledge".

BIOLOGY OF SPACE TRAVEL

A SYMPOSIUM on the "Biology of Space Travel", organized by the Institute of Biology, was held during September 29–30 at the Royal Geographical Society, Kensington.

For the opening session the chair was taken by Sir Lindor Brown. The first paper was by Air-Commodore W. K. Stewart, of the Royal Air Force Institute of Aviation Medicine, Farnborough, who gave an account of recent work on the physiological effects of acceleration. A semi-recumbent posture would allow acceleration for several minutes at about eight times gravity without severe physiological disturbance, and the accelerations on take-off of rockets would be close to this figure. However, little is known about the effects of vibration and of emotional disturbance under such conditions, and in such high accelerations the astronaut would find it very difficult to carry out any movements other than movements of the eyes and of the supported hands. The forces on re-entry would probably reach rather higher figures, in the region of ten times gravity, and provision would be needed for ensuring that the astronaut was correctly positioned in relation to the deceleration; if this were assured the forces would be tolerable for the short period expected. Wing-Commander T. C. D. Whiteside, also of the Royal Air Force Institute of Aviation Medicine, followed with a paper on the effects of the gravity-free state. Although no data are available for man for prolonged periods of weightlessness, it is probable that the physiological effects would not be severe. Eating would be easy, but fluids would have to be sucked from plastic containers. Locomotion would be easy in the dimensions of a small space-vehicle. However, it seems likely that muscular weakness would develop in a few days due to lack of exertion in a weightless environment, and this might reduce the tolerance to deceleration on re-entry. Regular exercises would

be needed to combat this problem. An unsuspected difficulty in low gravitational fields might occur if artificial gravity was produced by rotation of the space-vehicle itself, since even in large vehicles the Coriolis forces in the labyrinth of the ear produced on moving the head might give rise to disabling giddiness.

Lieut.-Colonel W. R. Turner, of the United States Air Force Aerospace Medical Division, Ohio, described the exacting series of physical and psychological tests employed in selecting candidates for the "man-into-space" projects such as "Project Mercury". The candidates were chosen from men with high basic qualifications, including a degree in engineering and 2,000 hr. of piloting jet aircraft. The examinations included exhaustive medical and psychological examinations and tests under conditions simulating those anticipated in space flight, such as high temperatures, acceleration and vibration. Other tests estimated noise-tolerance, patience with complicated and confusing machinery, and the ability to tolerate long periods of isolation. It was found that, given a normal physique, the motivation of the candidate played a surprisingly large part, and keen but level-headed men of about thirty-five years were the most successful at these tests.

For the second session the chair was taken by Sir Solly Zuckerman. Dr. D. McK. Kerslake read a paper by Flight-Lieutenant J. Billingham, of the Royal Air Force Institute of Aviation Medicine, on the maintenance of the thermal environment in space vehicles. When in orbit the temperature of the cabin would be maintained at a comfortable level by fairly simple air conditioning together with suitable insulation of the walls. On re-entry, however, the frictional heating of the exterior might cause severe over-heating of the interior, particularly if the time for descent was prolonged for any reason. Whether such over-heating will cause skin burns or heat stroke will depend largely on the rate of the rise in temperature. Both these dangers can be avoided by a special suit in which cold air is piped to the skin, and some impressive experiments were cited in which a man was well protected for several hours by this means in an environment at 125° C.

Mr. N. W. Pirie, of the Rothamsted Experimental Station, Harpenden, discussed the problem of the synthesis or re-cycling of oxygen, food and water on longer space flights. Water is unlikely to be a severe problem since most of the expired water vapour can be readily condensed and distillation of urine would allow the recovery of most of the remainder. The astronaut would require about 1 kgm. of oxygen a day, and the expired carbon dioxide would have to be absorbed: for short voyages potassium tetroxide would be suitable for this dual purpose. For longer voyages it has been suggested that algae such as *Chlorella* could be used to regenerate oxygen and foodstuffs by photosynthesis. There would be many technical problems in this. Outside the orbit of Mars the intensity of sunlight would fall to a level too low for effective photosynthesis: the algae would be very difficult to handle, maintain and process, and they would not in any event be suitable as the sole source of food. Complex chemical re-syntheses would require weighty and complex apparatus. An exciting possibility is that some way may be found of readily converting energy into essential biochemical intermediates, so that one could 'recharge' one's energy supplies in a manner analogous to recharging an electric accumulator.

Mr. S. W. F. Hanson, of Armour and Company, Ltd., London, read a paper on the supply of food to astronauts. He described recent progress in packaging food in a suitable form, and in particular the advantages for long journeys of dehydrated and pre-cooked foods, which can be prepared in wide variety; this is of great importance from the psychological point of view. He believed that at the most *Chlorella* would prove to be only an adjunct to the diet of astronauts, even if the technical problems of growing it were overcome. He showed a film which illustrated some of the problems of feeding under conditions of weightlessness.

On the morning of the second day of the symposium Sir Harrie Massey took the chair. Dr. P. Alexander, of the Chester Beatty Research Institute, London, read a paper on radiation in space and its effects on man. Most of the ionizing radiation in space consists of electrons and protons. The majority of the electrons will be stopped by the walls of the space-vehicle, though they will generate X-rays in this process which could penetrate the vehicle; in the inner of the two equatorial Van Allen radiation belts this secondary radiation might deliver a dose of about 5 rads/hr. to the astronaut. The protons, although more penetrating than electrons, would only deliver about 1 rad/hr. The radiation in the outer Van Allen belt would be less than that in the inner belt. In deep space the dose-rate would be small, probably about 10 rads per annum. In a short flight through the Van Allen belts and back the astronaut would receive a total of about 15–20 rads, which would be well below the permissible level in these special circumstances, and, by choosing a polar route, the radiation would be reduced considerably.

A paper on the psychological problems of solitude and confinement was read by Dr. R. Beech, of the Institute of Psychiatry, Maudsley Hospital, London. Dr. Beech reviewed thoroughly the published research on this topic, and concluded that very little reliable data were available. The tendency for sensory deprivation to cause abnormal mental behaviour, such as hallucinations, was now well recognized, but the degree to which this might occur in space flights was problematic, and little was known on the best ways to combat it. Dr. W. Grey Walter, of the Burden Neurological Institute, Bristol, in a communication entitled "The Human Brain in Space Time", described some recent work on the ability to learn under difficult and confusing conditions, and he emphasized the marked individual variations in the ease with which certain associations were recognized and learnt. He also raised the interesting question of the mental qualities which would be most desirable in astronauts, and noted that outstanding pioneers in many fields have frequently been decidedly eccentric individuals.

The chair in the final session was taken by Dr. A. S. Parkes, president of the Institute of Biology. Dr. P. H. A. Sneath, of the National Institute for Medical Research, London, discussed the dangers of contaminating the planets with terrestrial micro-organisms, or of contaminating the Earth with planetary organisms, should these exist. Recent work suggests that some soil bacteria may be able to multiply under the conditions found on Mars, and if we contaminate Mars with such bacteria the loss of scientific information would be enormous. The sterilization of a space rocket poses some very difficult problems, which urgently need further attention. It would be very dangerous to bring back to the Earth samples from other planets, because of the

risk that they might contain organisms which could prove dangerous to the ecology of the Earth, and it would be advisable first to carry out experiments on these in closed ecology chambers on manned satellites.

The last paper was by Dr. Harlow Shapley of the Harvard Observatory, who discussed the probable environment of other planets. He felt sure that there must be many planets in the universe which would be suitable for life as we know it on Earth (quite apart from the possibility of life in other forms) and it would seem inevitable that some form of life would have evolved on many of them. Whether we can ever communicate with such worlds was another matter. An important factor in the evolution of higher life may be the ozone layer of the Earth's atmosphere (itself due indirectly to the photosynthetic production of oxygen by primitive plants) since this layer protects terrestrial organisms from short-wave ultra-violet rays. None of the other planets of our solar system appears to possess such an ozone layer.

In summing-up, Dr. Parkes discussed the possibility that astronauts might travel for most of their journey in a state of suspended animation, only to be revived when they reached their destination, and recent work on the freezing of whole animals shows that this is not a wholly fanciful suggestion. This also raises the question of whether man would have a useful part to play in the early stages of space travel, or whether it would be better to devise very elaborate machines to make the observations. The symposium had the excellent result of bringing together workers in many disciplines, and it showed that the remaining difficulties in short-range space flight were mainly engineering problems, while those affecting the astronaut himself would soon be largely solved.

INFLUENCE OF CLIMATE ON LIFE

ONE of the most obvious, and at the same time one of the most neglected, statements in the whole field of biology is that all life depends on its environment. Biologists and medical men of the past have made this the basis of much of their thinking, and engineers and architects have often built machines or houses to suit specific climates, but scientific journals still contain reports of biological experiments in which the experimental conditions were neither controlled nor recorded, and buildings or vehicles often fail to display any consideration for local climate. Even the impressive Unesco headquarters completed a few years ago in Paris are liable to cause heat exhaustion in people working there on sunny days, and it is well known that motor-cars are the hottest places to be found in many tropical countries.

At the other extreme, tables of comfortable environmental temperatures usually assume that simple mathematical expressions can be valid in biological processes, and ships ply through some of the climatically most pleasant seas of the world carrying with them the same constant artificial micro-climate which can be found in any office building in New York or London.

The International Society for Bioclimatology and Biometeorology held its second International Bioclimatological Congress recently in London with the avowed intention of improving knowledge about the influence of climate on life by bringing together people active in all parts of the world and in all branches of science whose work is related in some way to these problems. The success of the Congress was considerable, and its effects will probably be felt for some time to come. Some of the work helped to cross-fertilize or to dispel misconceptions by passing ideas and techniques between different specialties or different countries, but much new information of interest was also provided.

Symposia included one on life at high altitudes in which Prof. R. Margaria (University of Milan) related the problem of acclimatization to anoxia with space flying where less oxygen means less pressure which, in turn, means less weight. He also reported the results of experiments which showed that the carotid body chemoreceptors of man were sensitive to oxygen, in any event during anoxia, which was of interest in view of occasional criticisms against conclusions made from such studies on anæsthetized animals. A paper by Prof. A. von Muralt and Dr. W. H. Weihe (University of Berne) reported experiments carried out on the Jungfraujoch at about 11,000 ft. and mean barometric pressures of about 500 mm. of mercury which showed that the threshold for various stimuli, such as taste, touch or tendon reflexes, was reduced at high altitudes but returned to normal if oxygen was breathed in. Prof. R. Schumacher and Dr. R. Schindler (Hamburg) reported on the 'high-altitude disease' observed at about 16,000 ft. in the Andes, where cattle developed heart failure and œdema but recovered quickly after a descent of only about 1,500 ft., a condition reproduced experimentally in rats and observed sometimes in man. It is difficult to escape the conclusion from this that the pressures to be chosen for long journeys into space will not be the lowest to which people at rest can become acclimatized but the lowest which will avoid heart failure and œdema.

In a symposium on life in the tropics, Prof. Alrick B. Hertzman (University of St. Louis) suggested, among other things, that correlations between the cardiac output and the skin blood-flow were purely coincidental, as there were situations when one was high and the other low, for example, when the skin is cooled after the whole body has been warmed. However, it could equally be argued that the correlations between these are part of a system integrating many variables, which usually works in a given way but in which no single correlation is immutably fixed, thus conforming to what might be predicted in any complex control system and making the relationship between cardiac output and skin blood-flow somewhat more predictable than a mere coincidence. Dr. H. Boyko (Israel) showed some impressive photographs to illustrate how a patch of desert could be turned in a very short time into a lush garden by applying sound principles of bioclimatology. Dr. J. C. D. Hutchinson (now in Parramatta, Aus-

tralia, but well remembered from his Cambridge and Edinburgh days) surveyed the problem of domestic cattle in the tropics, especially from the point of selective breeding, and he showed, among other things, how clipping the fur could increase the rate of growth in farm animals, simply by improving heat tolerance. Prof. W. Richards (Bangor) discussed tropical plants, and he quoted recent evidence from Ibadan and Cambridge that the rapid growth of these plants was related to the favourable growth of their new leaf. He also quoted some odd rhythms in equatorial plants, for example, one in Singapore which has a rhythm of 2 years and 8 months, or the Malayan pigeon orchid which flowers quite irregularly though pigeon orchids in any given area always flower on the same day.

Prof. C. P. Luck (Kampala, Uganda) described his studies on elephant, giraffe, rhinoceros and buffalo, which he hunts with cross-bows and succinyl-cholin-impregnated arrows, so that he can collect sweat, blood and urine, measure body temperatures, or even inoculate animals against diseases, without harm to the animals and, one was glad to hear, with safety to himself. Prof. E. B. Edney (Salisbury, Southern Rhodesia) showed that crabs took increasing amounts of oxygen and survived greater temperatures after acclimatization to heat than before, and that tsetse flies were able to evaporate water from their spiracles, thus avoiding over-heating while engaged in the hard work of sucking blood in close proximity to a warm animal.

There were many small sessions dealing with more specialized problems. Dr. T. R. A. Davis and Dr. R. J. T. Joy (U.S. Army Research Laboratories, Fort Knox) reported that animals and man exposed to cold for 2 hr. daily showed a reduction of shivering after 21–24 days, which was accompanied by an increase of heat production in the muscles without any electromyographic evidence of shivering. Prof. J. Grayson (Ibadan, Nigeria) produced evidence of similar, apparently purely chemical, heat regulation in the liver, which could also play a part in improved cold tolerance after acclimatization to cold. Related to these findings were those of Prof. H. Hensel and his associates of Marburg, Germany, that cooling of the hypothalamus in animals produced an increase of metabolism in the rest of the body within a few seconds, but more so at lower than at higher environmental temperatures. Taken together, these data probably mean that there may exist a form of true chemical heat regulation not related to shivering, which is probably controlled by the temperature of the hypothalamus, and which can be modified either by thermal impulses from the skin or by a repetition or continuation of the cold stimulus.

Equally interesting was evidence, also from Prof. Hensel, that thermal receptors discharge at a constant level of activity during constant stimulation, so that in the absence of any environmental change the central nervous system receives a constant level of thermal information. In other words, thermal receptors would seem to become adapted extremely slowly or not at all. This fits in well with evidence from the London Hospital Medical College that the diminution of sensations and responses to repeated or continued stimuli which plays an important part in acclimatization is a result of a central nervous mechanism of habituation and not of any changes in the peripheral receptors.

Other discussions had a wide range, though some did not get beyond defining useful fields for further study. Among these was the problem of air pollution, which appears to be complicated by the fact that certain particles suspended in the air reinforce the action of others. Recognition of one or more potentially harmful substances in the air is therefore insufficient to assess air pollution, and predictions may have to be based on a better knowledge of synergistic actions of individual particles.

Difficulties of using scales of environmental comfort were stressed in a very active group on town planning under the chairmanship of Prof. J. K. Page (Sheffield). It appears that builders and engineers use at least four different comfort scales; but if one remembers the effects of habituation on thermal comfort it appears likely that many more comfort scales would be in use if more people had tried to compute such scales. Evidence was presented also that the provision of warmth is cheaper and easier in cold climates than the provision of cool air in hot places; but this may not always be so, as civilized communities have studied heating longer than cooling. Evaporating water, where it is available, from the roofs of buildings, as well as the use of solar energy to drive cooling compressors, might lead to simple and cheap ways of avoiding the overheating of buildings or vehicles in hot climates, and considerable improvements may be achieved by good design. Opinions were expressed suggesting that technology may soon remove the need for any physiological adjustments to changes of temperature, but by and large this Congress left the impression that we are still far from the days when uniformly clad people will live at a constant level of thermal acclimatization in one and the same environment anywhere on the Earth and outside it.

E. M. GLASER

COLONIAL DEVELOPMENT AND WELFARE

THE schemes made under the Colonial Development and Welfare Act in the period April 1, 1959, to March 31, 1960, which are detailed in the latest return, bring the total commitments, from April 1, 1946, under the Act to £221,023,632, of which £18,792,837 is for research schemes*. The totals for the year in question are £33,001,222 for development and welfare and £2,370,261 for research schemes. Of this last, £1,009,974 is for agriculture, £560,600 for pesticides, £375,080 for medicine, £167,180 for locust control, £63,860 for fisheries, £57,289 for products research, £45,160 for tsetse fly and trypanosomiasis research, £41,697 for social science, and £7,796 for economic research.

Of the actual research schemes, £313,032 is for the Colonial Pesticides Research Unit, Arusha, Tanganyika, as well as a supplementary £57,139, 1960–

* Colonial Development and Welfare Act. Return of Schemes made and of Loans approved under the Colonial Development and Welfare Act in the Period from 1st April, 1959, to 31st March, 1960. Pp. 50. (London: H.M. Stationery Office, 1960.) 2s. 6d. net.

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63; £181,000 for the agricultural research services, North Borneo, with a further £73,625 for the establishment of agricultural research stations; £124,755 for the Regional Research Centre at the Imperial College of Tropical Agriculture, Trinidad, and £47,459 for herbicides research at that College; £69,500 for the Anti-Locust Research Centre and its extra-mural activities, 1960–61; and £51,009 for the Colonial Pesticides Research Unit, Porton, 1960–63. £47,892 went to the East African Agriculture and Forestry Research Organization, £33,504 to the East African Trypanosomiasis Research Organization, and £33,283 to the East African Veterinary Research Organization; £38,250 was for trials with anti-typhoid vaccines; £55,506 to the Wellcome Institute for research on foot-and-mouth disease; £57,295 to the West African Rice Research Station, Rokupr, 1960–61; £77,911 for improvement and extension of agricultural facilities, Sarawak; and £33,350 for the study of dental leishmaniasis, British Honduras.

Other major research schemes include a supplementary £17,174 to the Fish Culture Research Institute, Malacca; £18,503 for research on spraying techniques and trace element deficiencies at Long Ashton; £42,968 for trachoma research in London and in The Gambia; £25,920 for the Desert Locust Survey; £16,607 for research into farm production costs, Kenya; and £39,650 for cereals research, Kenya, as well as £21,235 for research on coffee berry disease there, 1960–62; a supplementary £20,153 for cotton pest research, Nyasaland; £22,930 for the Joint Fisheries Development and Research Unit, Sierra Leone, 1960–62; a supplementary £19,489 for the Colonial Microbiological Research Institute, Trinidad; and £15,126 for the East African Virus Research Institute; £27,882 was for the Colonial Pesticides Information Service, 1960–64; £16,500 for Overseas Research Fellowships, 1960–64; and £15,000 for Colonial Medical Research Studentships, 1960–64.

Development and welfare schemes of scientific interest include £17,232 to the Overseas Geological Surveys for age determination of rocks at the Geological Museum, University of Oxford; £25,930 for the Desert Locust Survey; grants totalling £376,633 to the Agricultural Department, Kenya, for the intensification of African agriculture, 1958–59; a supplementary £74,974 to Somaliland for scholarships and training abroad; £182,000 for the establishment of a Nature conservation area in the Ngorongoro Crater Highlands, Tanganyika; £68,500 for intensified control in Tanganyika of the Sudan dioch (grain-eating birds); and a supplementary £157,685 for forestry development, British Honduras. Educational grants include, besides £250,000 for a student hostel block, University College, Ibadan, Nigeria, a number of grants totalling more than £169,000 to the Nigerian College of Arts, Science and Technology; £210,000 and £233,250 for the second and third phase, respectively, of the expansion of general education in Lagos; £308,120 for building of schools in Northern Nigeria (with £341,500 for the development of health services); £368,000 to Fourah Bay College, Sierra Leone, for constructing and equipping two halls of residence, as well as £360,000 for the construction and equipment of Freetown Teacher Training College, Sierra Leone, and miscellaneous grants totalling more than £780,000 to the University College of the West Indies.

CONTROL OF INFECTIONS

DUE mainly to vaccination, fewer persons now suffer or die from such diseases as diphtheria, poliomyelitis and tuberculosis. If immunization programmes using the best available vaccines were more generally applied, the risk of infection from certain diseases could still further be reduced. Some of the problems raised by vaccination procedures are discussed in a recently published report of a European Technical Conference on the Control of Infectious Diseases through Vaccination Programmes*.

The report gives a broad picture of the legislation in force regarding vaccination in Europe. Compulsory vaccination varies considerably from one country to another; many use a mixed system in which some vaccinations are compulsory while others are not, and the general tendency is to substitute effective health education for compulsion by law. An important aspect is that of inspection and the recording of vaccinations, which makes it possible to obtain reliable data regarding their effectiveness. Generally the cost of vaccination programmes is borne by the health authorities; in some cases the cost has to be met by the patient himself, which may adversely affect the success of the campaign.

The report gives a brief account of the value and present state of the most important vaccinations. Although smallpox does not exist as an endemic disease in European countries, it was generally felt that it was still necessary to maintain a relatively high level of immunity in the population through continued vaccination programmes. It was agreed that BCG vaccination should be considered as part of the over-all tuberculosis control programme of any country. The report discusses the types of anti-polio vaccines used at present; inactivated virus vaccine and attenuated live virus vaccine, which have been successfully applied in the Soviet Union to more than twelve million persons. The use of triple vaccine against diphtheria, tetanus and pertussis is recommended, and consideration is given to the suitability and effectiveness of many other vaccines, such as those against influenza, typhoid, paratyphoid, tularæmia, brucellosis, rabies, etc., as well as those used against quarantinable diseases (yellow fever, typhus and cholera).

After dealing with the risks and techniques of different vaccinations, the report discusses the importance they may have in the control of infectious diseases. It finally suggests models for programmes which, in the opinion of the conference, might be adopted in the various countries according to the degree of development of their health services and their own particular problems.

* World Health Organization. Publication No. 198: European Technical Conference on the Control of Infectious Diseases through Vaccination Programmes, Rabat, Morocco, 23–31 October, 1959. Pp. 21. (Geneva: World Health Organization; London: H.M. Stationery Office, 1960.) 1 Swiss franc; 1*s.* 9*d.*; 0·30 dollars.

OPTICAL IMAGE ASSESSMENT

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In recent years considerable attention has been devoted to developing methods for assessing optical image quality. A realistic criterion for the performance of optical systems has long been sought, and the advent of communication theory in optics has brought forth the concept of frequency response[1-4]. The relative merits of conventional testing methods such as the star test, the square wave or bar test chart, edge response, energy density in the point image and the like have been adequately discussed. However, it is not widely recognized that for incoherent illumination all these criteria are simply interrelated and derivable from the basic point spread function of the optical system.

The need to assess the image quality of a lens system arises, first at the lens design stage, when the designer is forced to make compromises in order to balance the residual aberrations in the optical system, and secondly, when the lens is at the construction and assembly stage. The lens designer would like to estimate the information transfer characteristic of the system under its true operational conditions. Here the effects of aberrations, diffraction, contrast of the object domain, air turbulence and scattering, emulsion and development conditions and even mechanical vibrations need to be accounted for. On the other hand, the manufacturer and user of lens systems is interested in measuring the lens performance according to some meaningful criteria after it has been constructed. This article describes two methods for assessing lenses both at their design stage and after construction. A method has been devised which enables images of pictorial objects to be synthesized from data on the lens design and thus enables the lens designer to evaluate realistically the influence on the image of various image-degrading parameters. This system is expected to evolve into an accessory to an electronic computer. Also, an electro-optical bench has been constructed which is capable of presenting simultaneously the frequency response and phase curves of a lens system on a cathode ray oscilloscope, thus allowing measurement of lens performance at various field angles and focal positions in a relatively short time.

High-Speed Image Synthesizer

A method for convoluting the images of a pictorial test object from the lens design data has been described before[5]. The convolution integral can be written in two dimensions as:

$$h(x,y) = \iint_{-\infty}^{+\infty} a(x-\eta, y-\xi) f(\eta,\xi) \mathrm{d}\eta \mathrm{d}\xi \qquad (1)$$

where the function a is the point spread function of the optical system, $f(\eta,\xi)$ is the object intensity function, and $h(x,y)$ is the image intensity function. One must assume incoherent illumination for the object to allow superposition of the point intensity functions. The spot diagram is a close representation of $a(x,y)$ for optical systems not limited by diffraction and the analysis is valid over regions of the image plane where the aberration function remains constant.

In order to synthesize the optical images of various types of test objects, the intensity distribution function in the point image in the form of a spot diagram (bright spots on a dark background) has been used to illuminate the test object plane (Fig. 1). The convoluted image of the two-dimensional test object is received on an image plane in the form of a shadow of the test object. It is obviously desirable that the test object should not give rise to scattering, therefore test objects on thin emulsions have been used. The distances d and d', and the relative sizes of the object, image and the point spread function simulate the appropriate conjugate relationship and the magnitude of the aberrations under true operating conditions.

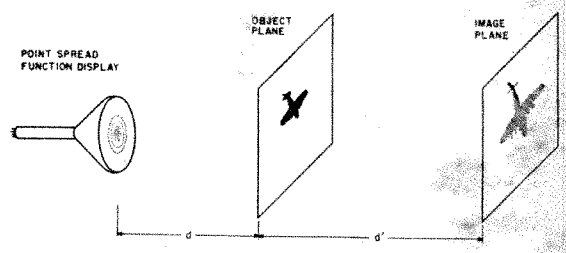

Fig. 1. Optical arrangement of the image synthesizer

The magnification of the test object at the image plane is given by:

$$M_{(\text{object})} = \frac{d + d'}{d} \qquad (2)$$

and the magnification of the point spread function is given by $M_{Sd} = d'/d$. If a periodic line test object is used, the resolution is given by:

$$R = (\text{test object scale})\ (\text{spot diagram scale}) \frac{M_{Sd}}{1 + M_{Sd}} \qquad (3)$$

This system has been used for measuring image quality in the presence of various types of aberrations using periodic as well as pictorial test objects. Fig. 2*a* shows the theoretical and synthesized intensity gradient in the image of an edge for an $f/2{\cdot}8$, 50 mm. photographic objective at 23° 50′ obliquity. Fig. 2*c* shows the square-wave response for the same lens in the sagittal and tangential directions as measured on the image synthesizer using the calculated spot diagram of the lens system. The pictorial images convoluted by this method have proved to be almost

indistinguishable from actual images produced by the lens built according to the same design. It is also possible to take account of such factors as diffraction, air turbulence and mechanical vibrations by using the point spread function in the presence of these image-degrading parameters. Fig. 2*b* shows the theoretical and experimental edge intensity gradient for a perfect lens as produced on the image synthesizer by approximating the intensity distribution in various rings of the Airy disk with areas of varying spot density.

Having established the performance of the image synthesizing technique and its ability to simulate not only the geometrical aberrations but also other complex phenomena, its application as an accessory to the electronic computer in assisting the lens designer becomes obvious. An approach that seems to offer much promise is the generation of the spot diagram upon the fluorescent screen of a cathode ray tube, the tube screen replacing the photographic plate in the image synthesizer. Thus, the co-ordinates of the spots representing the energy density in the point image can be calculated on an electronic computer, stored digitally either on magnetic tape or paper tape (Fig. 3*a*), and then displayed as successive bright spots on a cathode ray oscilloscope. Basically, the spot pattern is generated automatically by passing the tape through a digital-to-voltage converter using the output voltage from the latter to deflect the electron beam in two orthogonal co-ordinates. In general, it is found that of the order of 300–400 spots render a faithful synthesis of the image. Fig. 3*b* shows the photograph of spot representation of computed data on a cathode ray oscilloscope. As indicated in Fig. 1, this cathode ray oscilloscope is

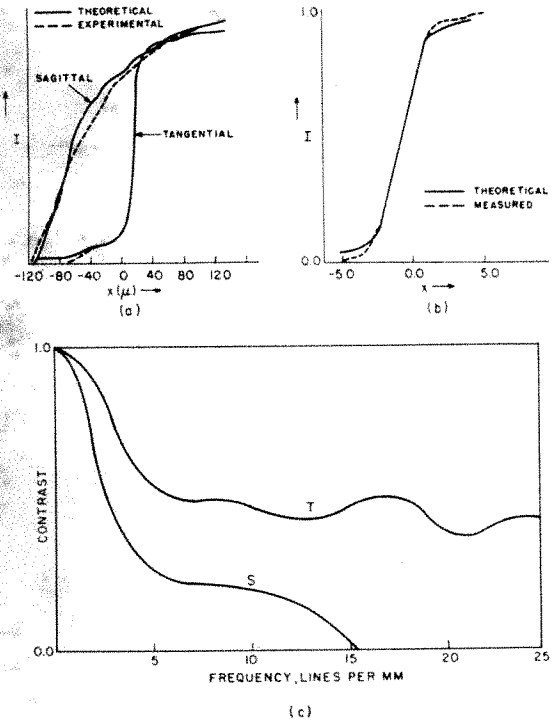

Fig. 2. Image synthesis data: (*a*) theoretical and synthesized edge response of an $F/2{\cdot}8$, 50 mm. lens at 23° 50′ field angle; (*b*) theoretical and synthesized edge response for a perfect lens, using Airy disk point spread function; (*c*) square wave response for the same lens position (as in Fig. 2*a*) measured on the image synthesizer

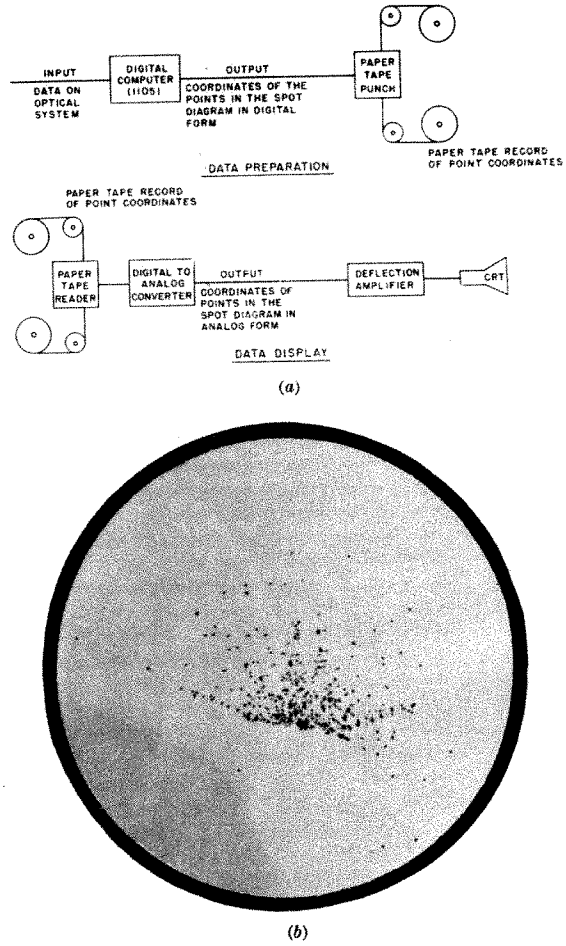

Fig. 3. High-speed image synthesis: (*a*) block diagram of the arrangement for computation of the point spread function and the cathode ray tube display unit; (*b*) a spot diagram displayed on a cathode ray tube

then followed by a simple device consisting of a test object holder and a viewing screen or a photographic plate with variable intermediate distances d and d'. This system is thus used for high-speed image synthesis of optical systems while the optical system is still at the design stage.

Measurement of Frequency Response and Phase Shift

In order to measure the spatial frequency response and the phase shift introduced by optical systems after construction, an electro-optical lens bench has been designed. It is well known[6] that the unidirectional spatial frequency response of an optical system is given by the Fourier transform of its line spread function, that is:

$$F(\omega) = \iint_{-\infty}^{+\infty} a(x,y)e^{-2\pi i\omega x}\mathrm{d}x\mathrm{d}y \qquad (4)$$

where $F(\omega)$ is the response for the spatial frequency (ω) and $a(x,y)$ is the point spread function of the optical system. Here, it is assumed that the point spread function does not vary over the slit-length. Furthermore, for incoherent illumination the simple unidirectional integration of the point spread function yields the line spread function.

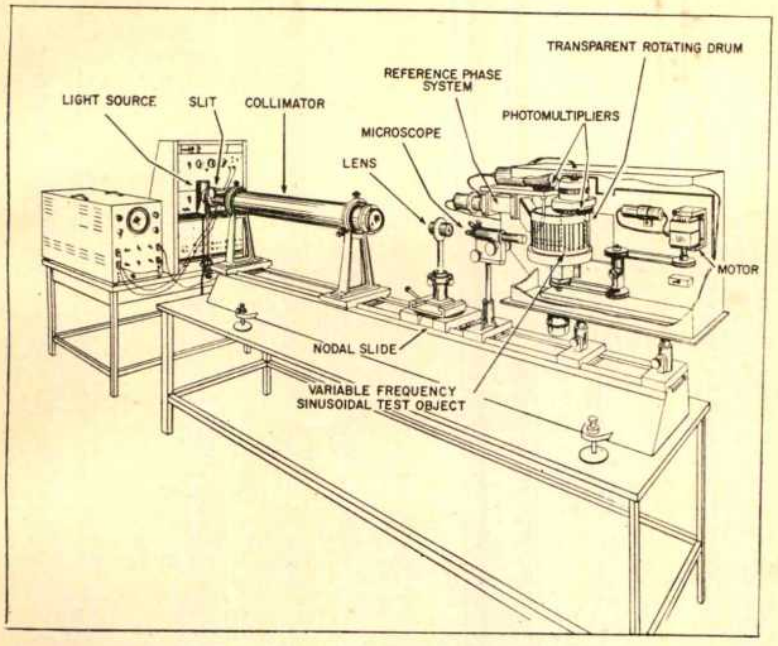

Fig. 4. Illustrating the lens bench for measurement of frequency response and phase of lens system

The principle of this lens bench consists of imaging the line spread function of the lens under test on a rotating glass drum with variable frequency sine wave test objects mounted around it. A photomultiplier receives all the flux, and the contrast in the received signal is a direct measure of the frequency response of the lens. Furthermore, a comparison of this signal with another reference signal yields the phase shift. Both the frequency response and phase shift are presented on a dual beam display scope.

The optical system of the lens bench is illustrated in Fig. 4. A fine slit is placed at the focal plane of a collimator lens, and the lens under test is placed on a nodal slide. The line image formed by the lens under test is imaged at a magnification on the rotating glass drum using a well-corrected microscope objective. The rotating glass drum has mounted around its periphery variable frequency sine wave test objects[7] consisting of 13 frequencies varying in steps of $\sqrt{2}$ and having 24 cycles of each frequency. A stationary photomultiplier placed in the rotating drum receives the signal when different frequencies are presented to the line spread function. The contrast of the received signal, given by the following expression, is a direct measure of the response for that frequency :

$$F(\omega) = \frac{I(\omega)_{\text{max.}} - I(\omega)_{\text{min.}}}{I(\omega)_{\text{max.}} + I(\omega)_{\text{min.}}} \qquad (5)$$

where $I(\omega)_{\text{max.}}$ and $I(\omega)_{\text{min.}}$ are the magnitudes of the signal for a given frequency ω at the maxima and minima, respectively.

In order to present the frequency response curve on an oscilloscope, the signal from the photomultiplier is amplified linearly, half-wave rectified and applied to an integrator. Using a logarithmic potentiometer geared to the shaft of the rotating glass drum the integrator output is made proportional to the input. This output is gated to a clamp circuit which displays the magnitude of $F(\omega)$ on a cathode ray oscilloscope. Fig. 5*a* shows the frequency response of an $F/6{\cdot}8$, 125 mm. lens system at a 5° field angle with defect of focus, presented on an oscilloscope. The phase shift and spurious resolution are observable at higher frequencies.

The optical system devised to measure the phase change is also shown in Fig. 4. A reference slit is imaged on another portion of the sine wave test object using a highly corrected lens system and the signal is received by another photomultiplier. It is, of course, necessary that the reference slit and the line spread function of the lens under test be in good alignment. The comparison of signals from the two photomultipliers, with the use of appropriate electronics, yields the phase information simultaneously with the frequency response. Fig. 5*b* shows the phase change introduced by the $F/6{\cdot}8$, 125 mm. lens system at a 5° field angle and with a defect of focus, presented on an oscilloscope.

(*a*)

(*b*)

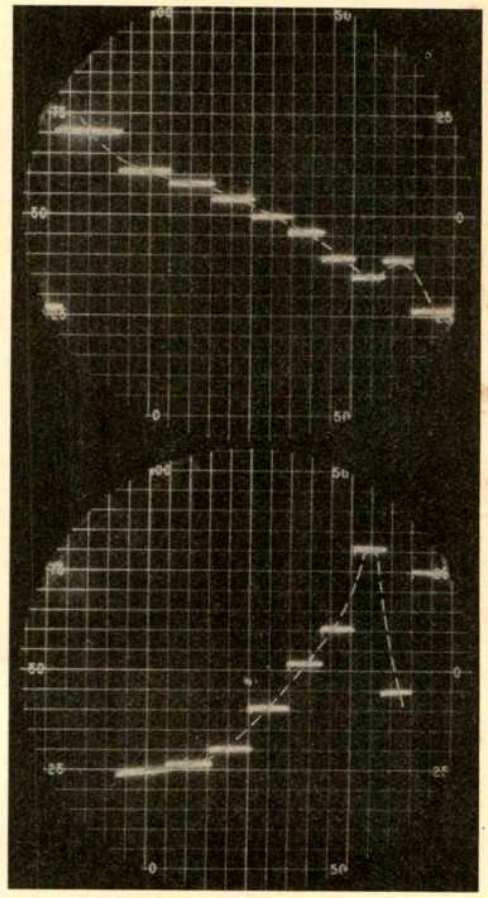

Fig. 5. Cathode ray tube display of frequency response (*a*) and phase (*b*) curves for an $F/6{\cdot}8$, 125 mm. lens system at 5° field angle with defect of focus

Conclusions

The two techniques described in this article seem to hold considerable promise for optical image assessment both at the lens design stage and after construction, and further work using these methods will be reported elsewhere. The high-speed image synthesizer is useful for evaluating realistically the influence of aberrations, diffraction, atmospheric turbulence and film characteristics, etc., on image quality without having to construct the lens system. Its uniqueness lies in the fact that it is capable of synthesizing images of pictorial test objects as well as conventional test objects. Therefore it can be used to evaluate the influence of psycho-physical effects on recognition and detection. A detailed programme incorporating the image synthesizer with a *Univac* 1105 computer is in progress. As a research tool the image synthesizer is capable of synthesizing images formed by other electro-optical systems such as cathode-ray tube and image intensifiers. Its application to the evaluation of X-ray image-forming systems and high-energy radiographic systems is at present being studied.

An interesting extension of the image synthesizer technique would achieve automatic lens design based on a most meaningful test method. Accordingly, use would be made of a correlation device that compares the synthesized picture with a standard and feeds back an error signal into the computer (Fig. 3*a*). Thus the lens design can be continuously tested on the basis of its 'picture quality', and appropriate changes in the design be made automatically until the correlation function reaches a desired value.

The electro-optical lens bench is particularly valuable for investigating the influence of aberrations and diffraction on spatial frequency response and phase shift of lens systems. Since both curves are presented on the oscilloscope simultaneously, the change introduced at various focal positions and field angles can be studied in much detail. It seems to offer promise as a routine lens bench for lens assembly and evaluation work.

Acknowledgment is due to A. J. Kliore, R. E. Keim and S. H. Cameron for their most valuable assistance.

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THE ACTION OF NITROUS ACID ON ALIPHATIC AMINES

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ALTHOUGH T. W. J. Taylor in 1928[1] indicated the correct experimental conditions for carrying out the reaction of aliphatic amines with nitrous acid, the essential items in these conditions appear to have been overlooked by other workers who have used other conditions and, not surprisingly, have obtained little or no reaction. As part of a study of the mechanism of deamination by nitrous acid of aliphatic primary amines[2], an investigation of the products formed in the reaction of methylamine with nitrous acid was undertaken; this has not been reported before, because it in turn led to a study of diazotization, which, as the more convenient reaction for detailed kinetic treatment, became for a time the leading sector of attack on the problem of deamination mechanism in general[3].

Taylor described the kinetics of the reaction between methylamine and nitrous acid[1], but so many incorrect statements, most of them in text-books, have been made about the products, that a new account of the matter seems desirable, though it was actually investigated some years ago[4] and in a broader context. There was little doubt that methyl alcohol could be obtained from the reaction of methylamine with nitrous acid, as this had been shown by Linnemann[5], who passed the gas evolved in the decomposition of faintly acidified solutions of methylamine nitrite through water and, on fractionation of this, had obtained the alcohol in good yield (50 per cent). The reaction was next investigated by Whitmore and Thorpe[6], who were apparently unaware of Taylor's fundamental investigation, and, using quite unsatisfactory conditions, these workers were unable to obtain any methyl alcohol. In view of the wide acceptance given to these negative findings, the following observations on the products that are obtainable in the methylamine – nitrous acid reaction are recorded.

The conditions used were those indicated by Taylor's work as being essential for reaction to take place, namely, a solution of the amine containing nitrous acid but—and this is important—no excess of mineral acid. As solutions of nitrous acid are unstable and evolve oxides of nitrogen at concentrations greater than 0·05 *M*, this acid was generated slowly *in situ* during the reaction by gradually adding mineral acid to the amine solution containing dissolved sodium nitrite. In a typical experiment, the methylamine hydrochloride (0·5 mole) was dissolved in water (550 c.c.) together with sodium nitrite (1·5 moles). Sulphuric acid (2 *N*, 0·4–0·6 equiv.) was then run in slowly beneath the surface of the solution. A brisk and steady evolution of gas ensued and the reaction proceeded readily at room temperature until less than 1 per cent of the amine remained. The evolved gas was passed through a container immersed in solid carbon dioxide/acetone mixture and then through a bubbler containing potassium permanganate (to remove oxides of nitrogen from decomposition of the nitrous acid) before being collected in a gas receiver. The products of the reaction in (*a*) the reaction vessel (*b*) the low-temperature trap and (*c*) the gas-holder were then investigated.

Distillation of the pale yellowish-green reaction solution in (*a*) caused the colour to darken to yellowish-brown, which then became opaque-green and much gas was evolved, part of which was carbon dioxide. The colour of the solution then became less intense

and finally pale yellow. A pronounced odour of bitter almonds was observed during the distillation, and this later changed to an ammoniacal odour. These colour changes and odours were shown to be caused by methylnitrolic acid that had been formed in the reaction. Fractionation of the distillate gave, at 64–85°, a two-phase liquid, the upper layer of which was shown to be aqueous methyl alcohol and the lower layer was shown to be mainly nitromethane.

The pale yellow liquid collected in the low-temperature trap (*b*) was shown to consist of a mixture of methyl nitrite (pale yellow, b.p. −18·5°) and methyl chloride (colourless, b.p. −24°). If methylamine hydrobromide was used in the reaction, then methyl bromide (colourless, b.p. 4·6°) was collected in the trap instead of the chloride.

The volume of gas obtained from the reaction at room temperature was slightly greater (3 per cent) than that expected from the reaction:

$$CH_3NH_2 + HNO_2 \rightarrow CH_3OH + N_2 + H_2O \quad \text{(I)}$$

The gas was shown to be nitrogen contaminated by a small amount of carbon dioxide.

Table 1. PRODUCTS FORMED WHEN METHYLAMINE HYDROCHLORIDE (0·5 MOLE) + SODIUM NITRITE (1·5 MOLES) IN WATER (550 C.C.) WAS SLOWLY ACIDIFIED WITH 2 *N* SULPHURIC ACID (0·4–0·6 EQUIV.). ROOM TEMPERATURE

	Per cent
Methyl alcohol	6–25
Methyl nitrite	45–35
Methyl chloride	13
Nitromethane	6
Methylnitrolic acid	10–12
Evolved gas (nitrogen + carbon dioxide)	103 'theoretical'

These findings may be summarized:

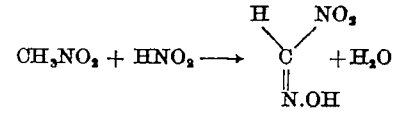
(1) Methylamine readily reacts with solutions containing nitrous acid. *Methyl alcohol* is formed.

(2) *Methyl nitrite* is, however, the major product. This escapes from the reaction vessel owing to its volatility (b.p. −18·5°), and this escape is facilitated by the nitrogen evolved during the reaction. (Identical behaviour is observed in the reaction of ethylamine with nitrous acid and the major product, ethyl nitrite (b.p. 17·4°), condenses in the low-temperature trap.) The methyl nitrite is probably formed by two processes: (*a*) the direct and rapid esterification of the methyl alcohol by the aqueous nitrous acid; and (*b*) interaction of the methyl carbonium ion at the oxygen end of the ambivalent nitrite ion. The ratio *a*/*b* is not known, but a considerable proportion of the methyl nitrite must be formed via the esterification route since, for a given concentration of sodium nitrite, the amount of methyl nitrite collected in the low-temperature trap was greater the greater the volume of acid added during the reaction. There was a corresponding diminution in the amount of methyl alcohol that could then be isolated from the reaction vessel. This correlation is indicated in Table 1 by the ranges given for the first two items, which should be read together, that is, a low yield of methyl alcohol corresponds to a high yield of methyl nitrite and vice versa.

(3) *Methyl chloride* (*or bromide*) is formed in the presence of chloride (or bromide). It was shown that under the conditions of the reaction, the methyl halide was not formed by esterification of the methyl alcohol by the acid halide. These compounds must therefore be formed as direct reaction products and not arise from secondary reactions.

(4) *Nitromethane* is formed in appreciable amount, and its formation is consistent with the formation of the methyl halides. It was shown by experiment that the nitromethane was not formed by re-arrangement of any of the methyl nitrite, nor was it formed in the direct esterification of the methyl alcohol by the nitrous acid.

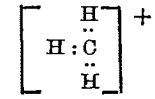
(5) *Methylnitrolic acid* is formed. Experiments confirmed that part of the nitromethane, formed directly in the reaction, had reacted with nitrous acid to give the nitrolic acid in a secondary reaction:



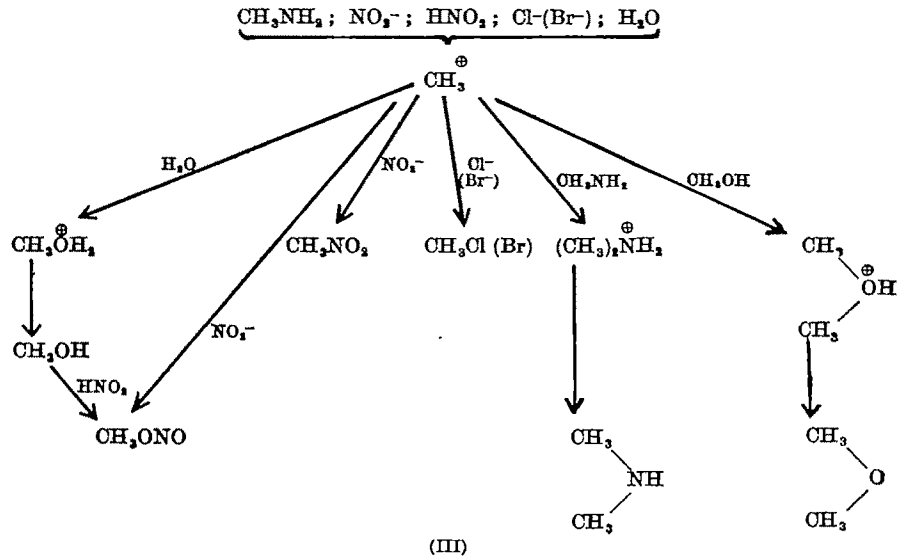
(II)

This acid is unstable and decomposes via well-established reactions and accounts for the colour changes and odours (hydrogen cyanide, ammonia) observed when the reaction residues were heated. It was also shown that the amount of decomposition undergone at room temperature accounts for the slight excess (3 per cent nitrogen and carbon dioxide) of gas collected during the amine–nitrous acid reaction.

The multiplicity of products formed in the above reaction is rationally explained if one assumes that the electron-deficient entity,



is formed—a suggestion originally put forward by Whitmore[7] for this type of reaction. The methylcarbonium ion could interact with a water molecule

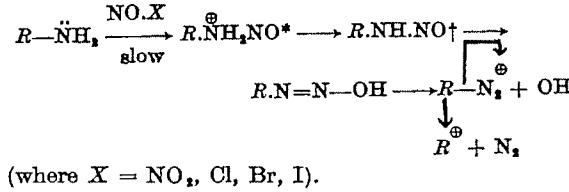


(III)

giving $CH_3\overset{\oplus}{O}H_2$, which, by loss of a proton to the solvent, would give methyl alcohol. It could unite directly with Cl^- or Br^- giving methyl chloride or bromide respectively. With the ambivalent nitrite ion, a considerable amount of interaction occurs at the *N* atom to give nitromethane. Some attack probably occurs at the O atom to give methyl nitrite directly. Although no secondary amine derivative was isolated from the reaction mixture, such compounds could arise by the $CH_3^{\oplus}$ interacting with some of the unchanged amine, and the formation of secondary amine products has definitely been established by others in this type of reaction[5]. There is also the possibility of formation of ether. This could result from the reaction of the $CH_3^{\oplus}$ with the alcohol formed in the reaction. This is not likely to occur to any appreciable extent in the reaction of methylamine, for the alcohol is swept out of the system as the very volatile nitrite ester. Of course, if an alcohol is used as the solvent for the reaction, it would be expected that the ether would then be the principal product. These reactions may be depicted as in scheme III.

With higher amines yet other reactions are possible for the carbonium ion. Proton loss can result in the formation of olefins and hydrogen, or alkyl groups, from other parts of the ion may migrate to the electron-deficient centre and in so doing create a fresh centre of electron-deficiency at the site vacated. The reactions noted above may then occur at the new centre of electron-deficiency.

The steps leading to the carbonium ion have also been established. Taylor's kinetic findings were confirmed, and the investigations led logically into the aromatic field[2]. Although Piria[9] discovered the 'amine–nitrous acid reaction' by noting the effect of dissolved oxides of nitrogen and assumed that nitrous acid was the effective reagent (thereby setting the pattern of thought for a hundred years) it has now been shown that molecular nitrous acid, as such, is not a participant in the initial interaction with the amine. The squared-term for the nitrous acid in Taylor's kinetic expression has been shown to stand for N_2O_3 ($\alpha[HNO_2]^2$), and this as the effective nitrosating entity, originally suggested by Hammett[10], has been placed on adequate experimental foundation together with NOCl, NOBr and NOI. The initial, and rate-determining, step involves an electrophilic attack by N_2O_3, NOCl, etc., on the free amine giving a N-nitrosoalkylammonium cation. The inhibiting effect of free mineral acid on the aliphatic amine–nitrous acid reaction is thus readily seen. These amines are so much more basic than their aromatic counterparts that any appreciable protonic concentration will cause the amount of free amine to diminish to vanishing point. Once the N-nitrosation has occurred, the base-weakening effect of the nitroso-group permits ready deprotonation of the nitroso-alkylammonium cation and the primary nitrosoamine then formed undergoes ready tautomeric shift to the diazo-hydroxide. This rapidly ionizes to the diazonium cation which, in the absence of resonance stabilization of aromatic groups, rapidly loses nitrogen giving the electron-deficient carbonium ion. The carbonium ion then undergoes the reactions already noted.



(where $X = NO_2$, Cl, Br, I).

(IV)

* If the original amine was tertiary the nitroso-alkyl ammonium cation could lose an alkyl group giving rise to a N-nitroso-secondary amine.

† If the original amine was a secondary amine the reaction would stop at this stage and the secondary nitrosamine can be isolated.

I thank Sir Christopher Ingold and Prof. E. D. Hughes for their help and encouragement in this work, and the Trustees of the Ramsay Memorial Fellowship Trust for the award of a fellowship at University College, London.

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CORRELATION OF BIOLOGICAL ACTIVITY AND THE ELECTRON SPIN RESONANCE SIGNAL STRENGTH FROM GUINEA PIG ADRENALS

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In a previous communication[1] an improved low-temperature technique for the study of free radicals in biological materials was described. This method has now been used to study the relation between electron spin resonance intensities and the level of functional activity in mammalian tissue.

Adrenal glands from large adult male guinea pigs were used. Highly active adrenocortical tissue was produced by daily injections of 5 clinical units of gel-adrenocorticotrophic hormone, followed by a single 5-unit injection of aqueous adrenocorticotrophic hormone 2 hr. before excision of the adrenals. High rates of steroidogenesis and adrenal glutathione turnover[2] are known to occur under these conditions. Hypofunctional glands were produced by suppression of endogenous secretion of adrenocorticotrophic hormone. For this purpose animals were given

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4 mgm. hydrocortisone phosphate by injection daily for five days, followed by a sixth injection of the same amount 2 hr. before being killed. These animals, as well as equal numbers of untreated controls, were killed by decapitation and the adrenals excised as rapidly as possible. Adrenals from 2–3 animals (together with a small amount of isotonic saline to displace trapped air bubbles) were placed in borosilicate glass sample holders of 10 mm. diameter and immersed at once in liquid nitrogen. The weight of tissue plus saline in these samples averaged 1·7 gm. Electron spin resonance measurements were carried out at −180° C. in a conventional x-band transmission type spectrometer[3]. The instrument was calibrated before and after each determination, using a secondary standard of coal dispersed in anhydrous dextrose. The resonance absorption had a g value close to that for free electrons ($g = 2{\cdot}0023$). The signal intensity from each sample was adjusted to account for minor changes in cavity Q which occurred from sample to sample. Electron spin resonance runs were also made on sample tubes containing only the frozen saline solution. These measurements showed that essentially none of the resonance absorption obtained from tissue samples could be attributed to the sample tubes or saline solution. As the line-width and shapes for the resonance absorption signals were essentially identical for all samples, the relative electron spin resonance signal strength and thus the relative unpaired electron content could be determined by measuring the peak-to-peak height of the normal electron spin resonance derivative curves. Though no attempt was made to determine the absolute number of paramagnetic species present per gram of sample, the electron spin resonance signal strength obtained for a given amount of tissue was roughly one-fifth of that obtained from freeze-dried rat liver, which contained the order of 10^{-8} mole of free electron spin per gram wet tissue[1].

Following electron spin resonance measurement, the non-protein sulphydryl concentration of a number of the samples was determined by a method described elsewhere[3].

Table 1 summarizes the results obtained in five sets of experiments. The intensity of the electron spin resonance signal in the control adrenals varied from 15·1 to 60 1 with a mean value of 31·8. The values of the adrenocorticotrophic hormone-stimulated adrenals ranged from 15·5 to 30·4 with a mean value of 24·2. Statistical analysis shows that this difference has a

Table 1

Exp. No.	Control		ACTH-stimulated		Cortisone-suppressed	
	ESR signal intensity	SH conc. γ/100 mgm.	ESR signal intensity	SH conc. γ/100 mgm.	ESR signal intensity	SH conc. γ/100 mgm.
1	35 7 60·1		23 7 15 5			
2	19 4 15·1 26 9				39 4 34 3	
3	37 5 31·0 31 0		28 1 30 4 27 2			
4	31 6	11 5	20 1	15 7	32 7	11·8
5	28 5 33 0	28·6 16 6	24 3	30 8	35 1 20 9	11 6 15 8
Mean	31 8		24 2		32 5	

ESR, electron spin resonance; ACTH, adrenocorticotrophic hormone

t-value of 2·72 with 12 degrees of freedom, which is significant ($P = 0{\cdot}018$). One may also inspect these results on a non-quantitative basis, that is, that 7 out of 7 deviations (control minus adrenocorticotrophic hormone) are positive. On the basis of the null hypothesis, the probability of such a result occurring by chance is 0·016. The comparison of the electron spin resonance signal strength of the cortisone suppressed adrenals with the control adrenals is less revealing. The values for the cortisone-treated adrenals ranged from 20·9 to 39·4 with a mean value of 32·5. The probability of 4 out of 5 deviations being positive is 0·06. Thus it is reasonable to conclude that the control and adrenocorticotrophic hormone adrenals differ significantly, while no conclusion can be drawn about the suppressed adrenals.

It was of interest to compare these changes to the alterations in adrenal sulphydryl concentration and turnover at the various levels of adrenocortical activity. It has been shown in rats[2] that acute stimulation of the adrenal cortex causes a marked, transient increase in sulphydryl concentration and turnover. Inactivation of the adrenals (by hypophysectomy) causes no change in the sulphydryl concentration but some diminution of the turnover rate. Since some stable organic free radicals, as in the case of α,α diphenyl β-picrylhydrazyl[5], may be expected to react with available sulphydryl groups, one may well wonder whether or not the decrease in free radicals (and thus the electron spin resonance signal level) in stimulated adrenal tissue is not correlated with the known rise in glutathione. For this reason, adrenal non-protein sulphydryl determinations were carried out in experiments 4 and 5. Unfortunately, the individual variations in SH concentration were large, greatly exceeding those observed in homogeneous rat populations. This variation (and possibly that in electron spin resonance signal intensity as well) may be related to the fact that the largest and therefore oldest animals available were used, to provide the maximum amount of adrenal tissue. This variance precluded the possibility of demonstrating SH changes such as are known to occur in rat adrenals.

There are many possible interpretations of these data other than a potential relationship of the electron spin resonance changes to sulphydryl alterations. Other reducing agents such as ascorbic acid could act in the same manner as SH groups. However, under the conditions of the experiment the tissue concentration of ascorbic acid is sharply reduced rather than increased as is glutathione. It may be noted that our electron spin resonance findings are at variance with those of Commoner *et al.*[4]. However, these authors based their conclusions on a comparison of different tissues rather than on a study of the same tissue at different levels of activity, which we believe would be a far more valid criterion. Moreover, the high levels of electron spin resonance signal intensity found by Commoner in lyophilized tissues may well have been due to sorbed molecular oxygen[6]. The possibility that our tissue electron spin resonance signals were in part due to paramagnetic ions is recognized, and much work needs to be done to determine to what extent such ions contribute to the observed electron spin resonance signal. However, the work of Heggen and Strock[7] shows that for rat liver tissue the content of paramagnetic ions having a g value close to 2 00 can account only in part for the electron spin resonance signal intensities observed[1].

Whether or not the paramagnetic ion content of guinea pig adrenal tissue is high enough to contribute to the electron spin resonance signals observed is at present under investigation

It is also important to consider whether the electron spin resonance values obtained can be related to concentrations of free radical in a simple manner or whether the lifetime of the free radicals must be taken into account. The temperatures at which measurements were carried out (− 180° C.) tended to reduce this problem; moreover, our previous work on aged rat liver[1] indicates that at the temperature of observation the free radicals present are relatively stable.

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THEORIES OF SHAPE DISCRIMINATION IN *OCTOPUS*

SUTHERLAND, in a recent article[1], offers an evaluation of my theory of the relation of the plexiform zone in the octopus to its shape discriminatory capacity[2]. A critique is made both on general grounds of plausibility and in relation to specific points of experimental evidence. Dr. Sutherland seems to misunderstand my theory, for his article contains important errors. There are six main objections which will be dealt with in turn.

(1) It can be seen from Cajal's neurohistological work that the retinal fibres of the octopus terminate in the plexiform zone, which they penetrate at right angles. This plexiform zone is seen to consist of a large number of fibres lying in many layers parallel to each other. Each fibre runs only a certain distance among this plexiform zone and sends a process out of this zone deeper into the optic lobes. Beyond these neurohistological observations made by Cajal, I further proposed that we make two main suppositions. The first was that each fibre in the plexiform zone sent a message out only when two or more simultaneously active retinal fibres cross it. The second was that the fibres in the plexiform zone ran in a vertical direction in relation to the visual field of the octopus. Given only these simple suppositions, it was shown that the observed neurohistological arrangement would convert vertical distances between points into amounts of activity leaving the plexiform zone. The smaller the distance between two points, the larger the amount of activity. It was made explicit that no precise mathematical relation between distance and output was postulated. "It should also be stated that the present system has been left quantitatively flexible. It has been assumed, for example, that the vertical distance between two points leads to an output which is the reciprocal of this distance. There is no reason for supposing that the conversion is precisely this. The theory only has to assume that the conversion is something like this and then not over the whole range". The conversion will depend, among other things, on the distribution of fibre-lengths in the plexiform zone. Further, it was assumed that the output from all such vertical arrangements was summed to produce a message for each visual pattern presented to the octopus.

Sutherland, in his review, fails to mention the neural mechanism postulated. He says: "He suggests that octopuses count distances between contours in the vertical direction at all points along the horizontal axis. The count is made in such a way that the reciprocal of the distance between contours is taken". Having thus omitted my qualifications, he then points out that as a result the number infinity will be obtained from shapes containing intersections of lines away from the vertical or horizontal axis. Apart from such considerations that, within the neural system described, counts of infinity are impossible, that infinity can be arbitrarily assigned some low value in terms of frequency of impulses, it was clearly stipulated in one of the two accessory assumptions made by me, that "excitations on the same vertical arrangement inhibit each other over a small distance".

(2) On the mechanism put forward, all shapes are transformed into a point on a dimension of amount of neural activity. Sutherland writes: "On general grounds this theory is rather implausible, since it is possible to find a horizontal or vertical rectangle which is on the same point on this dimension as any other shape however complex: it would be difficult to test this prediction, but it seems most unlikely to be correct". First of all, the deduction which Sutherland draws is incorrect. This is simply demonstrated by imagining the longest and narrowest horizontal rectangle the octopus can see. A pattern not equivalent to this can obviously be constructed by placing another such horizontal rectangle some distance above it. Such a procedure can be repeated until we have a whole field of horizontal stripes, which evidently cannot be equivalent to any horizontal rectangle. Conversely, there will be complex shapes which are not equivalent to any horizontal rectangle but to some field of stripes. What is of more interest is that he himself suggests a principle of classification for the octopus at the end of his article and in other publications on which precisely analogous equivalences can be constructed. He suggests that an analysing mechanism in the octopus is present which computes the total contour of a shape relative to its area or to the square root of its area.

Further in support of his suggestion, he reports an experiment in which there was good transfer from a butterfly shape to an elongated rectangle. Though these considerations are not claimed in support of

my theory, it is difficult to see why Sutherland regards my theory as "rather implausible" on grounds which apply to his suggestions and which, as he himself recognizes elsewhere, his own experiments tend to refute.

(3) A further criticism of my theory concerns the result of transfer tests to the same shape of different sizes. On my theory, transfer to the same shapes of different size would be predicted to varying degrees depending on both the shapes used in the original training. If we assume some kind of reciprocal relation between distance and amount of excitation on the vertical axis, then doubling the distance of two points will decrease the excitation emerging from the plexiform zone. On the other hand, if we enlarge a shape, we not only increase the distance between the contours in the vertical axis, but also increase the number of pairs of points on the horizontal axis. So, when we increase the distance vertically, we also increase it horizontally, so that the total amount of excitation for certain classes of shapes, such as squares, when scaled up or down tends to remain the same. It follows, as I further wrote: "Transfer from one shape to another will depend on two factors: (*a*) the shape used; and (*b*) the other member of the pair from which the octopus has learnt to make the discrimination. . . . As regards the first point, it will be readily seen that, if we take a V shape lying on its side and a scale enlargement of it, the scale enlargement will produce a greater output. The small V shape is a part of the larger V shape. . . ".

"This brings me to the second point. If the total amount of output from the shape to be discriminated from the other member of the pair was larger, then the increase in output due to the enlargement of this shape will not destroy the discrimination, because the effective distance along the continuum is increased. . . . There may actually be an improvement if the other parameters which the octopus derives from the stimulus also increase the distance between discriminanda"[2]. Sutherland, however, states: "Thus the theory predicts good transfer to different sized rectangles, but poor transfer to different sized triangles. These predictions are not confirmed: there is diminished transfer to all figures including vertical and horizontal rectangles when the area is reduced by a quarter. There is usually better transfer to larger figures than to smaller, though even this transfer is sometimes less than complete. The results of transfer tests to different sized figures thus constitute a direct refutation of one of the most interesting predictions made by *B* (Deutsch's theory)".

I am sorry that Sutherland has missed the point that overall trends in efficiency of transfer to different sizes are of little theoretical interest given his experimental situation. It is the comparative efficiency for a given shape, when it is being discriminated from a certain other, that is of interest. Here there are indications of variation, though the results are unfortunately confounded through a process of averaging. For example, Sutherland[4] reports that with certain pairs of shapes the transfer to shapes of 4/9 the area is better than to the originals. He also ignores similar interesting discrepancies from his generalization to be found in another of his papers[5]. It should be clear that, for some reason, Sutherland ignores the stipulation concerning the other member of the pair of shapes being discriminated which was clearly made. In fact, so far from making the transfer to different-sized triangles worse, I actually quoted an example from Sutherland's results in support of my theory, in which there was an improvement in accuracy of discrimination between a triangle and a square when the triangle was made larger.

I was well aware of the data on worse transfer to smaller shapes and comparatively better transfer to larger shapes which Sutherland quotes and which, according to him, "cannot be directly explained on any current theory", and for which he postulates some effect of noise in the neural analysing mechanisms. These data I carefully avoided discussing to spare Sutherland the embarrassment of pointing out that this may be explained as a simple artefact of his training situation, in which the octopus swims up to the shapes presented, thus exposing itself to progressively larger projections of the shape before it is finally rewarded or punished; however, no analogous shrinking of the shape to a smaller size than that presented is allowed to occur. We cannot, therefore, regard it as surprising that transfer to larger shapes is better than that to smaller.

In view of this, I was careful to quote only evidence which compares the effectiveness of transfer for different shapes. Sutherland has not denied the validity of these data.

(4, 5, 6) Three of Sutherland's further criticisms are again due to a failure to take note of one of the two accessory assumptions made by me:

"Before proceeding, I should make clear that for the purposes of prediction two accessory assumptions must be made . . . (2) that the octopus can also discriminate relative vertical positions of the output converted in the above way. This second appears to be a residual factor left when we have explained the rest of Sutherland's results". Though this is certainly not an explanation, it clearly limits the scope of my theory. In spite of this, the theory is criticized as if no such limitation had been made (Sutherland's points under his headings 2, 4 and 10). This failure is especially outstanding in the case of 10. I state: "It is found that the octopus can discriminate some up–down mirror images. This would be covered by assumption 2". Sutherland, however, says: "*B* [my theory] cannot account for any discrimination between mirror image shapes of this sort . . .". Such criticisms are all the more remarkable as in the very same paragraph he imports special assumptions into his own theory to explain these findings, " . . . behaviour is more accurately controlled by differences in the horizontal projection (on which up–down mirror images differ) than by differences in the vertical projection". He then goes on to state that using this principle of more accurate analysis on the horizontal projection to predict, it would be the case that "horizontal rectangles of different lengths will be more readily discriminable than vertical rectangles of different lengths (this follows because horizontal extent is more accurately analysed than vertical extent). This prediction was strikingly confirmed". If it were, then it disproves the theory, or shows it to be nonsense. If "behaviour is more accurately controlled by differences in the horizontal projection (on which up–down mirror images differ)" then vertical rectangles ought to be more readily discriminated, as they will differ on the same projection as up–down mirror images. The same confusion between vertical and horizontal (which Sutherland has shown the octopus can discriminate) is shown

when Young's[6] neuroanatomical data on the dendritic fields of pick-up fibres from the input to the optic lobe are quoted by Sutherland in support of his own theory. "Moreover, there appear to be more fields orientated in the horizontal than in the vertical axis: this would be expected on the theory if the function of these cells was to compute horizontal and vertical extents". Young[6], however, states about these structures: "Measurements on Cajal preparations show the greatest number and total length of dendrite to be in the vertical direction". Such a statement is amply borne out by the numerical analysis given by Young in Table 1 of his paper.

Young's work is fully consistent with my own theory, and his new findings enable the mechanism suggested in the theory to be applied to explain data which previously were outside its scope (for example, Sutherland[4]). It is hoped to deal with this in another publication.

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IN a recent article on shape discrimination in the octopus[1], I reviewed the behavioural evidence and its bearing on three theories which have been proposed. One of these theories was that put forward by me[2], a second was a modified form of this theory suggested by Deutsch[3].

In the foregoing communication, Deutsch attempts to rebut four of the criticisms made of his own theory in the light of the evidence, and also criticizes my theory at two points. Both the experimental evidence and its bearing on theory are now rather complex, and Deutsch appears to have misunderstood some of my original article: because of the complexity of the evidence and the brevity with which it was summarized, it is possible that parts of this article were not clear to others besides Deutsch, and the present communication will attempt to expand those points at which Deutsch's article reveals that there is a possibility of misunderstanding. His points will be dealt with in turn using the same numbering as in his communication above, and an attempt made to clarify dispassionately the questions at issue.

(1) One crux in Deutsch's theory is to specify what happens when the contours of a figure approach one another in such a way that the vertical distance between contours approaches continuously to zero. Fig. 1 shows four shapes, in three of which this occurs at the corners marked with a vertical line. Deutsch's mechanism analyses shapes in terms of the closeness in the vertical direction of their contours: when the vertical distance between contours falls below a certain distance (D) no count is taken. The vertical lines in the corners of shapes in Fig. 1 represent an example of what this distance might be. I did not fail to recognize that such a distance (D) could be specified in my article[1]—indeed, in my summary of Deutsch's theory I wrote that "to prevent

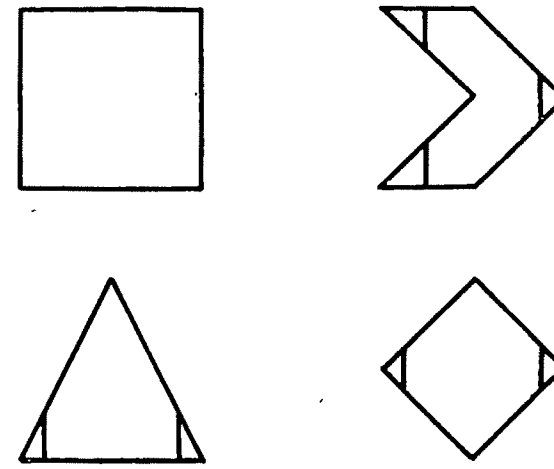

Fig. 1

obtaining infinity from such shapes, it would be necessary to specify some small vertical distance between contours within which no count is taken". The point at issue is that Deutsch has failed to specify what this distance is, and until it is specified it is impossible to make predictions on his theory about the discriminability of shapes with contours approaching one another in this way. This of course includes the vast majority of shapes in the octopus's normal environment, so that without specifying this distance the theory has little predictive value. However, once this distance is specified the theory would make different predictions from my own at some points. The question arises why Deutsch has failed to make his theory more precise by specifying a distance, and the answer would appear to be that whatever distance is selected predictions about some pairs of shapes are yielded which the experimental evidence already in existence shows to be false: the points at which false predictions will occur will of course vary with the actual distance specified. A second problem which Deutsch has not considered is that it is difficult to know whether to specify the distance (D) in terms of the physical size of the shape, or in terms of retinal angle. We find ourselves in a dilemma: the former alternative would require an elaborate neural mechanism to achieve constancy of visual size independent of how far from the eye a shape is placed operating before the count of vertical extents is taken. The latter alternative would mean that the count yielded by a shape would vary with its distance from the eye. Thus the question of what the vertical distance (D) is within which no count is taken is critical for Deutsch's theory since, until it is specified, the theory cannot make predictions about most shapes, and there are serious difficulties in specifying such a distance.

(2) Deutsch's claim that it would be possible to find a pattern of stripes not equivalent to a horizontal rectangle on his theory is irrelevant to the argument. My claim was that it would be possible to match any shape (not any pattern) by a vertical or horizontal rectangle of appropriate dimensions. How one evaluates the plausibility and biological utility of a mechanism which makes confusions of this sort is a matter for individual judgment. The point at issue is that Deutsch's mechanism confuses every closed shape with the appropriate horizontal or vertical

rectangle: the mechanism I proposed only confuses certain shapes, and has led to tests for whether or not these confusions actually occur.

(3) The predictions Deutsch should make about transfer to different-sized shapes can be stated succinctly as follows. Let us suppose that an animal has learned to discriminate between two shapes *A* and *B*, where *A* occupies a higher position on the dimension under analysis according to Deutsch than the position occupied by *B*. For some shapes (for example, horizontal and vertical rectangles, a square), changing their size does not alter their position on this dimension; for other shapes (for example, triangles, cf. Fig. 2 (*b*) in ref. 1), if the shape is enlarged, its position on the dimension is increased; if it is reduced in size, its position is decreased. We can now make the following predictions: (i) For all shapes of the former sort, transfer should be perfect to both smaller and larger shapes. This applies to both *A*- and *B*-type shapes, since neither changes its position on the dimension. This prediction has been shown to be wrong with no fewer than six pairs of shapes (horizontal and vertical rectangles[4], square and vertical rectangle[5], square and horizontal rectangle[5] pairs *jk* and *lm* in Fig. 1 of ref. 1, square and cross). In all these cases transfer was found to be better to larger shapes than to smaller. The following predictions can be made of shapes which do change their position on the dimension when their size is changed. (ii) If shape *A* is enlarged transfer will be complete since it will be pushed further away from shape *B* along the dimension. It is even possible (but unlikely, cf. the experimental evidence in ref. 6) that performance may now be better than on the training shapes used. (iii) If shape *A* is made smaller, transfer will be imperfect since it is now closer to shape *B* on the dimension. (iv) If shape *B* is enlarged, transfer will be incomplete since it now lies nearer *A*. (v) If shape *B* is reduced in size, transfer will be complete (or better than complete) since it now lies further away from shape *A* on the dimension under analysis. Predictions (ii) and (iii) are of little interest since they are covered by the generalization that better transfer results with larger figures than with smaller. Nevertheless, Deutsch rests his whole case on a prediction of type (ii). From some 40 examples of transfer to shapes of different sizes to be found in my experimental papers, Deutsch selects one result and claims it supports his theory. In this experiment[7] I had trained four animals to discriminate between a triangle (shape *A*) and a diamond (shape *B*) and four to discriminate between a triangle (*A*) and a square (*B*). When an enlarged triangle was presented transfer was better than complete. The very same experiment from which Deutsch takes this result provides data on transfer tests to three other shapes of different sizes, every single one of which gives a result contrary to the predictions which would be made on Deutsch's hypothesis. Thus we would expect worse transfer to a small triangle than to a small square, since reducing the size of the triangle (shape *A*) brings the shape nearer to the square on the dimension under analysis (prediction iii). Yet transfer to the small triangle and to the small square was the same and was complete. Moreover, when we increase the size of a diamond we bring the figure nearer to a triangle on this dimension (prediction iv), yet performance was as good as with the original diamond. Finally, if we reduce the size of the diamond, performance should improve since it moves away from the position of the triangle (prediction v). Performance did not improve: it was the same as with the small triangle. Thus even in the one experiment which Deutsch cites as providing evidence favourable to his hypothesis on transfer, there are three cases (not mentioned by Deutsch) where the predictions his theory makes were found to be incorrect, and one (cited by Deutsch) where the prediction was right. It is about this question that he now writes, "Sutherland has not denied the validity of these data".

In his discussion of size transfer, Deutsch further writes that the better transfer to larger shapes than to smaller "may be explained as a simple artefact of his [Sutherland's] training situation". This might well have been true, were it not for two facts: (*a*) Better transfer to larger shapes than to smaller has been found to occur in all species tested, irrespective of the training situation used. (*b*) In a recent experiment (to be published), J. Z. Young has shown that better transfer to larger shapes than to smaller occurs quite independently of octopuses' previous experience with shapes of different retinal sizes.

(4) Deutsch in his original article claimed it would be possible to put a further mechanism into his theory which would account for the discrimination of up–down mirror images. In the foregoing article he says "this is certainly not an explanation": it was for this reason that I did not discuss his unspecified further mechanism. It should be noted, however, that even if a count of contour position in the vertical plane is kept, this will still not explain discrimination of left–right mirror image shapes: my original claim that Deutsch's theory "cannot account for any discrimination of mirror-image shapes of this sort" (that is, left-right) is therefore correct. It is not clear why Deutsch thinks his further mechanism is relevant to points (2) and (4) in my original article[1]. He appears to be claiming that at all points where his theory makes incorrect predictions it would be possible to propose some other mechanism which would make correct predictions: this claim is irrefutable.

(5) The allegation that the greater discriminability of horizontal rectangles of different lengths than of vertical rectangles of different lengths disproves my original theory is surprising. This experiment was performed in order to test a prediction made by my own theory. Fig. 2 should help to make clear on what the prediction was based. The vertical and horizontal projections respectively represent the amount of each shape in the vertical plane at each point on the horizontal axis, and the amount of each shape in the horizontal plane at each point on the vertical axis. It should be noted that the horizontal projections have been rotated clockwise through 90°. In all my papers on this subject, it has been stated that it was the heights of these projections which are analysed, not their breadths. It is clear from Fig. 2 that left–right mirror images (pair *b*) differ only in their vertical projections, whereas up–down mirror images (pair *a*) differ only in their horizontal projections. Up–down mirror images are better discriminated by octopuses than left–right. In terms of my theory this can only mean that when discrimination is based on an analysis of the horizontal projections performance is more accurate than when it is based on an analysis of the vertical projections. This enables us to construct a further test for the theory: two horizontal rectangles of different lengths differ in the height of their horizontal projections,

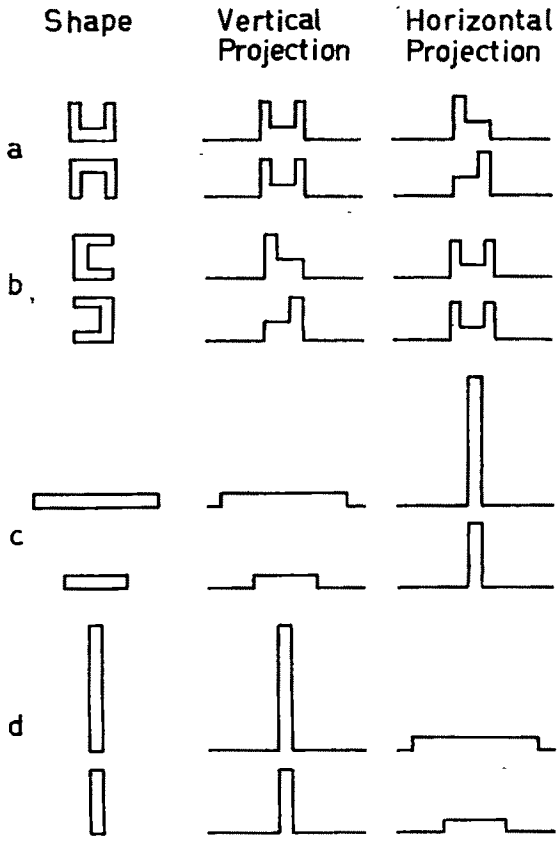

Fig. 2

two vertical rectangles differ in the height of their vertical projections (cf. Fig. 2, pairs *c* and *d*). The theory must predict that the horizontal rectangles will be better discriminated than the vertical. This prediction was confirmed. In my original article, I said it was "*strikingly*" confirmed; the difference in performance of animals trained on rectangles in different orientations was very large and was significant at better than the 0·00001 level of confidence[6]; also this was a new and (to common sense) unexpected discovery about the octopus, which would not have been found out if the theory had not been manipulated to yield predictions.

(6) Deutsch's final point appears to involve certain misconceptions about neuroanatomy and in particular about Young's recent findings[8]. From a functional point of view, what is likely to be important is not simply the total length of dendrite running in the direction corresponding to a given optical axis, but the orientation of dendritic pick-up fields. Young has tentatively interpreted his own findings to mean that there are more dendritic fields orientated in a plane corresponding to the visual horizontal than in any other plane. This might produce better discriminability of horizontal extents than of vertical, and is therefore in line both with the behavioural evidence and with my speculative interpretations. To consider only the direction in which fibres are running, which is what Deutsch appears to be doing, is like trying to draw conclusions about a radio set by looking only at the directions in which wires go without considering how they are linked up. On Deutsch's own theory we would expect to find better discriminability of vertical than of horizontal distances, and correspondingly more vertically orientated pick-up fields than horizontally orientated; thus the theory appears to be at variance both with the existing neuroanatomical and behavioural evidence.

In conclusion, it may be worth attempting to draw some lessons of a more general kind from this controversy. From behavioural data alone it is not possible to specify the exact neurophysiological mechanisms at work and it would be presumptuous for a psychologist to attempt to do so. Such specification must await the results of detailed neurophysiological and neuroanatomical studies: in the existing state of such studies it is only too easy for the psychologist to produce howlers in his attempts to interpret them. All the psychologist can hope to do is to specify the general lines along which data are processed in the system. I have attempted to work out by systematic experiment some of the ways in which visual data are processed by the octopus: any neurophysiological hypotheses I have proposed have been put forward only to give concrete instances of the sort of thing that may be happening, and as a help in framing hypotheses which may be tested at a behavioural level. Deutsch does not challenge the outlines of the data-processing system, that is, that there is an analysis of shape along the x and y co-ordinates with a greater accuracy of analysis on the horizontal co-ordinate. The point of neurophysiological speculation at this stage is only that thinking in concrete terms may help to produce hypotheses which can be tested by behavioural experiments: it is in fact heuristicly valuable and in the case of the octopus has helped me in the assembly of systematic data on this species' capacity for shape recognition, and in the discovery of some surprising facts. These facts may help in the interpretation of neurophysiological and neuroanatomical data when more complete data of this sort become available. Unfortunately, Deutsch's theory has not led to the discovery of any facts, nor has it yet made any new and correct predictions; if further specifications could be added, then it too might become valuable as a research tool. The body of experimental data on shape recognition in the octopus, collected by Young, Boycott, Muntz and Sutherland, is now fairly extensive; for almost any theory which could be proposed it would be possible to select a few facts out of many, quote them out of their experimental context and claim that these facts fit the theory. The progress of a science is not favoured, however, if in doing this we take no note of the facts which do not fit the theory; these may be the most important points at which to start further work.

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LETTERS TO THE EDITORS

PHYSICS

Pressure Dependence of Resistivity of Indium Antimonide to 70,000 Atmospheres

THE pressure dependence of the resistivity of indium antimonide has been measured by Keyes[1] up to 12,000 atmospheres. We have extended the range to 70,000 atmospheres. In addition to the type of change found by Keyes we have observed a resistance change on melting when the temperature was considerably below the zero pressure melting-point of 796° K.

The measurements were made in a tetrahedral apparatus constructed at the National Physical Laboratory following a design of the National Bureau of Standards[2]. This allows the use of a standard hydraulic press. In our apparatus the pyrophyllite tetrahedron had a side of ¾ in. and electrical connexions were made by the techniques described by Hall[3]. Cooling coils allowed the temperature to be lowered to 120° K. Pressure-versus-load calibration was made by measuring resistance changes in bismuth, thallium and barium specimens and using Bridgman's electrical data[4].

Fig. 1 shows typical behaviour of single-crystal specimens of indium antimonide at two temperatures. Initially, the resistance increases with pressure as found by Keyes, who showed that this effect comes mainly from a widening of the energy gap. In our room-temperature experiments, the resistance dropped sharply at a pressure of 30,000 atmospheres. This is attributed to melting, with a transition from semi-conduction in the crystal to metallic conduction in the liquid phase. In support of this, the ultimate resistivity reached here is close to the value obtained by Busch[5] for liquid indium antimonide at zero pressure. The small pressure dependence of the resistivity in the liquid phase is also consistent with the metallic behaviour demonstrated by Busch.

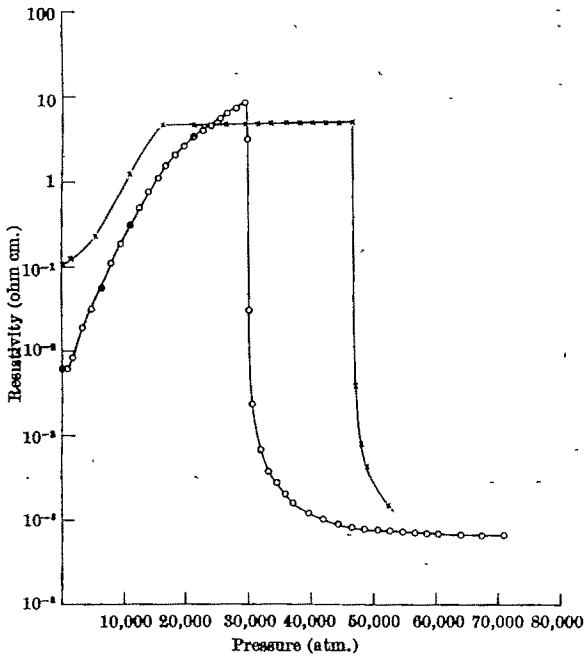

Fig. 1. Behaviour of single-crystal specimens of indium antimonide at two temperatures. n type ~ 4 × 10^{14} electrons/c.c. Specimen size, 1¼ mm × 1¼ mm. × 3 mm. ○, 293° K.; ×, 184° K.

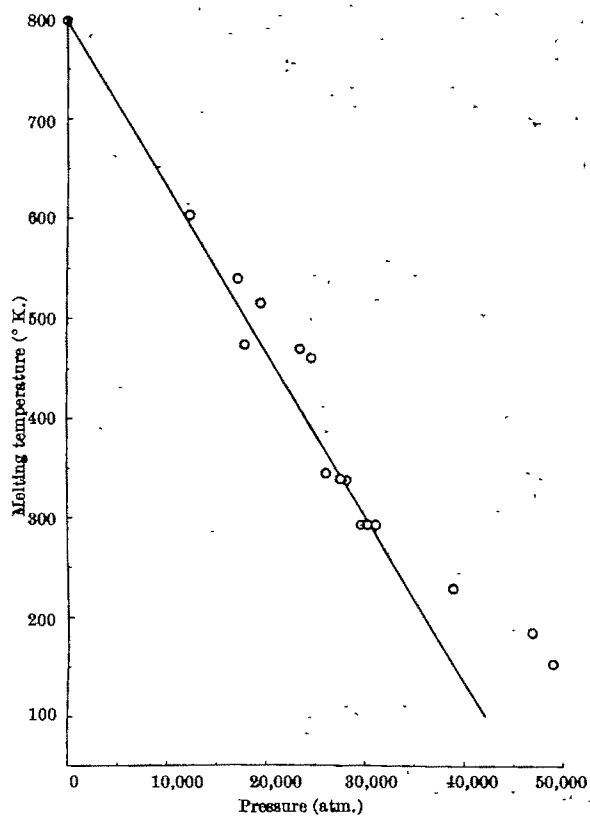

Fig. 2. Effect of pressure on the melting point of indium antimonide

Fig. 2 shows the melting point, as measured by the sharp fall in resistance, plotted as a function of pressure. It shows a decrease with increasing pressure which, qualitatively, is consistent with the known contraction in volume on melting shown by this compound. The decrease varies linearly with pressure to about 30,000 atmospheres, but significantly departs from this behaviour at higher pressures. By inserting a value of the slope of our melting curve at zero pressure in the Clausius–Clapeyron equation with a known value[6] of the volume contraction on melting ($\Delta v/v_{solid} = 0{\cdot}13$) a value for the latent heat of fusion can be found. This value of 27 cal./gm. does not agree with an experimentally determined value[7] of 47·2 cal./gm. The disagreement between these values might arise from the presence of complex phases in the liquid near the melting point[8]. In our experiments results are lacking below 10,000 atmospheres because the pyrophyllite gasket technique is not reliable.

It is interesting to compare the corresponding work on the melting of germanium by Hall[9]. In this he finds a variation of melting point with pressure which is substantially linear over the range 0–180,000 atmospheres. When his value of the slope of the melting curve is used to calculate the latent heat of fusion, using a measured value[10] of the volume change, a value of 84 cal./gm. is found which is in fair agreement with the experimentally determined value of 110 cal./gm.[11].

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Diffusion of Cadmium into Gallium Arsenide

DIFFUSION of cadmium-115 into gallium arsenide has been examined by a method identical to that described by us[1] in the case of zinc-65. The cadmium was diffused from a saturated vapour into a carefully prepared specimen of gallium arsenide approximately 1 cm. × 0·4 cm. × 0·2 cm. contained in a quartz tube 2 cm.^{3} in volume. After diffusion auto-radiographs of the specimen were taken to check the uniformity of activity across the surface and the diffusion profile was obtained by sectioning as described in the reference.

Fig. 1 shows typical diffusion profiles after diffusion for 40 hr. at 1,000° C. with the cadmium source held at 750° C.

The initial decrease in concentration from 2×10^{19} cm.$^{-3}$ at the surface is very rapid. Fitting this part of the curve to a complementary error function, an approximate diffusion coefficient, D, of 3×10^{-12} cm.^{2} sec.$^{-1}$ can be obtained. The concentration falls to a minimum, which is sometimes below the limit of detectability, but rises again to a maximum followed by a much more gradual decrease. Twelve different specimens have been examined and all have shown the same qualitative results. The half-life of the deeply penetrating activity has been measured and found to be the same as that of the irradiated cadmium, thus ruling out the possibility that the effect is due to an impurity in the cadmium. Although the steeply falling portion of the profile is reproducible, the concentration at the subsequent maximum has varied between 4×10^{18} cm.$^{-3}$ and $\sim 10^{16}$ cm.$^{-3}$ in a manner which is at present unaccountable.

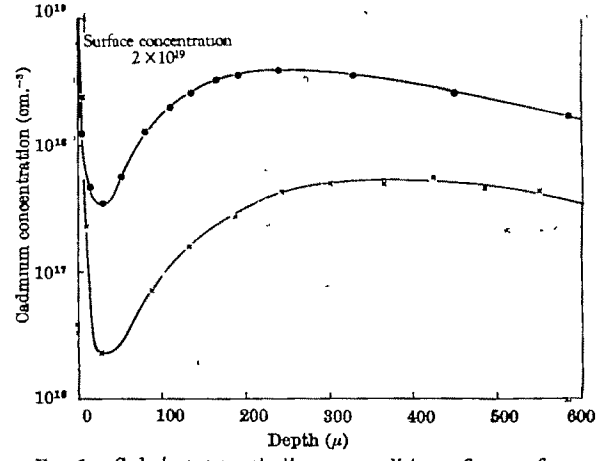

Fig. 1. Cadmium concentration versus distance from surface. Diffusion temperature, 1,000° C.; diffusion time, 40 hr.; cadmium source temperature, 750° C.

Goldstein[2] has also examined the diffusion of cadmium into gallium arsenide and fits his results to simple complementary error functions. The value of D which he obtains for 1,000° C. is somewhat higher than that which we obtain from the steeply falling portion of our curves. He does not report any anomalies in his results such as we have found. However, it should be noted that his conditions of diffusion are somewhat different from ours, and in particular he has chosen to carry out diffusion in the presence of an arsenic atmosphere.

In an attempt to explain this behaviour experiments have been performed using:

(1) crystals of different conductivity type;
(2) crystals orientated so that diffusion along [111], [$\bar{1}\bar{1}\bar{1}$]; [110] or [100] directions was examined;
(3) crystals strained to produce a large concentration of dislocations.

No correlation has been found between these crystal properties and the characteristics of the diffusion profile.

Further experiments to elucidate the mechanism of this diffusion are in progress.

We wish to thank the Admiralty for permission to publish this communication, Mr. W. R. Harding for supplying the gallium arsenide and Mr. N. Fleet for assistance with the experiments.

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Fine Structure of the Nuclear Magnetic Resonance Spectra of Solids: Chemical Shift Structure of the Spectrum of Phosphorus Pentachloride

THE static dipolar interaction between the nuclei in a solid causes its nuclear magnetic resonance spectrum to be much broader than that of a liquid. In the liquid state the isotropic re-orientation and diffusion of the molecules average their nuclear dipolar interaction almost to zero, often revealing a

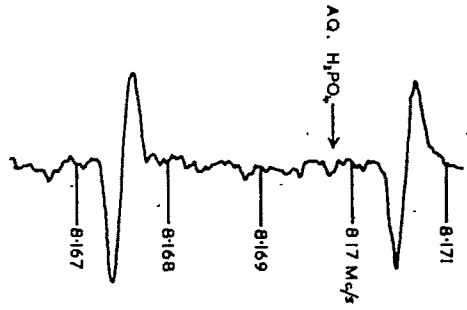

Fig. 1. Phosphorus-31 magnetic resonance spectrum of polycrystalline phosphorus pentachloride rotated at high speed. The resonance frequency of the reference compound (85 per cent aqueous phosphoric acid) is also indicated; this frequency was determined from recordings taken immediately beforehand and afterwards

fine structure originating from the different chemical shifts of the nuclei, and from their indirect spin–spin interactions. In solids this fine structure is obscured by the stronger dipolar interactions. As we have shown previously[1-3], the dipolar broadening may nevertheless be removed in solids also, the necessary averaging being achieved by high-speed rotation about an axis inclined at an angle 54° 44′ to the direction of the applied field. When the rotation-rate is comparable with the static line-width, the narrowed central line is resolved from the satellite lines which appear on either side of it at integral multiples of the rotation frequency. Thus, for example, rotation of solid sodium chloride at a rate of 800 c./s. gives a resolved sodium-23 spectrum consisting of a central line and three pairs of satellites[2]. At a rotation-rate of 1,600 c./s. the central line and only one pair of weak well-resolved satellites are observed, while at 2,500 c./s. only the narrow central line is visible.

High-speed rotation at the angle 54° 44′ thus opens up the possibility of observing fine structure in solid specimens, and may therefore be useful in studying insoluble compounds. There is in any event interest in comparing the fine structure of spectra for the same compound in both the solid and the liquid states.

A first example of the application of this method is provided by polycrystalline phosphorus pentachloride, which gave the phosphorus-31 resonance spectrum shown in Fig. 1. The sample was placed in an airtight container which was rotated about an axis making an angle of 54° 44′ with the steady magnetic field of about 4,740 gauss. The satellite lines were scarcely distinguishable from the noise background and the central spectrum consists of two sharp lines of approximately equal intensity. It is known from the X-ray diffraction examination by Clark, Powell and Wells[4] that in the solid state phosphorus pentachloride consists of equal numbers of tetrahedral $(PCl_4)^+$ and octahedral $(PCl_6)^-$ ions arranged on a tetragonal lattice. It is therefore reasonable to identify the two spectral lines with phosphorus nuclei in the two types of ion, the separation between the lines arising from their different chemical shifts. The spectrum has also been recorded in a field of about 3,550 gauss; the separation between the lines is found to be proportional to the field strength as the chemical shift explanation requires.

The chemical shifts of each line have been measured relative to the usual phosphorus standard, 85 per cent aqueous phosphoric acid, and are found to be +281 and −96 p.p.m. (The spectra were measured using a fixed field and a variable radiofrequency. The shift is therefore defined as $(\nu_r - \nu_c)/\nu_r$, where ν_c and ν_r are the frequencies for the compound and the reference respectively. This is equivalent to the usual definition $(H_c - H_r)/H_r$ when the frequency is held constant and the field is varied.) These shifts fall within the range +488 to −222 p.p.m. recorded for various liquid specimens[5]. Since there are equal numbers of the two types of phosphorus nuclei one cannot determine from the spectrum itself the assignment of the two lines to their respective ions. There is some indication that positive shifts arise when more than four atoms are connected to a phosphorus atom[6]. The shift for molecular PCl_5 in carbon disulphide solution is +80 p.p.m.[6] whereas for PCl_3 it is −215 p.p.m.[5]. The $(PF_6)^-$ ion, which like $(PCl_6)^-$ is an octahedral sp^3d^2 hybrid, has a shift of +148 p.p.m. in hexafluorophosphoric acid[7]. It seems likely, therefore, that the positively shifted line in solid phosphorus pentachloride arises from the $(PCl_6)^-$ ion, though this assignment cannot be certain. If the assignment is correct we have the following sequence of shifts in p.p.m. for four phosphorus chlorides: PCl_3 (−215), PCl_4^+ (−96), PCl_5 (+80), PCl_6^- (+281).

We have found evidence that when the rotation-rate is a submultiple of the separation between the two lines, so that the satellites of each line are superposed on the central line and satellites of the other, there is an exchange of energy between the two systems of nuclei. This feature is being examined in more detail.

One of us (G. J. J.) wishes to thank the Chief Scientist, Department of Supply, Commonwealth of Australia, for enabling him to study at Bangor.

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Line Breadths in the Ammonia Spectrum

The Van Vleck–Weisskopf formula for peak absorption and specified for the ammonia inversion spectrum in the microwave region can be written[1]:

$$\gamma_m = \frac{A}{\Delta\nu} f(J,K) \qquad (1)$$

where $A = \dfrac{6\pi^2 N f_\nu \mu^2}{3ckT} \sqrt{\dfrac{B^3Ch^2}{\pi(kT)^3}}$

and $f(J,K) = g\dfrac{(2J+1)K^2}{J(J+1)}$

$$\nu_0^2 \exp\left\{-\frac{14\cdot3}{T}\left(J(J+1)-0\cdot366K^2\right)\right\}$$

There is evidence that $\Delta\nu$ varies with rotational state for the $J = K$ transitions as $\left(\frac{K^2}{J(J+1)}\right)^{1/n}$, where n has the value[2] of either 2 or 3. If $\Delta\nu$ is normalized to the (3,3) line, as seems to be the present practice, then $f(J,K)$ in equation (1) should be multiplied by

$$\left(\frac{3J(J+1)}{4K^2}\right)^{1/n}, \quad n = 2 \text{ or } 3 \qquad (2)$$

The factor in equation 1 limiting an accurate prediction of intensity has been the value of $\Delta\nu$. Experimental intensity results have not previously warranted a more precise value of $\Delta\nu$. However, the development and construction of an improved microwave spectrometer at this University has allowed accurate measurements to be made on the intensities of absorption lines. A number of lines in the ammonia inversion spectrum have been measured ($J = K$, 1 to 6), and the results of these measurements are shown in Table 1. Column 3 lists the values predicted in Townes's "Microwave Spectroscopy"[4].

Table 1. TABLE OF PEAK ABSORPTION COEFFICIENTS OF AMMONIA MEASURED AT $T = 27°$ C. AND IN THE PRESSURE REGION OF 0·1–0·5 MM. MERCURY

(J,K)	γ_m measured ($\times 10^{-4}$ cm.$^{-1}$)	γ_m calculated (ref. 6) ($\times 10^{-4}$ cm.$^{-1}$)
1,1	1·81 ± 0·09	1·9
2,2	3·10 ± 0·11	3·2
3,3	7·87 ± 0·11	7·9
4,4	4·16 ± 0·03	4·3
5,5	3·87 ± 0·04	4·0
6,6	6·66 ± 0·08	6·9

The experimental values of γ_m have been plotted against $Af(J,K)\left(\frac{3J(J+1)}{4K^2}\right)^{1/2}$ in Fig. 1. The value of the line-breadth parameter found from the straight line is:

$$\Delta\nu = 25{\cdot}7 \pm 0{\cdot}2 \text{ mc./s. per mm. mercury at } 27° \text{ C.}$$

The results of this experiment did not distinguish between the values of $n = 2$ and $n = 3$ in expression (2). The value of $n = 2$ was chosen because of its more generally accepted theoretical basis[5].

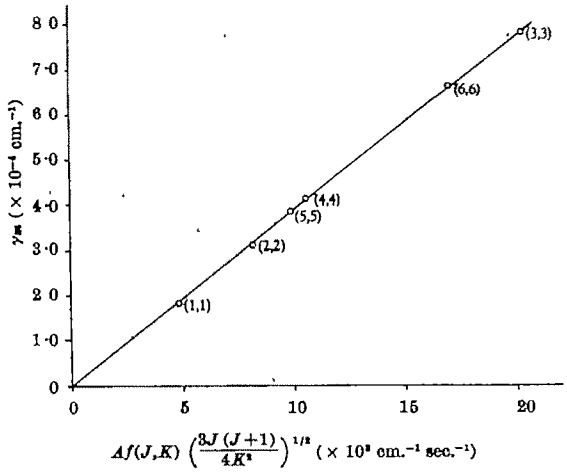

Fig. 1. Experimental intensity measurements of $J = K$, 1–6 ammonia inversion lines plotted against $Af(J,K)\left(\frac{3J(J+1)}{4K^2}\right)^{1/2}$

Yamano has measured $\Delta\nu$ and found it to be $27{\cdot}5 \pm 0{\cdot}1$ mc./s. per mm. mercury at 24·5° C. and to hold in the pressure region of 0·01–0·02 mm. mercury[6]. If $\Delta\nu$ is assumed to vary as T^{-1} then under similar temperature conditions the value obtained here is some 2·3 per cent less than that of Yamano.

A more detailed report will be published in due course.

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Sustained, Localized, Pulsed-Microwave Discharge in Air

SEVERAL recent publications[1–4] discuss possible methods whereby a localized gas discharge might be maintained by electromagnetic radiation. Recently a simple experiment to maintain an electrodeless discharge by focused microwave radiation was undertaken at this Laboratory. A small, localized discharge was obtained in low-pressure air. This discharge stands distinct and isolated from the generating apparatus and from any walls.

A pulsed, X-band radar transmitter is used as a microwave source. This unit emits pulses of approximately 0·5 μsec. duration, providing 40 W. average power and about 20 kW. peak power with an inter-pulse time of 290 μsec. These figures are nominal because stationary waves set up by the experiment cause deterioration of the magnetron. A pyramidal horn on the radar output is directed toward an 18-in. parabolic reflector 2 ft. away. An evacuated, roughly spherical glass chamber about 6 in. in diameter is placed at the focus of the paraboloid. A corona discharge from a Tesla coil is employed momentarily to provide the initial ionization within the chamber when the discharge does not occur immediately upon turning on the transmitter. A red or violet discharge is formed at the focus within the chamber. The size of the discharge is variable, the maximum dimension ranging from about 1 to 4 cm.

Several factors influence the appearance of the discharge. At pressures from about 3 to 20 mm. mercury its shape is irregular, exhibiting several striations. At higher and lower pressures, the discharge takes on the shape of one or two 'sausages' with their long axes in the direction of the electric vector of the microwaves from the transmitter. At about 0·3 mm. mercury, the lowest pressure at which it can be maintained, the discharge is red and diffuse. As the pressure is increased, the discharge gradually becomes definite in its configuration and violet in colour. At about 6 mm. mercury the colour is a bright violet and the edges are well defined. This remains true as the pressure is increased to 47 mm. mercury,

the highest pressure at which the discharge has been maintained.

Movement of the glass chamber modifies the shape of the discharge. This, as well as the striated appearance, is attributed to perturbations of the electromagnetic field by internal reflexions from the chamber walls. These reflexions can sometimes split the discharge into two or, rarely, three parts. However, the discharge does not move with the chamber. The position of the discharge is clearly determined by the transmitter-reflector geometry and can be obtained at any point within the chamber. If the discharge is brought into contact with the walls of the chamber, it will spread along a portion of the wall. If the focus is moved to the outside of the chamber, the discharge is extinguished.

There is no noticeable increase in the temperature of the chamber if the discharge is not brought in contact with the wall. When such contact occurs, the wall becomes warm and is uncomfortable to touch within 10 sec.

I wish to thank Messrs. Donald J. Ritchie and Carl P. Tresselt for their part in planning and carrying out these experiments.

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CRYSTALLOGRAPHY

Crystal Structure of $Ba_{0.5-x}TaO_{3-x}$

A STUDY of the barium–tantalum–oxygen system has produced the compounds $Ba_3TaO_{5.5}$ with an ordered perovskite structure[1], $Ba_5Ta_4O_{15}$ with a hexagonal layer structure[2], $Ba_{0.5}TaO_3$ with the tetragonal bronze structure[3], and $Ba_{0.44}TaO_{2.94}$, a hexagonal phase for which a trial structure has just been determined. The preparation of a powder and a single crystal of the reduced phase, $Ba_{0.44}(Ta^{IV}_{0.74}Ta^{V}_{0.26})O_{2.57}$, as well as analogous phases has previously been described[4]. It was later found that this reduced phase was produced only when the tantalum pentoxide used in the preparation was obtained from a particular source. The method of preparation is to mix appropriate quantities of tantalum pentoxide, tantalum metal, and barium oxide and heat in vacuum. Attempts to prepare larger amounts of the phase for density measurements after the original source of tantalum pentoxide was exhausted, were unsuccessful unless a barium chloride flux was added. The preparations obtained with the use of the flux, however, were not homogeneous, and good density measurements were therefore not obtained.

Single crystal studies indicate that the reduced phase has the same cell size ($a = 8 \cdot 96$ Å., $c = 7 \cdot 79$ Å.) and structure as the oxidized phase. Since crystals of the reduced phase were easier to prepare, they were used for the structure determination.

Intensities were obtained for $hk0$ and $h0l$ zones on a Buerger precession camera using molybdenum $K\alpha$ radiation. A sharpened $hk0$ Patterson projection was prepared. With the aid of a suggestion from Dr. A. D. Wadsley as to the possible structural relationship to $K_3V_5O_{14}$[5], it was seen almost at once that placing six tantalum ions in the positions $x, 0, \pm z$; $0, x, \pm z$ and $\bar{x}, \bar{x}, \pm z$ with $x = 0 \cdot 23$ would account for the most important peaks of the vector map. These were the positions of 3/5 of the vanadium ions in $K_3V_5O_{14}$. The bariums were placed in the potassium positions, $x, 0, z$; $0, x, z$; $\bar{x}, \bar{x}, z$, and x was determined as about $0 \cdot 63$, by an $h00$ Fourier line projection. Of the possible space-groups only $P62m$ would allow these positions.

From the $00l$ data, it was determined that a reasonable fit could be obtained if three tantalums were placed at $z = 0 \cdot 25$, three at $z = 0 \cdot 75$, and three bariums at $z = 0 \cdot 50$. An $h0l$ Patterson projection and a subsequent $00l$ Fourier line projection showed that z for the tantalums should be about $0 \cdot 24$ and $0 \cdot 76$ and the bariums should be at about $z = 0 \cdot 50$.

As for the oxygen packing the neatest arrangement would appear to be oxygens directly above and below each tantalum (a scheme that accounts so well for the axial length) and oxygens at the same z values as tantalum to make groups of three corner-sharing octahedra. The approximate co-ordinates for the atoms so obtained are given in Table 1.

Table 1

Atoms		x	y	z
3 Ba	in (g)	0 63	0	0 50
6 Ta	in (i)	0·23	0	0 24
$3O_1$	in (g)	0 23	0	0·50
$3O_2$	in (f)	0 23	0	0
$3O_3$	in (i)	0·84	0	0·24
$12O_4$	in (l)	0·47	0 18	0 24

Using the above parameters for the atoms a fair fit was found for observed and calculated $hk0$ and $00l$ structure factors ($R = 0 \cdot 24$).

The following points are disturbing about the trial structure: (1) There are marked deviations from Pauling's electrostatic valence rule in that the sum of strengths of electrostatic bonds to oxygens from adjacent cations is as low as $1 \cdot 23$ for some oxygens and as high as $2 \cdot 27$ for others. (2) The trial structure leads to an empirical formula of $Ba_{0.5}TaO_3$ with no obvious explanation of the observed fixed ratio of Ba : Ta of about $0 \cdot 44$. (3) There are only 18 oxygens occupying 24 crystallographically available positions (still fewer in the reduced phase), thus leaving considerable unfilled volume, again for no obvious reason. (4) The X-ray density based on the trial structure is lower than the observed range of values.

The obvious thing to try would be the inclusion of a greater number of cations, and therefore oxygens, in the structure. Judicious placement of the additional cations could favourably change the situation with respect to all the points raised above. However, so far, all attempts to add atoms to the structure have led to a greater deviation of observed from the calculated structure factors.

It is hoped that we shall be able to collect more complete data on this compound. Our intention is then to substitute a machine Fourier approach, with the described trial structure as a starting point, for the human semi-logical semi-intuitive approach we have so far been using. (It may be pointed out that this latter approach is somewhat handicapped because the structure is non-centrosymmetric.) Should these efforts prove fruitful, the results will be reported at another time.

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GEOLOGY

Spectral Reflectivity of Ore Minerals

IT would appear that there may have been some ambiguity in the use of the terms 'standard reference surfaces' and 'standard values' in our recent article on the above subject[1]. The standard reference surfaces specifically refer to a polished basal section of quartz and to liquid mercury under a coverslip, which were measured for us by the National Physical Laboratory. The intention was that these two surfaces would be readily reproducible by other workers. The confusion has arisen in that two other surfaces of intermediate reflectivity were also measured for us by the National Physical Laboratory to assist in the calibration of our equipment. It is entirely incidental that these two 'other surfaces' were hæmatite and pyrite; their identity is immaterial and the values of reflectivity quoted for them are not standard values, *sensu stricto*, since minerals will, in many cases, show a range of reflectivity due to variable composition and optical anisotropy.

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GEOCHEMISTRY

Pigments of a Fossil Echinoderm

SEVERAL years ago, I described[1] the discovery of crystallized organic pigments ('fringelite') in a fossil crinoid (*Millericrinus*) of upper Jurassic age. Additional specimens have now been collected at the two original locations (Fringeli and Liesberg, both in north-western Switzerland). The pigments are isolated by solvent extraction and separated by repetitive chromatography and fractional crystallization. Six pigments (fringelite *A*–*F*) have been isolated: additional pigments remaining in the fossil after exhaustive extraction with pyridine can be dissolved in concentrated sulphuric acid in which they exhibit an absorption spectrum similar to that of the more soluble fringelites. All these pigments are similar in respect to their absorption spectra, the colour of their solutions (red in organic solvents, green in sulphuric acid), the formation of green, insoluble sodium salts and the ease with which acetyl- and benzoyl-derivatives are formed. In all these properties the fringelites strongly resemble extended quinones of the type of aphin[2] or hypericin[3].

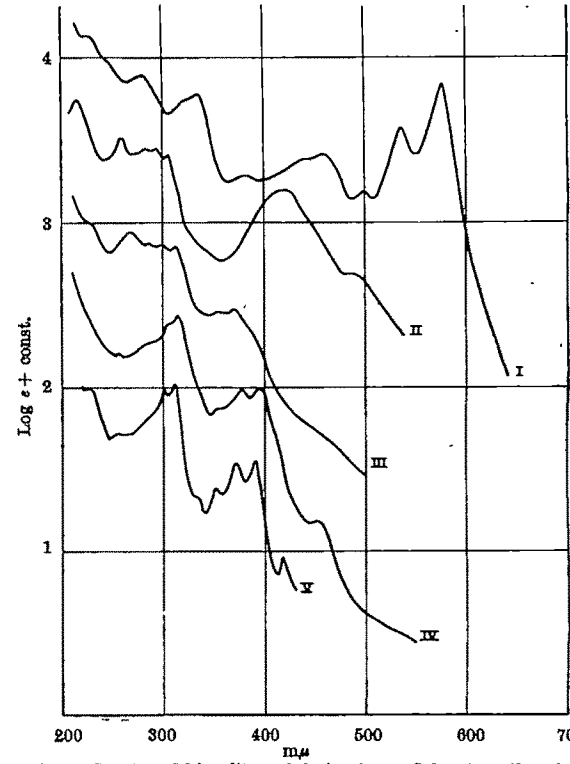

Fig. 1. Spectra of fringelite and derivatives. Solvent, methanol. I, Fringelite *E*; II, acetyl derivative of fringelite *E*; III and IV, hydroacetyl derivatives; V, fossil alkyl-benzperylene

They even give the characteristic aphin-reaction, a blue(-violet) colour, on treatment with acetic anhydride containing a small amount of sulphuric acid.

The visible and ultra-violet absorption spectrum of fringelite *E* in methanol (Fig. 1, curve I) shows a general resemblance to that of erythroaphin *fb* (ref. 4); however, differences in band positions and relative extinctions of the band systems at 450 and 550 mμ indicate the presence of a similar but not identical chromophoric system. The acetyl-derivative of curve II is obtained by exhaustive acetylation with pyridine-acetic anhydride. Hydroacetyl derivatives (curves III and IV) are formed by reduction with zinc dust in the same medium. Curve IV, except for a displacement to longer wave-lengths (amounting to 13·5 mμ for the main band at 298·5 mμ and 8 mμ at 383 mμ, both in methanol), is nearly identical with that of the 6-ring aromatic hydrocarbon 1.12-benzperylene; curve III shows the typical bands of highly substituted phenanthrenes. The same phenanthrene band system is also evident in curve II (the acetyl pigment) in addition to absorption at longer wave-lengths caused by the carbonyl groups of the quinone.

From these spectral data we conclude that the fringelites are polyhydroxyquinones of 1.12-benzperylene. The aromatic hydrocarbon is substituted by the quinone oxygens in such a way that three aromatic rings with phenanthrene configuration remain undisturbed. By hydrogenation this quinone is reduced to the hydroquinone with the benzperylene spectrum IV, which, by more vigorous treatment, is transformed into the phenanthrene-derivative III.

The ultimate reduction products obtained in the laboratory and in Nature provide further proof for

this structure. Zinc-dust fusion[5] leads to 1.12-benzperylene-type hydrocarbons of varying degrees of substitution, in addition to small amounts of a pyrene derivative. An alkyl-benzperylene also occurs naturally in the fossil sea lily[1].

The various fringelites seem to differ mainly in the number and position of their hydroxyl groups. The spectral data and the formation of a pyrene-derivative in the zinc-dust fusion suggest that the quinone-oxygens are located in 4 and 9 positions. The presence of alkyl substituents, the position of which is not yet clear, is indicated by a considerable spectral band shift from the synthetic benzperylene to the fossil hydrocarbon and the products of the zinc dust fusion. However, the 6 and 7 positions do not seem to be bridged by an alicyclic ring or substituted by an alkyl-chain since coronene is not formed in the zinc-dust fusion.

It has been suggested[6] that the pigments of recent crinoids are closely related to the hydroxynaphthoquinones of other echinoderms (echinochromes, spinochromes). In my previous paper I had suggested that the fringelites and the fossil benzperylene are the products of successive redox and condensation reactions between two echinochrome molecules, a hypothesis that has been further corroborated by the present findings. Fringelite *F* and the even more polar materials soluble only in concentrated sulphuric acid would be the primary condensation products; they are also the major pigments (several gm./kgm. of the fossil). The small amounts of the less polar pigments (mgm./kgm. for fringelites *D* and *E* and μgm./kgm. for pigments *A*, *B* and *C*) and the hydrocarbon have been formed from the major pigments by reduction and elimination of substituents.

The highest pigment concentration occurs in the massive (2–3 in. diameter) roots and lower parts of the stem; small stems ($\frac{1}{2}$ in. diameter) and crowns rarely contain more than traces of pigments. Other fossils of the same locations, including small sea urchins and their spines, are completely devoid of pigments. Apparently, conditions for the preservation of the pigments were sufficiently good only below the sediment-water interface where the roots and heavy stems accumulated during or immediately after the lifetime of the crinoids.

Discovery of the fringelites is geochemically significant, permitting for the first time the reconstruction of a complex reaction sequence, involving reduction, condensation, oxidation and further reduction and elimination of substituents under the final formation of a polynuclear aromatic hydrocarbon. A knowledge of such transformation reactions permits conclusions about the chemical environment and the organic reactivity in the sub-surface.

A more detailed report of this work is being prepared for publication in *Geochimica et Cosmochimica Acta*. This investigation has been supported by a research contract with the United States Office of Naval Research (Contract *NONR*-2196 (00)).

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Exposure Ages for Iron Meteorites

Schaeffer and Fisher[1] have given values for the exposure ages (that is, the time during which the meteorites were exposed to cosmic rays after having been broken out of a bigger body) of 18 iron meteorites. These ages vary between 20×10^6 to $1{,}900 \times 10^6$ years. I think these authors have made some mistakes in interpreting the results of their experimental work.

Exact determinations of the exposure ages of meteorites are only possible by combining the values of a stable and a radioactive cosmic-ray spallation product. For measurements of radioactive spallation products big samples are needed, and therefore only few such determinations were made. If one knows the size of the meteorite before passing the Earth's atmosphere and the location of the sample analysed inside the meteorite, it is possible to calculate the exposure age from the content of any stable spallation product alone. Unfortunately, we do not know the location of the samples or, better, their distance from the original surface of the meteorites.

Schaeffer and Fisher tried to calculate the 'depth' of the samples from the ratios of the content of different stable spallation products and based this calculation on two assumptions:

(1) The energy spectrum of the particles which produce nuclear spallation varies with the distance from the surface and with the size of the meteorite. Because of the secondary particles which have relatively low energies, the mean energy of the particles producing spallations decreases with the depth from the surface.

(2) The ratio of helium-3 to argon-38 is a measure for the mean energy of the particles.

Schaeffer and Fisher used this ratio to calculate the depth of the samples analysed and then determined from the total amounts of helium-3 the exposure ages of the meteorites.

There are errors in both of these assumptions.

(1) The energy spectrum of the primaries extends from at least 500 MeV. to several BeV. Especially from data on meteorites an extension down to about 200–300 MeV. seems very probable[2,3]. These low-energy primaries lie in the same energy-range as the secondaries. For particles of this energy-range of several 100 MeV., the diminution by loss of energy through ionization and excitation is not negligible apart from the diminution by nuclear absorption. By this loss of energy the mean energy of the primary particles increases with the distance passed in the meteorites. This increase of the mean energy of the primaries is balanced in big meteorites by the low-energy secondaries; and even the ratio of the flux of the secondaries to the flux of the high-energy primaries (with energies > 1 BeV.) reaches a nearly constant value already for a depth of about 30 cm. caused by the diminution of the secondaries by loss of energy through ionization and excitation[2].

(2) The ratio helium-3/argon-38 seems not at all a good measure for the energy of the particles which produce the spallation processes. This ratio should be nearly independent of the particle energy[4–6].

As neither assumption can withstand intensive examination, the exposure age based on them cannot be correct.

Some exact determinations of the exposure ages of meteorites are known, for which Schaeffer and Fisher

also have given values. Fireman[7], measuring argon-39 and helium-3, found the same age for Treysa and Sikhote-Alin meteorites; nearly the same results were found by me[5,9]. Schaeffer and Fisher, however, gave the age of Treysa as being more than ten times higher than that of Sikhote-Alin. I have also tried to find at least approximate values for the exposure ages of iron meteorites from the results of stable spallation products only; these results will be published in due course.

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IN our communication it was pointed out that it is possible to estimate a cosmic-ray exposure age for a meteorite from a measurement of the stable rare gas contents alone. The difficulty with such estimates in the past has been that it was not possible to estimate the cosmic-ray production-rate of a stable nuclide in the particular sample of the meteoroid measured, as the production-rate depends on the unknown depth of the measured sample in a meteoroid of unknown size. The proposed estimate of production-rate was made from the observation that for meteorites with low argon-39 and chlorine-36 activity (that is, low cosmic-ray nuclide production-rates) the ratio helium-3/argon-38 is lower than in meteorites with high argon-39 and chlorine-36 activities. It was also pointed out that the same is true for the ratios helium-3/helium-4 and neon-21/argon-38. The discussion of the dependence on energy of these ratios was included to give a possible explanation for the observed dependence. The only assumptions made were that the dependence is not a coincidence or an experimental error. This argument has been discussed by Wänke in the preceding communication. Contrary to Wanke's statement, the estimation of the exposure ages is not based on assumptions concerning the energy spectrum of the cosmic-ray particles producing the rare gases or on whether the ratios are a measure of the mean energy. The estimation is based only on experimental observations which indicate a relationship between the ratios helium-3/argon-38, helium-3/helium-4, neon-4/argon-38 and the production-rate of the radioactive nuclides chlorine-36 and argon-39 by cosmic rays.

The relationship found is to be expected from the results of the measured proton-production cross-sections cited by Wänke[1,2]. It was found that the proton-production ratio $\sigma_{He} + \sigma_T/\sigma_{Ar^{38}}$ (which is to be compared to helium-3/argon-38 in meteorites) changes from about 8 with 400 MeV. protons to 23 with 3 BeV. protons; while the proton-production ratio $\sigma_{He^3} + \sigma_T/\sigma_{He^4}$ changes from 0·19 at 400 MeV. to 0·26 at 3 BeV. The results on the neon production are at present too fragmentary for a comparison; however, from the systematics of spallation processes (Friedlander, G., private discussions and ref. 3) it is to be expected that the ratio neon-21/argon-38 will show a similar change. These cross-section measurements indicate that the proton-production ratios helium-3/argon-38, helium-3/helium-4 and neon-21/argon-38 change with proton energy and lead one to suspect that this is the reason for the variation of the ratios in meteorites.

On the other hand, more recent, but preliminary, results[4] indicate that the ratio helium-3/argon-38 does not vary with energy. In addition, recent measurements of Signer and Nier[5] indicate that in a given meteorite the ratio helium-3/argon-38 is constant to at least 5 per cent while the helium-3/helium-4 and neon-21/argon-38 ratios vary by about 15 per cent. Both these observations are in agreement with Wänke's statement that the ratio helium-3/argon-38 is not a good measure of the mean energy of the particles.

If this view is substantiated by further experiments, then the observed relation between cosmic-ray production-rates and the helium-3/argon-38 ratio must have some other explanation. For example, as pointed out by Wänke, the ratios of primary to secondary particles may vary depending on the meteorite size or location of the sample inside the meteoroid. In any event, the use of the helium-3/argon-38, helium-3/helium-4 or neon-21/argon-38 ratio to estimate a cosmic-ray production-rate is based on an empirical relationship and can be disproved only by further experiments.

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CHEMISTRY

Crystal Structures of 1-Chloro-2,4-Dinitrobenzene and 1-Bromo-2,4-Dinitrobenzene

THE rates of reaction for nucleophilic aromatic substitution are affected if the replaced group has one, or two, groups ortho- to it. In particular, the effects of nitro groups in these positions (and in meta- and para-positions) have been studied in many reactions. Generally, these groups contribute two competing effects which control the reaction-rate. First, a maximum activation through electron transfer is attained if the nitro group is planar with the benzene ring. However, spatial considerations often forbid this coplanarity in the case of ortho-substitution, and there exists a competing de-activation due to the twist of the nitro group from the plane of the benzene ring. In the extreme case of two ortho-substituents, the activating effect of the nitro groups

is greatly diminished by this steric effect and may result in a net de-activation.

The reaction-rates of many nucleophilic reagents with 1-halo-2,4-dinitrobenzenes have been measured in several laboratories[1-4] and a comprehensive review of the subject of nucleophilic substitution reactions and their mechanism has been published by Bunnett[5]. Kruger and Bednova[1] showed that, although chlorine normally accelerates reaction, the acceleration was weaker when it was ortho- to an activating nitro group, when reactions of methoxide with 1-chloro-2,4-dinitrobenzene were studied. The de-activation was attributed to rotation of the nitro group, thus interfering with the partial conjugation of the C—N bond. Parker[6], again investigating reactions of methoxide and 1-halo-2,4-dinitrobenzenes, observed these steric effects and found the order of de-activation to be I > Br > Cl > F, and suggested that this was due to the relative sizes of the halogen atoms causing varying angles of rotation of the ortho-nitro groups. As no direct measurements of the molecular dimensions of these molecules had been made, it was suggested by Dr. J. Miller, of the Department of Chemistry, University of Western Australia, that single-crystal X-ray diffraction structure analyses of the 1-halo-2,4-dinitrobenzenes be undertaken to measure accurately these angles of twist of the 2-nitro groups. Samples of the chloro-, bromo-, iodo- and fluoro-compounds were kindly provided by Dr. J. Miller for the investigation.

Preliminary studies of the compounds showed two of them, 1-chloro-2,4-dinitrobenzene and 1-bromo-2,4-dinitrobenzene, to be isomorphous, conforming to the orthorhombic space-group *Pccn* and having eight molecules in the unit cell. 1-iodo-2,4-dinitrobenzene crystallizes in a lower symmetry and 1-fluoro-2,4-dinitrobenzene is a liquid at room temperature.

The chloro- and bromo-compounds were chosen for initial detailed study. Their cell dimensions are :

Compound	a_0	b_0	c_0
1-Chloro-2,4-dinitrobenzene	8·937 Å.	11·035 Å.	15 675 Å.
1-Bromo-2,4-dinitrobenzene	8 898 Å.	11·244 Å.	15 753 Å.

Intensity data up to $\sin \theta/\lambda = 0{\cdot}515$ for the $(0kl)$ and $(h0l)$ zones of both compounds were measured on a single-crystal Geiger counter spectrometer. These were extended to the full range of the sphere of reflexion for copper radiation by standard photographic techniques.

The heavy-atom co-ordinates were found from Patterson and difference Patterson syntheses projected on the (100) and (010) planes. The remaining atomic positions were located in Fourier syntheses on these planes, the signs of the Fourier coefficients being determined, initially, by the contribution of the heavy atom alone and then, later, by the combined contributions of the heavy atom and seven postulated light atoms.

The (100) and (010) projections of both compounds have been refined by successive difference syntheses and the 'reliability indices' for the calculated and observed structure factors are $R\ (0kl) = 0{\cdot}137$ and $R\ (h0l) = 0{\cdot}118$ for 1-chloro-2,4-dinitrobenzene and $R\ (0kl) = 0{\cdot}097$ and $R(h0l) = 0{\cdot}087$ for 1-bromo-2,4-dinitrobenzene.

As expected, the planes of the 2-nitro groups are rotated from the planes of the benzene rings, the measured angles being 39° for the chloro-compound and 40° for the bromo-compound. The proximity of the 2-nitro groups and the heavy atoms in these compounds has also caused distortions of the heavy atoms from the positions collinear with the 1- and 4-carbon atoms of the benzene rings. Thus the C_1-Hal bond is at about 5° to the line joining C_1 and C_4.

In addition, the planes of the 4-nitro groups are rotated from the planes of the benzene rings. These twists (about 15°) are presumably due to field effects associated with the neighbouring molecules.

The average bond-lengths at the present stage of refinement are 1·20 Å. for the N—O bonds and 1·45 Å. for the C—N bonds.

Assumptions attributing chemical de-activation of these compounds to the rotation of the ortho-nitro groups out of the benzene ring planes have been found to be justified stereochemically. However, the conclusion of Parker[6] regarding the relation of the relative twists of these groups and their de-activating powers has not been verified.

Although all the points of chemical interest in the structures have now been elucidated, evidence for thermal anisotropic motions of the heavy atoms and the atoms of the nitro groups has appeared in the difference maps. An analysis of these vibrations is in progress and a full report will shortly be published elsewhere.

During the course of these X-ray investigations a brief preliminary report of an investigation of the structure of 1-chloro-2,4-dinitrobenzene was published[7], but the results of only one projection were given, and there was consequently no discussion of the chemical significance of the results.

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Magnetic Resonance of Protons in Glasses

WE have been interested in the effect of sodium fluoride and calcium fluoride on molten silicates and phosphates, and the principal reactions are being investigated using kinetic and infra-red techniques. We have also been interested in the elimination of water from the melts by the fluorides and have used a proton magnetic resonance technique for studying the elimination. The infra-red technique has recently been used to investigate water elimination from silicate-glasses[1], but it would be difficult to obtain results using the same technique for glasses containing phosphate since these pick up water to a great extent and very quickly.

Sodium metaphosphate and potassium metaphosphate can be prepared by heating the sodium and

potassium dihydrogen phosphates respectively. The metaphosphates are produced from their respective acid salts by dehydration processes; hence to prepare these compounds containing water it is only necessary to heat the acid salts for a short time. The sodium metaphosphate glass and potassium Kurrol salt were prepared by heating the respective A.R. quality salts for 6 min. at 900° C. Similarly, borate-glass containing water was prepared by heating A.R. ortho-boric acid for 6 min. at 900° C.

Mixtures of sodium disilicate and sodium metaphosphate plus sodium disilicate and sodium pyrophosphate were saturated with water by heating the melts in a stream of steam at 1,000° C. for 8 hr. Carefully dried, analytical reagent quality sodium fluoride was added to each of these samples to give 10 weight per cent mixtures and the mixtures heated in attempts to eliminate the water.

Samples were quenched on a clean stainless steel plate and immediately crushed and weighed out in dry boxes maintained at 30–35 per cent relative humidity. 1-gm. samples were sealed in 'Pyrex' tubes which had been carefully dried at 400° C. for two to three days. During the sealing process, the 'Pyrex' tubes were connected to a drying tower containing phosphorus pentoxide, so the sample was not exposed to the air.

Proton resonances were observed using a Pound–Watkins marginal oscillator of conventional design operating at a fixed frequency of 21·750 Mc./s. The magnetic field was varied by connecting a motorized d.c. supply across field-bias coils wound around the poles of a permanent magnet. Tuning of the radio-frequency amplifier stage was employed to facilitate production of low oscillation-levels. The field was modulated at 280 c./s. and the output of the marginal oscillator passed through a phase-sensitive detector to give a derivative signal to a chart recorder.

The specimens were found to be easily saturated, and the resonance signals were therefore rather weak. Line-widths were about 4 œrsteds, and a modulation amplitude of 1·5 œrsteds was found to give optimum signal-to-noise ratio. The oscillation amplitude was maintained at a constant level corresponding to about 100 mV. across the specimen coil. A 5-sec. time-constant filter was used in the output stage of the phase-sensitive detector.

The signal strength was taken as the distance between maximum displacements of the derivative curve. It was estimated that any water content exceeding ¼ per cent would give a resonance signal detectable with this apparatus.

In the sodium metaphosphate series, samples of the glass were heated for 5, 10 and 20 min. with sodium fluoride. The proton signals are shown in Fig. 1 and it can be seen that the water, which is bonded in the lattice, is eliminated.

Similarly, water is eliminated by sodium fluoride from potassium Kurrol's salt, boron trioxide and the disilicate–metaphosphate mixture containing 15 per cent phosphorus pentoxide.

Further, an estimate of the accuracy of the determination of the number of protons by the resonance method was made by preparing two samples of boron trioxide in which the water content can be determined by titration[2]. The ratio of water contents in the samples by direct titration and the ratio of signal-to-noise ratio for the two samples are 3·4/2·8 and 8·3/6·5 respectively. We have also located

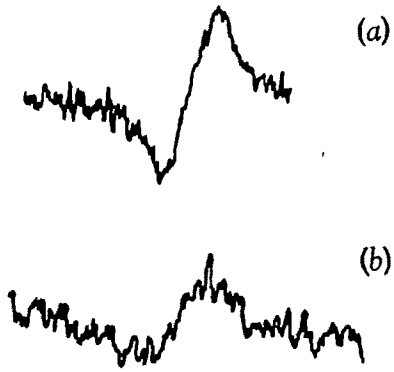

Fig. 1. (a) Proton resonance at 21 750 Mc./s. due to water in sodium metaphosphate glass.
(b) Proton resonance at 21·750 Mc./s. in the same sodium metaphosphate glass after being heated at 900° C. for 5 min. with dry A.R. quality sodium fluoride

proton resonance peaks in the other phosphate–silicate mixtures prepared.

Attempts to use the fluorine-19 chemical shift to determine the amount of P–F and Si–F bonding in the various samples were unsuccessful.

These results will be reported in more detail later.

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Atomic Polarizations of Chloro-, Bromo- and Iodo-benzene

IN 1940, Bottcher[1] suggested that the distortion polarization of a compound such as mono-chlorobenzene might be obtained by assuming it to be the mean of the total polarization for the parent compound, benzene, and for *p*-dichlorobenzene.

Dielectric constant and density measurements on benzene, chlorobenzene, *p*-dichlorobenzene, bromobenzene, *p*-dibromobenzene, iodobenzene and *p*-diiodobenzene, using carbon tetrachloride as solvent at 25°, have been made and the distortion polarizations of chloro-, bromo- and iodo-benzene calculated.

The atomic polarizations obtained by subtracting the electronic polarizations (R_D) from the distortion polarizations (P_D) determined in this manner are given in Table 1 under the heading P_A (exp.).

Table 1

Compound	P_A (exp.) (c.c.)	P_A (calc.)	0·05 R_D
Chlorobenzene	3·7 ± 0·4	2·8	1·6
Bromobenzene	2·5 ± 0·5	2·1	1·7
Iodobenzene	2·4 ± 0·7	1·8	2·0

The respective in-plane and out-of-plane bending frequencies (ν) for the mono-halogenobenzenes, as assigned by Pyler[2], have been substituted into an equation for a much simplified model of a halobenzene molecule. For this model the halogen

atom (X) is regarded as the 'bob' of a simple pendulum of length r, equal to the (aromatic) C—X distance; the bending force constants for the two bending modes is calculated from $k_B = 4\pi^2\nu^2 m_x$. When such values of k_B are substituted into the equation $P_A = (4\pi N\mu^2/3k_B)$ and these P_A values are added to the atomic polarization figure for benzene (1·6 c.c.), the P_A (calc.) figures listed in Table 1 are obtained.

Also listed in Table 1 are the estimates often used for the atomic polarizations, namely, that they are 5 per cent of the electronic polarizations.

Bottcher's method, when applied to the three mono-halogenobenzenes, gives values for the atomic polarizations of these molecules, which are in qualitative agreement with rough application of theory. Further, it indicates a decrease in atomic polarization with increasing mass of substituent in the series chloro-, bromo-, iodo-benzene, thus lending support to the idea[4] that atomic polarization cannot be assumed to be a fixed fraction of the electronic polarization of a molecule.

Details of this work will be published elsewhere.

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Ionic Conductances in Gels of Wheat Starch

POLYMERIC gel systems may be formed either by cooling a polymer solution, or by swelling a suspension of solid polymer particles in a suitable solvent. These two types of gelation process differ in one fundamental respect. Gel formation from solution is usually a thermoreversible process, and on warming, the system reverts back to a solution. On the other hand, gelation by swelling is thermally irreversible, and scarcely any shrinkage occurs on cooling.

Starch gelation in water is a typically irreversible process. Above 55°, granules of wheat starch swell irreversibly. On cooling, molecules from adjacent granules link up by hydrogen bonding and molecular entanglement to form a continuous network of swollen starch granules.

There is evidence in the literature[1,2] that gel formation from solution occurs with little or no change in the conductance of electrolyte present. This means that the water has a micro-viscosity similar to that of normal free water, although of course the bulk viscosity of the gel is considerably greater. However, it has previously been shown from the nuclear magnetic resonance spectra[3] that starch gelation has a very marked effect on the water structure. These changes should be reflected in the conductance, and it was therefore decided to study the conductance changes of sodium chloride in a number of starch–water mixtures during gelation. Conductivity measurements were made using a pair of platinum disk electrodes. The mixtures were heated slowly from 25° to 85° and afterwards cooled back to 25° again. During the early period of heating

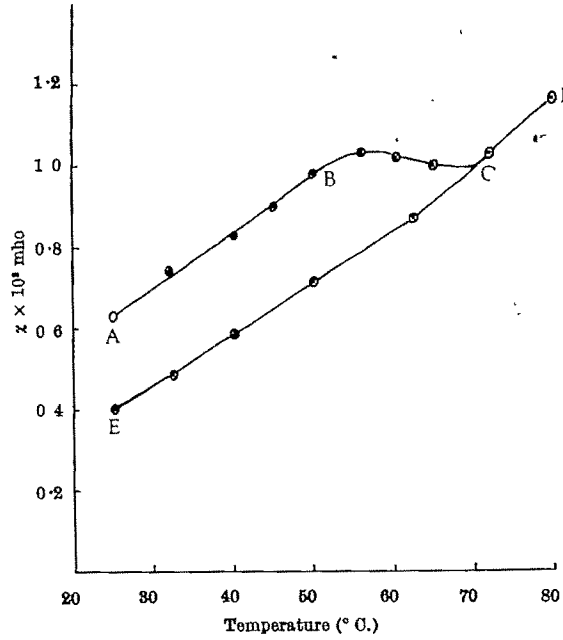

Fig. 1. Conductance of 0·412 per cent sodium chloride in 37 per cent starch

the system consisted of two phases, and the suspension was agitated before readings were taken. Above 55° gelation took place and the electrodes became firmly embedded.

Provided there was sufficient starch (12 per cent) to form a coherent gel, the conductances were always lower in the gel than in the suspension as expected. A typical example is shown (Fig. 1) in which the changes can be conveniently divided into three portions.

(1) The suspension AB before gelation has started. During this stage the changes in conductance are thermally reversible.

(2) The process of gelation BC during which the conductance falls. Gelation is an irreversible process and the line CB cannot be retraced if the system is cooled. On cooling from a point on BC, the conductance values fall on a line intermediate between AB and EC.

(3) The fully gelatinized system ECD. Gelation is complete at C and the conductivity starts to rise again with increasing temperature. The conductance is now thermally reversible, and on heating or cooling, the conductance values will always lie on the same curve ECD.

These changes in conductance can be correlated with the swelling behaviour of wheat starch. At 25° water is absorbed into the amorphous regions, and the granules swell about 30 per cent by volume[4]. Little further swelling occurs until about 55° when the granules suddenly begin to swell rapidly with increasing temperature[5]. This is the point B where the gel is first formed, at high starch concentration. The process of swelling and particle adhesion continues for about another 15°, the maximum swelling (at C) being governed by the amount of water available.

Having established the general pattern of behaviour, some more precise conductance (χ) measurements were made on suspensions and gels containing 37 per cent starch and varying amounts of sodium chloride, at 25° and 50°. Corrections for ionic

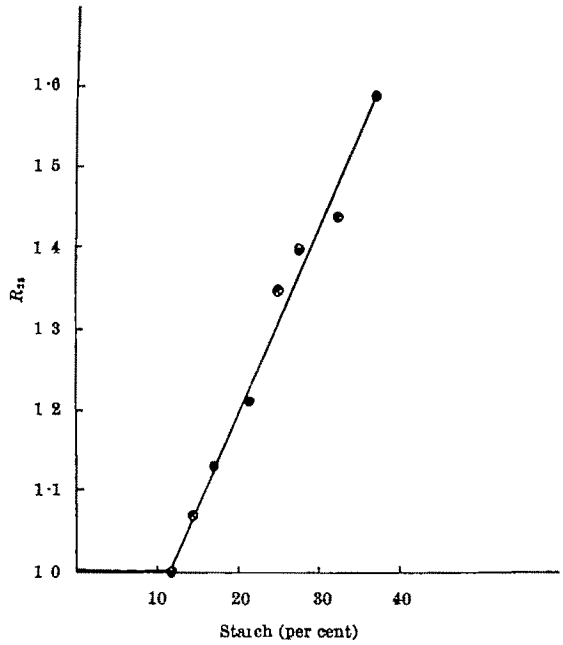

Fig. 2. Variation of R_{25} with starch concentration

impurity in the starch were made, by subtracting the values obtained during a blank experiment done in the absence of any added sodium chloride. The corrected results are given in Table 1 and Fig. 2.

It was found that $\frac{1}{\chi}\frac{\Delta\chi}{\Delta T}$ (and consequently the energy of activation for ionic mobility) over this temperature-range was 1·7 times greater in the gel than in suspension. This is in qualitative agreement with the increase in the micro-viscosity of the water after gelation, which has previously been established from the water proton line in the nuclear magnetic resonance spectra. The band-width of this line was found to increase on gelation, and there was no 'free' water line superimposed on the broader line. Therefore, all the water in the gel is in a more highly bound state, leaving no fibrils of free water, contrary to what has been postulated for some other gel systems.

The variation of the conductance behaviour with starch concentration follows a pattern similar to the variation of nuclear magnetic resonance water band-width. The ratio of conductance of sodium chloride in suspension and gel at 25° (R_{25}) increases almost linearly from 1·0 at 12 per cent to 1·6 at 37 per cent starch, showing that the water becomes increasingly bound as the starch concentration is increased above 12 per cent. Similarly the water proton line in the nuclear magnetic resonance spectra resembles that of pure water in swollen starch mixtures up to about 12 per cent concentration, but at higher concentrations the band-width increases. The similarity between these two sets of results suggests that the change in the water structure on gelation is the main factor contributing to the fall in conductance.

There may also be other factors. For example, it is possible that the ions do not penetrate into the granules, in which case the tortuous migration of ionic particles around the swollen granules would tend to reduce the conductance. However, it is known that some large molecules, for example the dye congo red, are easily absorbed by swollen granules even in the cold, and it therefore seems likely that sodium chloride penetrates into the granules. This is supported by the fact that swelling causes no detectable drop in conductance ($R = 1$) at starch concentrations just below the minimum starch concentration (12 per cent) for gel formation, where the swollen granules occupy about 50 per cent of the total volume.

It seems likely that these unusual conductance results are due primarily to the change in water structure. If this is so, the ratio R_{25} should be a rough measure of the micro-viscosity of the water in the gel, since the conductivity is approximately inversely proportional to the viscosity of the medium.

The increase in micro-viscosity on gelation has, on the basis of the nuclear magnetic resonance results, previously been attributed partly to the formation of a four co-ordinated water lattice around each starch hydroxyl group, and partly to the 'fixing' of these regions of solvated water, by the formation of a continuous polymer network on gelation. Both these factors become more marked at higher starch concentrations; this is reflected in the increase in R_{25}. It is worth pointing out that gelatin, which is itself ionic, shows no fall in conductance on gelation[1]. This is probably because gelatin has a smaller effect on the water structure due to its lower hydrogen bonding power and also because the polymer concentrations are lower in these gels. The anomalous behaviour of starch is due to its high degree of hydrogen bonding power, which has a marked effect on the water structure and also enables the starch to form a strong polymer network.

Table 1. CONDUCTANCE OF SODIUM CHLORIDE IN 37 PER CENT STARCH

	Sodium chloride (per cent)			
	0 206 per cent	0 412 per cent	0 824 per cent	1 647 per cent
R_{25}	1 64	1·62	1·51	1·50
Cg	0 026	0·030	0 028	0 027
Cs	0 016	0·015	0 016	0·016
$\frac{Cg}{Cs}$	1 6	2·0	1·75	1 7

R_{25} = Sodium chloride conductance in suspension at 25° / Sodium chloride conductance in gel at 25°

$Cg = \frac{1}{\chi}\frac{\Delta\chi}{\Delta T}$ for gel between 25° and 50°.

$Cs = \frac{1}{\chi}\frac{\Delta\chi}{\Delta T}$ for suspension between 25° and 50°.

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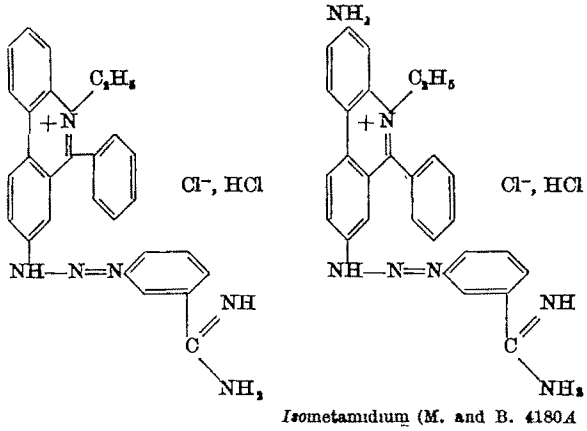
BIOCHEMISTRY

Structure of *Isometamidium* (M. and B. 4180*A*), 7-*m*-Amidinophenyldiazoamino-2-amino-10-ethyl-9-phenylphenanthridinium Chloride Hydrochloride, the Red Isomer present in Metamidium

THE trypanocidal drug, metamidium, first described by Wragg, Washbourn, Brown and Hill[1], was obtained from the coupling reaction between *m*-amidinobenzenediazonium chloride and homidium chloride. It was isolated as a mixture of purple and red compounds (55 and 45 per cent, respectively) which were

separated by fractional crystallization and shown to be isomeric. The red (M. and B. 4180*A*) was more active than the purple isomer, both therapeutically and prophylactically, against a laboratory strain of *Trypanosoma congolense* in mice. Wragg *et al.*[1], on the evidence available at the time, provisionally assigned diazoamino structures to these two isomers, and stated that work to verify these was being done. Several unsuccessful attempts were at first made to determine the structure of the red compound, and this has now been achieved by deamination which gave the desamino compound (I), which was identical in analysis, properties, and infra-red spectra with authentic specimens of (I) prepared by: (*a*) the coupling reaction of diazotized 7-amino-10-ethyl-9-phenylphenanthridinium chloride with *m*-aminobenzamidine, and (*b*) the coupling reaction of 7-amino-10-ethyl-9-phenylphenanthridinium chloride with *m*-amidinobenzenediazonium chloride.



*Iso*metamidium (M. and B. 4180*A*

(I) (II)

The evolution of nitrogen which occurred when the red and purple compounds were heated with 6 *N* sulphuric acid was given as evidence for the presence of a diazoamino group in both compounds (Wragg *et al.*[1]), although it was pointed out by these workers that for unexplained reasons the purple isomer gave considerably less than the theoretical volume of nitrogen. Further work has now shown that these reaction conditions were too drastic for a diagnostic test for the presence of a diazoamino group as distinct from an aminoazo system, and milder conditions will clearly differentiate the two systems. Thus, if the red compound (*iso*metamidium) is heated with cuprous chloride–3 *N* hydrochloric acid, the theoretical quantity of nitrogen is evolved in 7–9 min., while no evolution of nitrogen occurs even after prolonged heating of the purple compound under identical conditions. Thus only the red compound contains a diazoamino-group. Recent investigations into the structure of the purple compound have revealed that it is an isomeric aminoazo compound.

As a result of this work, the formulæ provisionally suggested for the two isomers by Wragg *et al.*[1] have to be modified, and the red isomer is now shown to have structure (II) (which was originally assigned to the purple compound).

Concurrently with this investigation the original coupling reaction has been studied and conditions[2] have been established under which *iso*metamidium (II) is the main product formed, the ratio of red : purple compound being as high as 9 : 1 (polarographic determinations carried out by Dr. P. O. Kane), and the pure product is readily isolated, by standard procedures, from the reaction mixture.

The trypanocidal activity of *iso*metamidium (M. and B. 4180*A*) has been confirmed in cattle, and the results of field trials in Africa are very encouraging.

Full details of the chemical work involved in the proof of the structure of *iso*metamidium and of the modified coupling reaction will be submitted in due course to the *Journal of the Chemical Society*.

I am grateful to Dr. H. J. Barber, Dr. J. N. Ashley and colleagues of this research organization for their discussions and helpful advice.

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1,3-Dialkyl-6-thioxanthines: a New Series of Bronchodilators and Coronary Va odilators

1,3-Dimethylxanthine (theophylline) is readily converted into the corresponding 6-thio derivative by treatment with phosphorus pentasulphide in pyridine. The choline salt (M. and B. 4926*A*) of this derivative is more active than choline theophyllinate in relaxing the bronchial muscle (guinea pig tracheal ring preparation) and in dilating the coronary vessels (dog heart-lung preparation). This result led us to prepare and examine a series of homologous compounds, the most active in these two respects being 3-*iso*butyl-1-methyl-6-thioxanthine (M. and B. 5924).

All the thioxanthines are obtained from the corresponding xanthines in high yield by refluxing for several hours with phosphorus pentasulphide in pyridine. It was established by spectroscopic and degradation studies that thionation occurs only in the 6-position.

The choline salt of 3-*iso*butyl-1-methyl-6-thioxanthine is a pale yellow, crystalline solid, m.p. 145–147°, which is more than 50 per cent w/v soluble in water at 20°. A 10 per cent w/v solution has a *p*H of 11. Choline 6-thiotheophyllinate, m.p. 146–149°, has similar solubility characteristics.

Pharmacologically the 6-thioxanthines are very similar to theophylline, the difference in their actions being essentially quantitative. Some of the 6-thioxanthines are very much more active as bronchodilators *in vitro*, M. and B. 5924 being about sixty times as active as choline theophyllinate. *In vivo* bronchodilator activity was assessed by determining whether pretreatment would protect guinea pigs against the lethal effects of a bronchoconstrictor aerosol. The 6-thioxanthines are effective, but the relative bronchodilator activity is much less than that observed with the isolated preparation. The 3-*iso*butyl-1-methyl derivative is also more active than choline theophyllinate in dilating the coronary vessels of the dog heart-lung preparation, in dilating the coronary vessels of the anæsthetized dog and in dilating the vessels of the hind leg of the dog perfused with heparinized blood. As diuretics, however, all the thioxanthines are less potent than choline theophyllinate. Comparative results are summarized in Table 1.

Table 1. RELATIVE ACTIVITIES OF CHOLINE THEOPHYLLINATE, CHOLINE THIOTHEOPHYLLINATE AND M. AND B. 5924
(The activity of choline theophyllinate has been expressed arbitrarily as 1)

Compound	Bronchodilator activity (guinea pig)		Coronary dilator activity (dog)	Diuretic activity (rat)
	In vitro	*In vivo*		
Choline theophyllinate	1	1	1	1
Choline thiotheophyllinate	5	1	2–3	< 1
M. and B. 5924	60	2	15	< 1

A full description of the chemical work will be submitted to the *Journal of the Chemical Society* and of the pharmacological work to the *British Journal of Pharmacology and Chemotherapy*.

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Ayapin, Scopoletin and 6,7-Dimethoxycoumarin from *Dendrobium thyrsiflorum* (Reichb. f.)

DURING the examination of plants for phenolic constituents, the orchid *Dendrobium thyrsiflorum* was found to contain three highly fluorescent constituents (E. C. Bate-Smith, personal communication). The substances were extracted from a leaf hydrolysate with amyl alcohol and chromatographed on Whatman No. 1 paper using several different solvent systems. All the substances concerned fluoresce strongly a light blue-violet colour which is changed to green when the paper is sprayed with 2 *N* sodium hydroxide. The R_F values in toluene/acetic acid/water (supernatant phase from 4 : 1 : 5 vol.) were 0·15, 0·77 and 0·85 and in 6 per cent acetic acid 0·43, 0·54 and 0·61. In Forestal solvent (hydrochloric acid/acetic acid/water) and butanol/acetic acid/water the R_F values were all too high to give good separation.

The reaction with sodium hydroxide strongly resembled that given by coumarin (R_F in toluene–acetic acid 0·9). The first substance, in fact, agreed in every respect with the well-known coumarin scopoletin. The other two substances, from their R_F values relative to those of scopoletin and coumarin, seemed likely to be polymethoxy- or methylenedioxy-coumarins. Samples of ayapin (6,7-methylenedioxycoumarin) and 6,7-dimethoxycoumarin were therefore synthesized, and a sample of the latter and also of 5,6,7-trimethoxycoumarin were obtained from Dr. F. E. King. The dimethoxycoumarin agreed in all particulars with the second unknown substance and ayapin with the third. Trimethoxycoumarin has virtually the same R_F as ayapin in toluene/acetic acid/water but its R_F value in 6 per cent acetic acid is much higher (0·76), and when the paper is sprayed with alkali its fluorescence changes to bright yellow-white. The hydrolysate was chromatographed on Whatman No. 3 paper in 6 per cent acetic acid, the three substances were eluted, and their ultra-violet absorption spectra compared with synthetic standards. All showed closely similar spectra with maxima at 345 mμ and 295 mμ, a shoulder at 260 mμ and minima at 270 mμ and 305 mμ. Since the absorption spectra are quite different from other related coumarins such as herniarin, daphnetin, limetin, it is concluded that 6,7-dimethoxycoumarin and ayapin are the substances present.

In order to determine the form in which these substances occur in the plant, an extract of a leaf was made with cold methanol. This was run on Whatman No. 3 paper in 6 per cent acetic acid. No free coumarins were present, but there were three distinct fluorescent bands which were cut out and eluted. On hydrolysis the slowest-running of these gave the dimethoxycoumarin, the second gave ayapin and the third gave a mixture of these two and scopoletin. It is concluded that these coumarins occur in combination, probably as the glycosides of the corresponding *o*-coumaric acids, and that the dimethoxycoumarin and ayapin both occur in more than one glycosidic form.

I wish to thank Dr. F. E. King for the specimens of dimethoxy- and trimethoxy-coumarins and Dr. E. C. Bate-Smith for helpful advice and the facilities of his laboratory.

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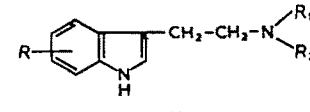
Reserpine Analogues

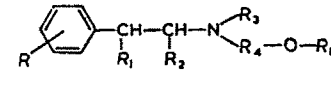
IT seems likely that the most interesting pharmacological properties of the natural alkaloid reserpine are mainly determined by three chemical groups in the molecule: (1) the β-indolylethylamine group, which is present in many other natural drugs (serotonine, ergot alkaloids); (2) a tertiary nitrogen atom which is substituted by three carbon chains, one of which (the ethyl group) is attached to the indole nucleus, while the other two form part of a ring system bearing (3) a hydroxyl group which is esterified by trimethoxybenzoic acid. The β-phenylethylamine group, which is very similar to the β-indolylethylamine group, is found in another group of drugs, the adrenaline family.

On the basis of these considerations we have synthesized a number of compounds the structure of which is more or less similar to that of reserpine, in the hope that these would have useful medicinal properties. These compounds fall into two classes: β-indolylethylamine derivatives, having the general formula I:



(I)

where R indicates the absence of substitution, or substitution by one or two hydroxyl or alkoxyl groups, and R_1 and R_2 are alkyl or hydroxy-alkyl groups which may be etherized or esterified; and β-phenylethylamine derivatives, II:



(II)

where R indicates the absence of substitution, or substitution by one to three hydroxyl or alkoxyl

groups, R_1 is H or OH, R_2, R_3 and R_4 are H, alkyl or alkylene groups, which may be partly cyclized to give piperidyl and *cyclo*hexyl rings, as in reserpine, and R_5 is an alkoxybenzoyl group.

We tested all these compounds for adrenolytic and spasmolytic activity, and for their effect on the central nervous system, the heart and the circulation, with the following results.

β-*Indolylethylamine derivatives*. Some of these show properties which are very similar to those of reserpine: they potentiate hexobarbital and ether narcosis in mice, like reserpine but to a lesser extent, and show a tranquillizing effect on the same animals. Some of these compounds also have a hypotensive effect on rats and dogs, and produce bradycardia in dogs.

β-*Phenylethylamine derivatives*. Unlike reserpine, these compounds have little or no effect on the central nervous system.

Those compounds in which the phenyl group is substituted by alkoxyl groups produce spasmolysis and bradycardia; two compounds of this group, with $R = p\text{-}OCH_3$, $R_1 = H$, $R_2 = CH_3$, $R_3 = C_2H_5$, $R_4 = —(CH_2)_4—$ and R_5 = 3,4,5-trimethoxybenzoyl or 3,4-dimethoxybenzoyl, show a strong papaverine-like spasmolytic effect, and also atropine-like properties. The other effects are considerably weakened.

Where the phenyl group is unsubstituted or substituted by hydroxyl groups (*p*- or *m,p*-), on the other hand, the depressor and adrenolytic activities predominate. Two such compounds, with $R = H$, $R_1 = H$, $R_2 = H$, $R_3 = C_2H_5$, $R_4 = —(CH_2)_3—$ or $—(CH_2)_2CH(C_2H_5)—$ and R_3 = 3,4,5-trimethoxybenzoyl, cause a depressor effect of long duration in narcotized cats. This effect begins instantaneously and is accompanied by a slight degree of bradycardia.

Clinical investigations are in progress. The chemical synthesis of these compounds and the pharmacological investigations will be described elsewhere.

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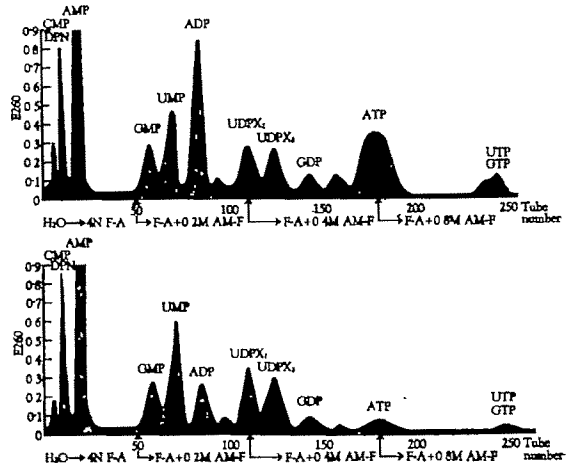
Effects of Short-term Weaning on the Acid-soluble Ribonucleotides of Rat Mammary Gland

THE physiological and biochemical changes which occur during early involution in the mammary gland are of great complexity; the gland regresses from a highly active secretory tissue to one in which the metabolic activity is greatly diminished. The ribonucleic acid and total protein content[1] has been reported to have decreased at two days of involution as does the activity of many enzyme systems[2]. Evidence is presented in this communication that marked changes occur in the acid-soluble ribonucleotides over as short a period of weaning as 12 hr.

Primiparous lactating rats of an albino strain were taken between the seventeenth to nineteenth day of lactation. The pups were removed from the mother at 9 a.m. except in experiments of 12 hr. weaning when the pups were removed at 9 p.m. Rats were killed by dislocation of the cervical vertebræ and the mammary glands were excised rapidly and put into liquid nitrogen. The acid-soluble ribonucleotides were extracted and examined by gradient elution on a 'Dowex-1' (formate form) column by essentially the method described by Hurlbert *et al.*[3].

The chromatogram obtained for the whole gland before weaning and after 12 hr. of weaning are shown in Figs. 1 and 2.



Figs. 1 and 2. Chromatograms of acid-soluble ribonucleotides extracted from the mammary gland of a late lactating rat before involution and after 12 hr. weaning, respectively. The nucleotides were eluted by the gradient elution method described by Hurlbert *et al* (ref. 3) with three changes of solvent, as shown, from 'Dowex-1' (formate form) ion-exchange columns and collected in 5 ml. fractions. In top chromatogram the optical absorptions greater than 1 0 for adenosine monophosphate were 1 8, 1 5, 1 5 for each 5 ml. fraction; in bottom chromatogram the figures were 1 8, 2 8, 2 8, 1 8 for each 5 ml. fraction.
Abbreviations. *C*, Cytidine, *A*, adenosine; *U*, uridine, *G*, guanosine; *MP*, *DP* and *TP*, mono-, di- and tri-phosphate, respectively, X_1, N-acetylglucosamine; X_2, glucose; *DPN*, diphosphopyridine nucleotide, *F-A*, formic acid; *AM-F*, ammonium formate

On comparison of these two chromatograms it will be noticed that there is a striking decrease in the content of adenosine di- and tri-phosphates, with a correspondingly large increase in the adenosine monophosphate. This dephosphorylation seems to be general for the other nucleoside phosphates, although the uridine diphosphate complexes of acetylglucosamine and glucose are unaffected. Since the adenosine phosphates are most abundant the time course of this dephosphorylation was followed by plotting the time of weaning against the ratios of adenosine di- and tri-phosphates to adenosine monophosphate. It should be borne in mind that adenosine triphosphate is not present as a pure fraction in the chromatogram but contains other nucleotides, uridine diphosphate being the main one. This fraction at late lactation normally contains about 65 per cent adenosine triphosphate[4].

Table 1

Animals used in experiment	Hours of weaning	Total acid-soluble ribonucleotide (μmoles/gland)
2	0	16 7
1	2	14 5
1	4	10 2
1	6	10 5
1	8	15·5
2	12	13 5
	Hours of lactation after 12-hr weaning	
2	2	20 5
1	4	14 7
		Mean = 14 5 S E M. = 1·09

Fig. 3 shows these ratios decrease slightly up to about the sixth hour, after which they fall rapidly to the eighth hour ; from here the low values attained are constant. When lactation is restarted after 12 hr. weaning, by the re-introduction of the pups, the ratios can be seen to rise steeply, the normal lactating values being reached by 2 hr. After 4 hr. of suckling these values are still obtained. This indicates that the phenomenon is unlikely to be wholly due to diurnal variations and that even after 12 hr. weaning the dephosphorylation of adenosine di- and tri-phosphates can be reversed. Another point which emerges (see Table 1) is the constancy of the total acid-soluble ribonucleotide content of the gland throughout all the experiments undertaken. This would suggest that the catabolism of the nucleotides is not enhanced by the weaning period of 12 hr.

It has been reported by Turner[5] that weaning affects the fat composition of milk ; longer periods of weaning giving rise to a lower fat content of the milk. It has been suggested that the cause is the retention by the mammary cells of fat components due to the high pressure developed in the mammary gland during weaning while the more permeable components are secreted into the alveoli of the mammary gland.

The presence of alkaline phosphatase in milk has been reported by Morton[6], and, although its function is not clearly understood, there seems little doubt that it originates in the alveolar cells of the mammary gland. It is conceivable that weaning would lead to a complete or partial retention of alkaline phosphatase in the same manner as occurs with fat under similar conditions. Such a retention would render the acid-soluble ribonucleotides vulnerable to enzymic dephosphorylation.

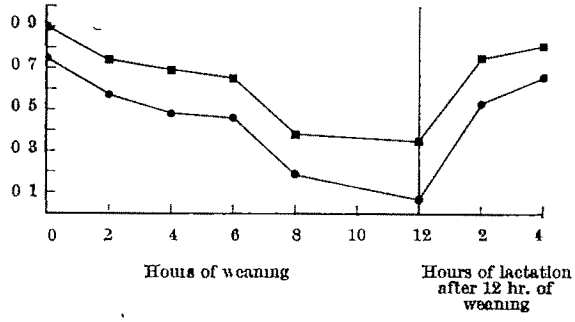


Fig. 3. Time course of dephosphorylation of adenosine polyphosphates. ■, Ratio of adenosine di- to mono-phosphate ; ●, ratio of adenosine tri- to mono-phosphate

Further support for this suggestion of retention by the cell of phosphatases comes from the observed rise in pressure during weaning. Tgetgel[7] has shown that in the cow pressure in the udder increases slowly up to about the fourth hour and thereafter rapidly Assuming a similar type of pressure curve in the rat mammary gland the drop in the ratios of adenosine triphosphate and diphosphate to monophosphate mirrors remarkably this increase.

Since adenosine di- and tri-phosphates are known to play an important part in many biosynthetic reactions which are active in the lactating mammary gland, it is possible then that the levels of the mono-, di- and tri-phosphorylated nucleosides could govern the rates of biosyntheses. Thus the rate of milk production of the rat mammary gland may be maintained by a 'feed-back' mechanism involving an increasing phosphatase activity in the cell coupled to an increasing accumulation of milk in the mammary gland.

My thanks are expressed to Drs. A. L. Greenbaum, and T. F. Slater for their guidance and helpful criticism. This work was made possible by a Medical Research Council Studentship award.

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Reduction of α-Ketobutyrate by Human Serum

DURING the course of investigations into serum transaminase activities[1], it was observed that α-ketobutyrate (2-oxobutanoate) underwent enzymic reduction in the presence of serum and reduced diphosphopyridine nucleotide. At the time this was interpreted as being due to serum lactic dehydrogenase because a commercial sample of crystalline lactic dehydrogenase prepared from rabbit skeletal muscle reduced α-ketobutyrate almost as readily as its normal substrate, pyruvate[2]. Further work, however, has indicated differences between the action of serum on α-ketobutyrate and its action on pyruvate.

Dehydrogenase activities were measured spectrophotometrically at 340 mμ in 0·067 *M* Sørensen phosphate buffer at *p*H 7·4 (ref. 3). Temperature corrections were applied and all results were adjusted to 25°. The results of a typical experiment on the effect of variation of substrate concentration on the dehydrogenase activity of normal human serum is shown in Fig. 1. Maximum activity against pyruvate occurred when the substrate concentration was $0 \cdot 33 \times 10^{-3}$ *M* and at higher concentrations appreciable substrate inhibition occurred. When α-ketobutyrate was used, activity was maximal at a concentration of $3 \cdot 3 \times 10^{-3}$ *M*. The Michaelis constants calculated from these were $Km = 1 \cdot 0 \times 10^{-4}$ for pyruvate and $6 \cdot 7 \times 10^{-4}$ for α-ketobutyrate. These figures are of comparative value only since no account has been taken of the presence in serum of possible inhibitors.

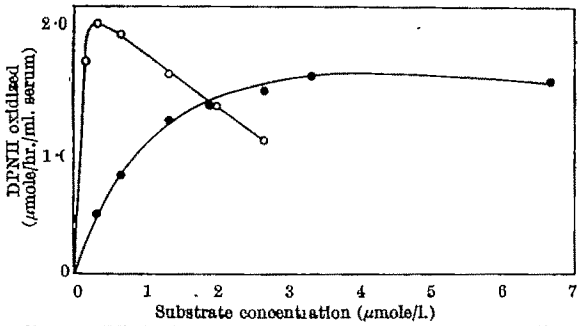

Fig. 1. Effect of changes in substrate concentration on the dehydrogenase activity of serum against pyruvate (○) and α-ketobutyrate (●)

but repetition of the experiment with other normal sera gave similar curves.

The effect of *p*H variation was measured using optimal substrate concentrations and the results appear in Fig. 2. The activity against α-ketobutyrate was maximal at *p*H 7·4 and was appreciably less at *p*H 8·0 whereas that against pyruvate was increased at the higher *p*H value.

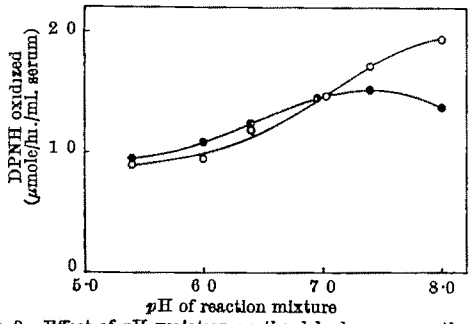

Fig. 2. Effect of *p*H variation on the dehydrogenase activity of serum against pyruvate (○) and α-ketobutyrate (●)

Over the range 21–28°, the temperature coefficient was found to be linear in both cases, but was slightly greater for pyruvate (8 per cent/deg. C.) than for α-ketobutyrate (6 per cent/deg. C.).

No inhibition of enzymic activity by a final concentration of $1 \cdot 67 \times 10^{-3}$ *M* azide, fluoride, cyanide, iodoacetate, sequestrate or oxine was observed, but $6 \cdot 67 \times 10^{-3}$ *M* cyanide reduced the activity against both substrates to a similar extent.

Four normal sera were fractionated by means of continuous paper electrophoresis using barbitone buffer of *p*H 8·6 ($\mu = 0 \cdot 05$). Lactic dehydrogenase activity was detected in the α_1-, α_2-, β- and γ-globulin fractions. The enzyme present in the β- and γ-globulin fractions, however, was much more active against pyruvate than against α-ketobutyrate whereas that in the α-globulin fractions showed only slightly greater activity against pyruvate (Fig. 3).

The dehydrogenase activities of a number of normal and pathological sera were examined. The ratio of the activities against pyruvate and α-ketobutyrate was found to vary between 1·4 : 1 and 1·1 to 1, figures well outside the limits of experimental error.

The differences in temperature coefficients, Michaelis constants and *p*H optima shown by serum towards the two substrates could possibly be explained by the effect of substrate variation on a single enzyme system. This is unlikely since serum lactic dehydrogenase has been shown to be electrophoretic-

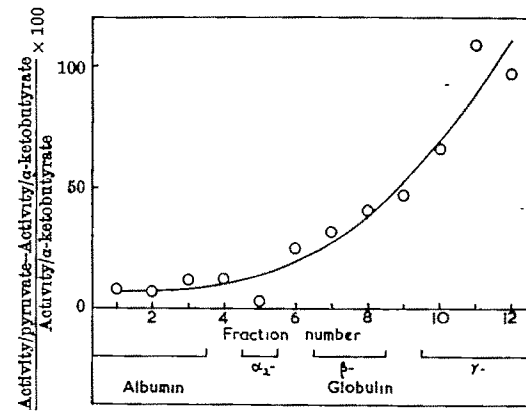

Fig. 3. Percentage differences in the dehydrogenase activity of electrophoretic fractions of human sera towards pyruvate and α-ketobutyrate. 2 ml. serum was separated into 12 fractions which were assayed separately for enzyme activity. Each point represents the mean percentage difference in the activities against these substrates exhibited by four different sera. Differences were not included when the total activity was less than 0·20 μmole/hr.

ally heterogeneous[4–7], and we have demonstrated that, although each globulin fraction exhibits activity against both pyruvate and α-ketobutyrate, the relative activities in each fraction are not parallel. It is therefore suggested that this variation indicates a difference in the properties of the components of serum lactic dehydrogenase or that there exists in serum an enzyme other than lactic dehydrogenase capable of reducing α-ketobutyrate.

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Composition of the Free Fatty Acid Fraction in the Plasma of Human Arterial Blood

The importance of free fatty acids as the main form in which fat is mobilized from depots and extracted by tissues has been stressed during the past few years. Several methods for their estimation in plasma are now available. One of the most widely used is that of Gordon *et al.*[1], which seems to measure the long-chain fatty acids[2] more specifically than any other. The exact composition of the fatty acids which are extracted from human plasma by this method has not, however, been determined. Their composition is of importance in metabolic studies where a knowledge of the mean molecular weight, double-bond index, and oxygen equivalent may be required.

We have analysed the free fatty acids extracted from the plasma of arterial blood by Gordon's method in eleven people who had fasted overnight. After titration, the soaps of the fatty acids in the alkaline ethanol–water phase were reconverted into free fatty acids which were methylated by means of diazo-

methane. The methyl esters were then diluted in diethyl ether and analysed in a Pye argon chromatograph. Polyvinyl acetate was used as the stationary phase, supported on 'Celite' (100–120 mesh). This stationary phase gave a separation at least as good as polyethylene glycol adipate and it had the further advantage of easier preparation and greater stability in the operating temperature (160–165° C.). The identification of the chromatograph peaks was made by using pure standards, supplemented by the method described by F. P. Woodford and C. M. Van Cent[3]. The area of each peak was measured by the triangulation procedure.

The main constituents are listed in Table 1. They are expressed as percentages of the total area of the major peaks. Oleic acid accounted for almost half. Apart from these major components, small traces of other fatty acids were found. These appeared to consist of *n*- nonanoic (pelargonic), decanoic (capric), pentadecanoic (15 : 0) and heptadecanoic (margaric) acids. Branched-chain fatty acids were also found as branched 14 : 0, 15 : 0, 16 : 0 and 18 : 0. The double-bond index[4] was 24·41 ± 3·7 (mean ± *S.D.*). The mean molecular weight was found to be 270 8, which is lower than it has previously been assumed. The mean number of oxygen molecules required for complete oxidation of one equivalent of fatty acid found during titration was calculated to be 24·32.

Table 1

Fatty acids		Mean (per cent) *S.D.*
Lauric	(12 : 0)	0·62 ± 0 16
Myristic	(14 · 0)	3 91 ± 1 87
Myristoleic	(14 . 1)	0 70 ± 0·34
Palmitic	(16 : 0)	25·12 ± 1·51
Palmitoleic	(16 : 1)	7·52 ± 2·14
Stearic	(18 : 0)	9·43 ± 2 33
Oleic	(18 : 1)	45 54 ± 4·42
Linoleic	(18 2)	7 04 ± 1·59

The results are different from those obtained by Dole *et al.*[4], who used Dole's method of extraction[5] of free fatty acids from plasma of human venous blood. The chief difference is in the percentage of oleic acid present, which Dole *et al.* found to be 28·9 per cent, and in the double-bond index which they found to be 28.

These differences may be due to variations in the diet of the subjects studied. Theoretically they could also be due to changes which might occur between arterial and venous blood. Work which is being carried out in this laboratory, however, suggests that the changes in composition of free fatty acids during the passage of blood through a resting limb are very small. It seems likely, therefore, that the composition of the free fatty acids extracted depends on the method used.

We are grateful to Dr. S. Paul and Mr. T. D. Heyes of the Research Department, Lever Bros., Ltd., for technical advice and for providing us with pure standards of fatty acids

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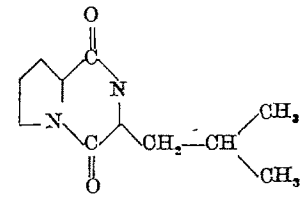
A New Cyclic Dipeptide from Peptone

WHILE investigating the antifungal principle derived from cultures of a *Bacillus subtilis* strain, a crystalline substance was obtained as one of the by-products. It was necessary to decide whether the crystals were a metabolite of the organism or originally contained in peptone used as a dietary essential. The same procedure succeeded in isolating the same crystals from peptone. The peptone was commercially available as 'Mikuni peptone' in Japan.

Purification was effected by recrystallization from a benzene–petroleum ether mixture. The crystals, purified as colourless needles, melted at 159·5° and was readily soluble in alcohols, chloroform and benzene and insoluble in water, ether and hydrocarbons. Carbon–hydrogen and nitrogen analysis and molecular weight measurement by Rast's method indicated molecular formulæ of $C_{11}H_{16}N_2O_2$. The infra-red spectrum showed absorption at 3,260 cm., 1,670 cm. and 1,630 cm, but no absorption of the 1,550-cm. region, which is characteristic of a cyclic amide. Significant optical rotation in methanol solution was observed as $[\alpha]_D^{2} = -132{\cdot}8°$. Hydrolysis with 6 *N* hydrochloric acid in a sealed tube at 110° for 20 hr. produced amino-acids. Qualitative analysis for the amino-acids by paper chromatography indicated equimolecular quantities of proline and leucine. All the results are in agreement for a cyclic dipeptide composed of two parts, proline and leucine.



It is perhaps of some interest that one of the 2,5-piperazinediones is contained in a natural substance, although certain proof of its original existence in raw meat evidently needs further investigation.

Work on the biological activity of the peptide is being carried on in several organisms.

We are grateful to Dr. Ichiji Mibuchi, Shizuoka College of Pharmacy, for discussion.

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Stabilization of Thymidylate Kinase Activity by Thymidylate and by Thymidine

WE have recently reported that an increase in thymidylate kinase activity occurs in rat liver and kidney following injection of thymidine into the intact animal[1]. Subsequent work has revealed that this enzyme activity is labile in the absence of, but stable in the presence of, thymidylate or thymidine. In this communication we wish to report the results of this work on stabilization of thymidylate kinase activity, and to consider the possible relation of these observations to the increase in kinase activity which follows thymidine administration.

Liver and thymus were removed from 200–300 gm. male Wistar rats, which were killed by decapitation. Regenerating liver was obtained from rats subjected

to 70 per cent hepatectomy[3] under ether anæsthesia 48 hr. earlier. Frozen calf thymus was obtained from commercial sources. Tissue extracts were prepared by grinding in an all-glass homogenizer 200 mgm. of acetone powder[3] with 2 ml. of ice-cold 0·1 *M tris*-(hydroxymethyl)aminomethane (*tris*) buffer, *p*H 7·5, or 1 gm. of fresh tissue with 5 ml. of buffer, followed by centrifugation at 0° for 10 min. at 10,000 r.p.m. Nucleosides and nucleotides of the highest purity commercially available were used. Thymidine and thymidylate were further purified by ion exchange and paper chromatography. Thymidylate-^{32}P was synthesized chemically from thymidine and ^{32}P-orthophosphoric acid by the procedure described by Hurwitz for cytidylic acid[4] and purified by ion exchange and paper chromatography. 98 per cent of the radioactivity in the final product was hydrolysed by snake venom phosphatase and 99 per cent by semen phosphomonoesterase[6]. Thymidylate kinase activity was assayed by a slight modification of the method of Lehmann *et al.*[5]. In the first stage of the procedure three components were employed: 0·1 *M tris* buffer, *p*H 7·5 (150–195 µl.), tissue extract (5–50 µl.), and substrate mixture (100 µl.) of the following composition: 40 µmoles of *tris* buffer (0·1 *M*, *p*H 7·5), 4 µmoles of magnesium chloride, 2 µmoles of adenosine triphosphate and 40 mµmoles of thymidylate-^{32}P containing 50–200 c.p.m./mµmole. The sequence of addition of each component was found to be important (see below), and for maximum enzyme activity the reaction was started by adding tissue extract as the last component. The reaction mixture was incubated for 15 or 30 min. at 37°, and the reaction was stopped by heating in a boiling water-bath for 2 min. In the second stage the unreacted thymidylate was hydrolysed with semen phosphomonoesterase as described[6]. Finally, the phosphomonoesterase-resistant material was adsorbed on charcoal, which, in turn, was collected on a membrane filter ('Ultraflex', Schleicher and Schuell Co.), washed thoroughly with cold water, dried, and counted with a micromil end-window counter. All values were corrected for a blank containing no enzyme. A unit of enzyme activity is defined as that amount of enzyme which in 1 hr. renders 100 mµmoles of thymidylate resistant to phosphomonoesterase. The specific activity is expressed as units per mgm. of protein, determined by the method of Lowry *et al.*[7].

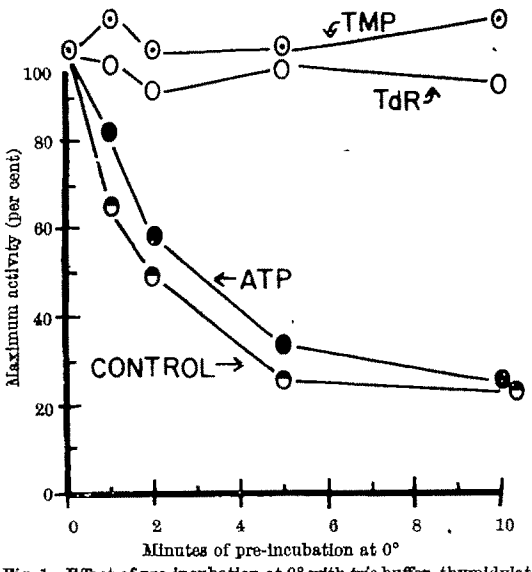

Fig. 1. Effect of pre-incubation at 0° with *tris* buffer, thymidylate (TMP), adenosine triphosphate (ATP) and thymidine (TdR) on thymidylate kinase activity. 5 µl. (200 µgm. protein) of an extract of 48-hr. regenerating rat liver acetone powder was pre-incubated at 0° with 195 µl. of *tris* buffer alone ('control'), or with buffer containing 1 mµmole of thymidylate, 10 mµmoles of thymidine, or 10 mµmoles of adenosine triphosphate in a final volume of 200 µl. At the intervals indicated, enzyme activity was determined by adding 100 µl. of substrate mixture (cf. text) and incubating at 37° for 30 min. The results are expressed as percentage of maximum enzyme activity, determined by assaying the extract without pre-incubation

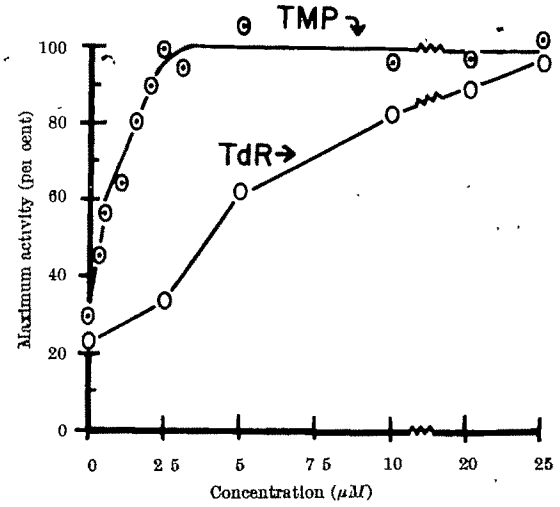

Fig. 2. Effect of thymidylate (TMP) and thymidine (TdR) concentration on thymidylate kinase activity during pre-incubation at 0°. Tissue extract (as in Fig. 1) was pre-incubated at 0° for 10 min. with 195 µl. of *tris* buffer containing the indicated amounts of thymidylate or thymidine. The activity was assayed and the results expressed as in Fig. 1

For studies of enzyme stability a dilution test was devised. Tissue extract was diluted with *tris* buffer to a final volume of 200 µl., and the mixture was 'pre-incubated' at 0°, usually for 10 min. Substrate mixture, 100 µl., was then added and thymidylate kinase was assayed as described above. Compounds tested for their ability to protect the enzyme were incorporated into the buffer used for dilution.

'Pre-incubation' of tissue extract in *tris* buffer at 0° prior to incubation at 37° with the substrate mixture resulted in a rapid, irreversible decrease of enzyme activity to a minimal value of 20 per cent (curve marked 'control' in Fig. 1) of that found in the same extract assayed without pre-incubation. This observation suggested that a substance in the substrate mixture was protecting the enzyme against loss of activity. Hence, adenosine triphosphate and thymidylate were added separately to the buffer in which the tissue extract was diluted and pre-incubated. Enzyme activity was protected fully when thymidylate was present in the diluent (curve marked TMP in Fig. 1), but adenosine triphosphate had no effect. Thymidine also protected enzyme activity (Fig. 1), but for full protection 10 times as much thymidine (25 µ*M*) was required as compared with thymidylate (Fig. 2). The following compounds at concentrations of 2·5 µ*M* and 25 µ*M* did not protect thymidylate kinase activity in the dilution test: the monophosphates of adenosine, guanosine, cytidine and uridine, and the corresponding deoxyribonucleotides; cytidine, uridine, deoxycytidine, deoxyuridine, and thymine. Bovine serum albumin, ribonucleic acid and deoxyribonucleic acid were also without effect. The supernatant solution obtained by boiling

liver extract for 2 min. followed by centrifugation protected the enzyme in the dilution test. Boiled extract from regenerating liver exerted a greater protective effect than did that from resting liver. The protective factor in boiled extract could be adsorbed on activated charcoal and eluted with ammoniated ethanol. Although it has yet to be identified, it is presumed to be thymidylate or thymidine in view of the specificity of these compounds with respect to enzyme stabilization.

The inclusion of 10 m*M* thymidine in the buffer used for extracting fresh tissue or acetone powder has resulted not only in stabilization of thymidylate kinase activity in the dilution test, but also in a larger yield of enzyme activity (Table 1). This observation has proved of practical value in our present efforts to purify the enzyme. With preparations from regenerating rat liver full recovery of kinase activity is achieved following dialysis against thymidine at *p*H 7·5, but in the absence of thymidine activity is completely lost. This is also true for other manipulations, such as salt fractionation and gel adsorption.

Table 1. EFFECT OF THYMIDINE IN THE EXTRACTION MEDIUM ON THYMIDYLATE KINASE ACTIVITY

Preparation	Extraction medium	Thymidylate kinase activity (units/mgm. protein × 10^3)	
		Control	Pre-incubated for 10 min.
48-hr. regenerating rat liver acetone powder extract (5 μl.; 200 μgm. protein)	*Tris* buffer	26·9	6·1
	10 m*M* thymidine in *tris* buffer	32·1	30·9
Resting rat liver extract (50 μl.; 900 μgm. protein)	*Tris* buffer	1·3	0·7
	10 m*M* thymidine in *tris* buffer	2·4	2·7
Rat thymus extract (20 μl.; 140 μgm. protein)	*Tris* buffer	74·2	15·7
	10 m*M* thymidine in *tris* buffer	132·0	144·0
Frozen calf thymus acetone powder extract (5 μl.; 100 μgm. protein)	*Tris* buffer	84·0	22·0
	10 m*M* thymidine in *tris* buffer	117·0	120·0

The demonstration that thymidylate kinase activity is labile under certain conditions, but is stabilized by thymidylate and by thymidine, suggests that the increase in enzyme activity in rat tissues following *in vivo* thymidine administration is at least in part attributable to protection of the enzyme by its substrate. Work now in progress with purified enzyme preparations is designed to test this hypothesis and to elucidate the mechanism of enzyme protection by thymidine and by thymidylate.

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PHYSIOLOGY

Specificity of the Effects of Cardiac Glycosides on the Rhythmic Contraction of Single Cultured Cardiac Muscle Cells

FROM fragments of embryonic chick hearts treated with trypsin, single, rhythmically contracting cells can be grown in a fluid, semisynthetic culture medium[1]. Exposure of these cells to cardiac glycosides in concentrations as low as 10^{-9}–10^{-8} *M* results in an increase in the rate of beat[2]. In addition the pulsations appear to become stronger. At concentrations of 10^{-7} *M* and above, the acceleration of pulsation is soon followed, or is accompanied, by disturbances of automaticity and of co-ordinated contractile activity. By means of phase-contrast, high-speed microcinematography of cells anchored to the glass surface these effects could be studied in greater detail[3]. The motion pictures revealed changes at the cellular level which strikingly resembled some of the familiar manifestations of digitalis poisoning in the heart of animals and of man. Such phenomena as partial and complete block of propagation of the contraction wave (presumably due to block of conduction), bigeminal rhythm, ectopic beats, tachycardia, and fibrillation could all be observed in single isolated ventricle cells.

It seemed worth while to find out whether these effects were specific in the sense that they are elicited solely or preferentially by compounds possessing the various molecular features required for the characteristic action of the cardiac glycosides on the intact heart. By the use of compounds lacking one or the other of these features, but possessing the rest of them, it has been possible to establish a fairly high degree of structure-dependent specificity for the action of cardiac glycosides on cation movement in erythrocytes[4] and on respiratory cardiac tissue metabolism[5], and to rule out such specificity for certain effects exerted on contractile heart muscle proteins[6].

Two compounds of this type, hexahydroscillaren *A* and allocymarin, were selected for the experiments described below. They were compared to the closely related, biologically potent natural glycosides, scillaren *A* and cymarin. Hexahydroscillaren *A* is derived from scillaren *A* by hydrogenation of the doubly unsaturated six-membered lactone side grouping and of the 4,5-double bond in the steroid nucleus, the C_5-hydrogen atom assuming the α-orientation (*trans* junction of rings *A* and *B*). Allocymarin (17-*iso*cymarin) is formed from cymarin by inversion of the substituents at C_{17} of the nucleus, the butenolide ring becoming α-oriented. Except for an antagonism exhibited under certain conditions against scillaren *A*, hexahydroscillaren *A* has no significant effect on the heart, while the potency of allocymarin is about 1/100 that of cymarin[7]. Solutions of the glycosides in ethanol (5 mgm./ml.) were prepared and were appropriately diluted with culture medium prior to use.

Single pulsating myoblasts were grown under sterile conditions in sealed and inverted hollow-ground slides by the method referred to above from enzymatically and mechanically dissociated ventricular cardiac muscle of 13 days old chick embryos. After 24 hr. of incubation at 37° C. the initially spherically shaped cells had flattened on, and become fastened to, the surface of the cover slip. The culture

Table 1. COMPARISON OF THE EFFECTS OF HEXAHYDROSCILLAREN *A* AND SCILLAREN *A* AND OF ALLOCYMARIN AND CYMARIN ON ISOLATED PULSATING MYOBLASTS CULTURED FROM EMBRYONIC CHICK HEART VENTRICLES

Culture No	Glycoside	Concentration		Number of cells observed	Rate of pulsation, Mean ± standard deviation	*P*	Irregularities of pulsation
		μgm./ml.	μmoles/l.				
7	—	—	—	44	52 ± 17	~0 25	No
7	Hexahydroscillaren *A*	1 0	1 43	50	57 ± 17		No
7	—	—	—	22	55 ± 16	< 0 005	No
7	Scillaren *A*	0·1	0 14	13	84 ± 35		Yes
1	—	—	—	22	52 ± 21	~0 5	No
1	Allocymarin	1 0	1 82	48	57 ± 20		No
8	—	—	—	45	54 ± 28	< 0 005	No
8	Cymarin	0 1	0·18	87	72 ± 34		Yes

medium was then changed several times in order to ascertain that the rate of pulsation was not affected by fresh medium. A final change was made to medium containing glycoside or ethanol, the concentration of the latter corresponding to that of the alcohol in the glycoside solution (0·002 and 0·02 per cent). The cells were observed at 37 ± 0·3° C. with a phase-contrast microscope equipped with a warm stage.

Table 1 summarizes the results of experiments in which scillaren *A* and cymarin were used in final concentrations of 1·4 and 1·8 × 10^{-7} *M*, respectively, while the concentration of their structural analogues was set at 1 4 and 1 8 × 10^{-6} *M*. The results show that scillaren *A* and cymarin caused a significant increase in the rate of pulsation. They also caused previously quiescent cells to pulsate. In a number of cells disturbances of rhythm and contraction were observed, terminating in some instances in fibrillatory movements and stand-still. Hexahydroscillaren *A* and allocymarin on the other hand, though present at ten times higher concentrations than their cardio-active congeners, were without significant chronotropic action, did not induce rhythmicity in quiescent cells, and produced no irregularities of beat. Thus the structural requirements for the display of biological activity by steroid lactones are as stringent in the cultured embryonic heart cell, at least so far as the present structure–activity relationships are concerned, as they are known to be in the adult vertebrate heart.

These findings make us feel rather confident that in our previous work on the behaviour of cultured heart muscle cells in the presence of cardiac glycosides we had not been dealing with irrelevant phenomena. One is encouraged to pursue the study further of this variety of a cardiac cell for whatever new information it might yield on the cellular basis of cardiac glycoside action.

We are indebted to Prof. A. Stoll, Basle, for a gift of hexahydroscillaren *A* and scillaren *A* and to Prof. T. Reichstein, Basle, for a gift of allocymarin and cymarin.

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Adrenaline and Blood Lipids

ADRENALINE has a powerful effect on carbohydrate metabolism. The effect of this hormone on nitrogen excretion has also been studied[1]. However, little is known about its effect on blood lipids. In the present work, adrenaline was administered in doses of 1 mgm. to normal individuals after a 14-hr. fasting period. Blood samples were taken initially and every hour for 4 hr. after the injection. In all samples total lipids and phospholipid phosphorus were measured. For the determination of total fats the following method was used[2]: 0·1 ml. of plasma was applied to a filter paper and dried. The filter paper was previously washed with alcohol/ether solution 3 : 1. The paper with the dried plasma was soaked for 60 min. in a sudan black solution (100 mgm. of the dye in 100 ml of 50 per cent ethanol) and then washed three times for 15 min. with 50 per cent ethanol. The spots were cut and eluted in 6 ml. of 25 per cent acetic acid in ethanol. The colour density was determined at 590 μm. The results are expressed in mgm. of lipids per 100 ml. A calibration curve was prepared by using a standard solution of purified olive oil (1 per cent in a hot mixture of alcohol/ether 3 : 1). It was noticed from preliminary experiments that by this method nearly all lipids are measured. This method is more sensitive for determination of plasma lipids than visible lipæmia, and proved satisfactory for routine work.

For determination of phospholipids the Zilversmit–Davis method was used[3]. The results are expressed in mgm. of phospholipid phosphorus per cent.

The effect of adrenaline on plasma lipids is presented in Table 1. Normal untreated individuals show a trend towards an increase in total lipids in plasma, due probably to mobilization of depot fats. The phospholipid phosphorus remains practically constant. Individuals treated with adrenaline showed a slight decrease in total lipids accompanied by an increase in phospholipid phosphorus.

Table 1. EFFECT OF ADRENALINE ON PLASMA LIPIDS

	Control			Adrenaline		
	T.L.	*P.P.*	*R.*	*T.L.*	*P.P.*	*R.*
Before injection	307 ± 13 7	9·85 ± 0 22	3 17	312 ± 11 2	9 75 ± 0·81	3 12
First hour	317 ± 11 3	9·25 ± 0 29	2·93	300 ± 5·6	10·30 ± 0 09	3 43
Second hour	320 ± 9 4	9·30 ± 0·24	2 90	302 ± 4·1	11 90 ± 0·08*	3 94
Third hour	332 ± 6·3	9·50 ± 0·19	2 90	307 ± 8·2	12·70 ± 0·18*	4 09
Fourth hour	340 ± 7·2	10·00 ± 0·20	2·94	305 ± 9 3	10 40 ± 0·25	3·49

T.L., Total lipids (mgm. per cent); *P.P.*, phospholipid phosphorus (mgm. per cent); *R*, ratio *P.P./T.L.* The values represent the average of 18 individuals, after a 14-hr. fasting period Adrenaline was given, 1 mgm. subcutaneously.
* $P < 0·02$.

The effect of adrenaline on plasma is better illustrated by calculating the ratio phospholipid phosphorus/total lipid. There is a definite increase in this ratio after administration of adrenaline, which is evident after the first post-injection hour and lasts 1–3 hr.

That adrenaline may have an effect on lipid metabolism is suggested by the observation that large doses of adrenaline (1 mgm. per kgm. body-weight) in rabbits produce a calorigenic effect, 2–3 hr. after injection, along with a decrease in plasma fatty acids[4]. However, this experiment gives no information on phospholipid phosphorus, and the doses used do not approach any physiological or therapeutic dose. From our experiment the conclusion is drawn that adrenaline increases the percentage of phospholipid component of serum lipids.

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Catalase Activity of Mouse Liver and its Relation to the Condition of the Animal

IN papers dealing with methods of determining catalase activity in animal tissue, while dealing with the experimental conditions, usually little attention is paid to the condition of the animal. We have found the latter to be of utmost importance.

The two methods mostly employed in the determination of catalase activity in animal tissue, the titrimetric and gasometric method, have been compared by Greenstein[1] and by Dounce and Shanewise[2]. The former found different values; the latter workers obtained the same values in both methods. Chance[3] made a thorough spectrophotometric investigation of the decomposition of hydrogen peroxide by catalase.

In our experiments we used the apparatus described by Appleman[4]. The animal was killed by decapitation, the liver removed, weighed and homogenized with 3 ml. water in a Griffith tube. After centrifugation the supernatant was diluted with 0·1 *N* Sorensen phosphate buffer of *p*H 7·0. 3 ml. of this solution—equivalent to about 0·9 mgm. of tissue—were mixed in the Appleman apparatus with 5 ml. of 3 per cent hydrogen peroxide buffered with 0·1 *N* Sörensen phosphate buffer solution at 29° C. The unit of catalase activity (activity factor) is expressed as ml. oxygen per gram tissue (dotted lines in Fig. 1) or per whole liver (solid lines in Fig. 1) per second. The reproducibility was better than 5 per cent.

We used male homozygotic Swiss mice in order to exclude possible differences in liver catalase activity of the two sexes as reported by Adams[5].

We expected a normal distribution curve (symmetrically, positively or negatively J-shaped) of the activity factors of normal mice. Curve I was obtained (dotted lines, activity factors per gram; solid lines, per whole liver).

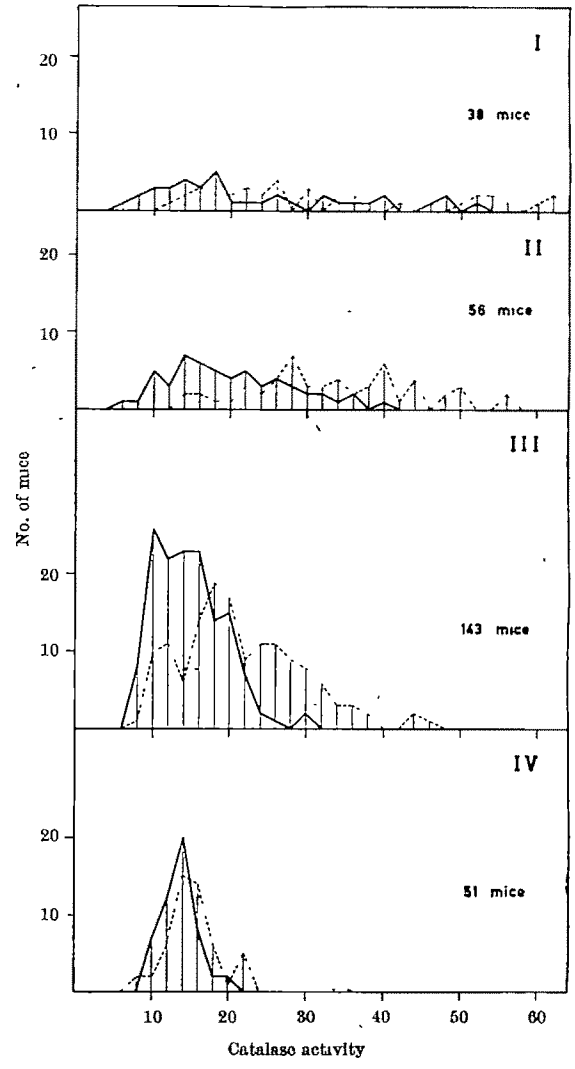

Fig. 1

Fasting the mice for 24 hr. before the analysis gave a slightly better picture (curve II).

We then reasoned that placing the animal in a 'steady state' probably would give better results. We imagined the liver to be composed of machinery (enzyme systems) and products (glycogen, proteins). When all mice receive the same food (quality and quantity) and have to produce the same amount of energy every day, one would expect that the liver would be in a 'steady state', and therefore the enzyme apparatus in all the mice livers would be practically the same. For the determination of liver catalase in this way we used mice 38–57 days old, which we raised in a stable at 24° C. They were exposed to artificial light from 8.30 until 17.00 hr. Every mouse of the same age received the same quantity and quality of food. Water was given *ad libitum*. The results are reproduced in curve III.

During cold nights the stable did not reach 24° C., so finally we set up an experiment using constant temperatures in the stable. Only normal growing mice—controlled by weighing—were used. All organs of the mice used were checked macroscopically for abnormalities; if any were found, the respective

activity factor was excluded. All mice were adult (about 90 days old). The result is shown in curve IV.

The spread in liver catalase activity factors per whole liver was thus reduced from 4–54 (curve I) to 8–22 (curve IV) or to 28 per cent of the original value.

With this method we tested substances separated from cancer tissue. When injected in mice the substances produce a marked decrease in liver catalase activity. Our results agree with those of Nakahara and Fukuoka with 'toxohormone'[6].

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Toxicity of a Single Subcutaneous Dose of Sodium Selenite in Pigs

SINCE the activity of 'factor 3' in liver necrosis in rats and exudative diathesis in chicks was shown to be dependent on selenium[1], compounds of this element have been shown to prevent other diseases induced by tocopherol-deficient diets. Sodium selenite (0·2 p.p.m.) as well as tocopherol acetate inhibit muscular degeneration in pigs fed grain, which causes field outbreaks[2]. Muscular degeneration in pigs is associated with a rise in plasma glutamic-oxaloacetic transaminase, but normal ornithine-carbamyl transferase[3]. When the disease is manifested, high glutamic-oxaloacetic transaminase levels rapidly return to normal after subcutaneous administration of 0·02 mgm. selenium (as Na_2SeO_3) per kgm. body-weight daily for three days (Orstadius *et al.*, unpublished work).

In veterinary medicine selenium has long since been known as a cause of poisoning in farm animals ('blind staggers', 'alkali disease'). 6–8 mgm. selenium per pound of body-weight as a single oral dose of sodium selenite is the minimum lethal dose for pigs[4]. Intoxicated animals showed emesis, diarrhœa, apathy, unwillingness to move, shivering and sometimes paresis before death. No thorough examination of the muscles was done.

Sodium selenite was given subcutaneously to pigs weighing 30–70 kgm. 2·0 mgm. and 1·2 mgm. selenium per kgm. body-weight caused death after 4 hr. and five days, respectively, during which time the pigs showed trembling, ataxia and paresis. Plasma glutamic-oxaloacetic transaminase was significantly increased (Fig. 1); but plasma ornithine-carbamyl transferase was normal, indicating that muscle but not the liver was affected[2]. At post-mortem examination the body musculature showed extensive dystrophy; but other organs, including the liver, showed no significant changes.

0·9–1·1 mgm. selenium per kgm. body-weight caused slight to moderate elevation of plasma glutamic-oxaloacetic transaminase in about half the

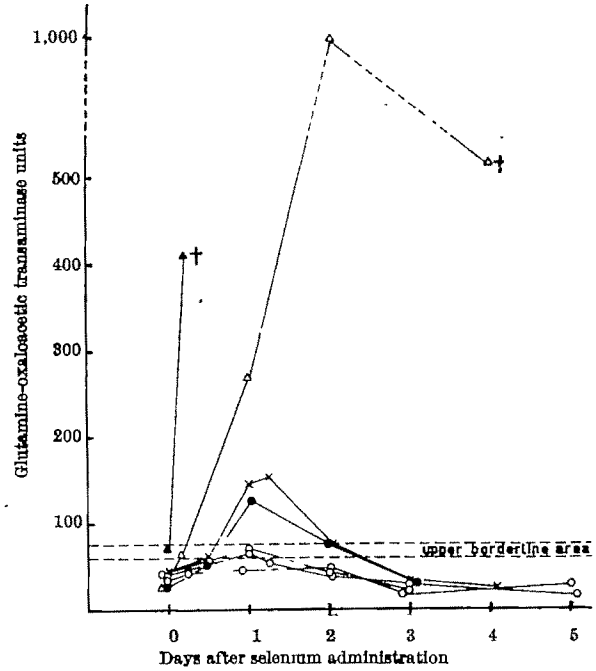

Fig. 1. ×, 0·9; ○, 1·0; ●, 1·1; △, 1·2; ▲, 2·0 mgm./kgm. body-weight

number of pigs so treated, but otherwise no symptoms of disease. The ornithine-carbamyl transferase values were normal. The elevations of glutamic-oxaloacetic transaminase returned to the starting-level after a day or two. Biopsy specimens from the longissimus dorsi showed no changes at microscopical examination.

0·8 mgm. selenium per kgm. body-weight or smaller doses gave no increase of transaminase.

It is remarkable that the anti-muscular degeneration effect of low selenium doses corresponds to a high vulnerability of the muscles to increased selenium doses.

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Effects of γ-Aminobutyric Acid and Picrotoxin on Spontaneous Activity in the Central Nervous System of the Crayfish

SINCE the extraction of an inhibitory substance (factor I) from mammalian brain[1], one constituent of which was identified as γ-aminobutyric acid[2], this constituent has been tried on a number of invertebrate preparations[3]. It imitates the action of inhibitory neurones in crayfish and on injection into the animal results in flaccidity[3]. The action of γ-aminobutyric acid is very similar to that obtained on stimulation of the inhibitory fibres in crayfish stretch receptors[4]. The effects of γ-aminobutyric acid are counteracted by picrotoxin in this preparation[3] as well as in crayfish hearts[5]. Picrotoxin

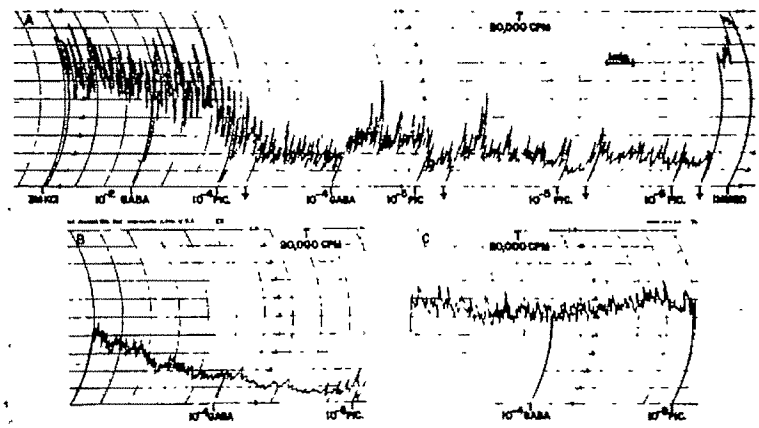

Fig. 1. Records of integrated electrical activity in β-γ-aminobutyric acid-picrotoxin antagonism experiments. Records should be read from right to left. Full scale is 20,000 impulses per min.; vertical lines delineate 1 min. periods of recording; arrows indicate periods of rinsing in van Harreveld's solution; '*IMMED*' shows activity recorded immediately after isolation of the ganglion. *A*, *p*H 7·5; *B*, *p*H 6·6; *C*, picrotoxin *p*H 7·5, γ-aminobutyric acid *p*H 6·6

by itself is a convulsant in crayfish[6,7] although no effect on synaptic transmission is observed using $2 \cdot 5 \times 10^{-4}$ *M* picrotoxin[8]. However, concentrations greater than 10^{-6} *M* progressively decrease the effect of inhibitory nerve stimulation in crayfish claws[9].

Although only peripheral inhibition has been demonstrated in the crayfish, it is not unreasonable to expect that inhibitory pathways may be present in the central nervous system. If this is so, it might be possible to demonstrate them if the transmission process is blocked by picrotoxin and depends on γ-aminobutyric acid.

The preparation used was the fifth abdominal ganglion of the crayfish, *Orconectes virilis*. The ganglion was held between electrodes and the electrical activity counted by electronic scalers, integrated and then fed into a graphic ammeter. (The details of the technique used are in the thesis, "Spontaneous Electrical Activity in the Crayfish Central Nervous System", by J. K. Hichar, Harvard University, 1958, *J. Cell. Comp. Physiol.*, 55, 195; 1960). Control-levels of activity were obtained by recording the activity from the ganglion in a layer of oil after it had been immersed in a van Harreveld's solution[10] for a period of at least 15 min. After the control-level was established the ganglion was then immersed in a test solution for 1 min. and the activity recorded again after raising into the oil layer. For each level of activity obtained after contact with a drug, the preceding activity was used as the control. Normally, when the effects of a particular drug were being tested, the progression of concentrations was from weak to strong concentrations. All drug solutions were made up in van Harreveld's solution and the experiments were conducted at room temperature, which varied from 24° to 26° C.

In 4 out of 5 experiments γ-aminobutyric acid, in concentrations of 10^{-10} to 10^{-2} *M*, had no effect on spontaneous activity of the fifth ganglion; β-alanine was found to have effects similar to those of γ-aminobutyric acid on the crayfish stretch receptor but to be 1/20 as active[2]. On the ganglion β-alanine caused a gradual enhancement of the activity, commencing at 10^{-4} *M* and inhibition occurring at 10^{-2} *M*.

The effects of picrotoxin were more striking. As the concentration increased from 10^{-8} *M* there was a gradual increase in activity until 10^{-4} *M* was reached, when the activity was maximal. After exposure to 10^{-4} *M* picrotoxin for approximately 3 min. depression occurred. This was more obvious when yet higher concentrations were used. It was common for units to fire repetitively when treated with picrotoxin. These bursts began long before increases in overall level of activity were apparent; in most cases before a concentration of 10^{-7} *M* was reached. These effects were irreversible after periods of washing as long as 30 min.

Several experiments were then conducted in order to determine whether pre-treatment with picrotoxin and the resulting excitation could be influenced by subsequent treatment with γ-aminobutyric acid. The results of one such experiment appear in Fig. 1*A*. In this experiment after the usual picrotoxin excitation subsequent treatment with 10^{-4} or 10^{-2} *M* concentrations of γ-aminobutyric acid failed to influence this high level of activity.

To determine if a lower *p*H would change the activity in any way, as was suggested by Florey[1], a nerve cord was soaked in 10^{-2} *M* picrotoxin for 30 min. at a *p*H of 6·6. The activity was recorded for 5 min., after which the preparation was immersed in 10^{-4} *M* γ-aminobutyric acid of the same *p*H for 2 min. The electrical activity was again recorded for 5 min. and the results appear in Fig. 1*B*. Here it can be seen that the increase which began after the treatment with picrotoxin continued at close to the same rate after immersion in γ-aminobutyric acid.

Other experiments were conducted where nerve cords were soaked for 30 min. in 10^{-9} *M* picrotoxin at *p*H 7·5. Activity was recorded for 5 min. which was followed by immersion in 10^{-4} *M* γ-aminobutyric acid at *p*H 6·6 for 2 min. and recording again done. Results of this experiment appear in Fig. 1*C*. Here it can be seen that the initial increase in activity after soaking for 30 min. in the picrotoxin solution was in no way influenced by the considerably higher concentration of γ-aminobutyric acid, and the level remained constant.

The suggestion was made that acetylcholine and factor I are the transmitters of opposite action in crayfish[5,11]. Since no evidence was obtained for a neurohumoral function of γ-aminobutyric acid in the preparations used here, it appears that the situation may not be so simple. It may be that γ-aminobutyric acid is a precursor of factor I[12]. On the other hand, there is no *a priori* reason to assume that in an inhibitory pathway (or in any pathway for that matter) the same transmitter must be used at all synaptic junctions. It is entirely possible as in the vertebrate autonomic system that different transmitters are involved. Thus γ-aminobutyric acid might be the inhibitory transmitter at the periphery, and not be utilized in the central nervous system. However, a few experiments done on an intact animal where γ-aminobutyric acid was injected into a walking leg and proprioceptive responses were elicited from a sensory neurone, did not give evidence of any effect of the substance, although it was found to block the lobster seventh median thoracic stretch

receptor, which has no inhibitory synapse[13]. This would suggest that γ-aminobutyric acid or a substance similar to it is not a general peripheral inhibitory transmitter.

The different effects of β-alanine at central synapses found here and peripheral ones[2] suggest a central inhibitory transmitter that differs from that at the periphery. The different effects of picrotoxin observed in these two areas also support this hypothesis. The results presented here show picrotoxin to be highly irreversible in the crayfish central nervous system, whereas it appears to be easily reversible at the periphery[7,9]. Picrotoxin in low concentrations does not alter the spontaneous activity of the stretch receptor neurone, but it antagonizes the inhibitory effect of factor I[7]. Van der Kloot *et al.*[9] reported that picrotoxin blocks the effect of stimulation of the inhibitory nerve in crayfish chela muscle. Elliott and Florey[7] also reported that picrotoxin had convulsive effects in crayfish and it was found to excite the ganglia. Thus the effect of picrotoxin differs peripherally and centrally. These observations indicate that the drug may have a different action at central synapses from that at peripheral ones where the transmitters involved may differ. That is, picrotoxin may, as van der Kloot *et al.*[9] suggest, block the action of the inhibitory transmitter peripherally in a curare-like manner by joining the receptor molecule. Its central action, however, may be quite different.

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Incorporation of Amino-Acids labelled with Carbon-14 in Nerve Proteins during Activity and Recovery

THAT nerve proteins may take an active role during nerve impulse propagation has been proposed in many publications[1]. In a paper, now in the press, I have suggested that a small fraction of the nerve proteins may split, probably to the level of amino-acids, during nerve activity, and that this process should be fully reversible, appearing as an increased turnover of proteins during impulse conduction or shortly afterwards. The purpose of the present communication is to present evidence in support of these suggestions.

In each experiment, 4–6 desheathed sciatic nerves (800–1,600 mgm. of nerve) from the South American frog *Callyptocephalus gally* were immersed for 1 hr. in 10 c.c. of Ringer solution containing 20–40 μc. of a mixture of amino-acids labelled with carbon-14 (hydrolysate of *Chlorella* protein). Then half the nerves were placed on electrodes and stimulated for 30 min. with square pulses of 0·2 msec. duration at 1–2 V. at a frequency of 120/sec. To control conduction and the maximal response, the activity of the nerves was continuously displayed on an oscilloscope. The other half of the nerves were also placed on electrodes for the same length of time, but were not stimulated. At the end of the 30 min. period, both groups were washed twice, for 15 min. each time, in Ringer solution without amino-acids. After washing, the nerves were frozen and crushed with ground glass in a mortar, and their proteins extracted in 0·1 *M* potassium chloride (15 c.c. of extract). The extracts were clarified in a refrigerated centrifuge at 20,000*g* for 1 hr. and the supernatant of each sample was treated with the same volume of 20 per cent trichloracetic acid and left overnight. Next day, the precipitates were filtered and washed with 5 per cent trichloracetic acid and with alcohol–ether (three times each). The precipitates were retained in filter papers, which were then transferred to aluminium planchets and the radioactivity of the precipitated protein was measured with a gas-flow counter (Nuclear Chicago Model *D* 47 with micromil window). Afterwards, the nitrogen content of each filter paper and precipitate was determined by micro-Kjeldahl analysis. The nitrogen content of the protein was obtained by subtracting the average nitrogen content of the filter paper.

Amino-acid incorporation of the experimental (stimulated) and control (not stimulated) samples was compared from their specific activities expressed in terms of counts/min./mgm. of nitrogen. Table 1 shows the results of seven experiments. It can be seen that the proteins from the stimulated nerves incorporated more activity than those of the controls. The average increase in activity due to stimulation was 48 per cent with a high standard deviation of 23.

Table 1

Exp. No.	1	2	3	4	5	6	7
$E\left(\frac{\text{counts/min.}}{\text{mgm. N}}\right)$	136	151	118	135	175	185	139

E = standardized specific activity of the experimental group, taking the value for the control group as 100.

These results can probably be interpreted as due to an increase in protein turnover during nerve impulse propagation or shortly afterwards. Similar observations have been made with respect to the protein turnover in the central nervous system after intense stimulation[2] (although in this latter case glucose labelled with carbon-14 was used as the source of markers). However, as the results presented here were obtained on isolated peripheral nerves, they support more directly the idea that nerve proteins have a more active role in impulse propagation and recovery than those obtained using the central nervous system, where other processes may be involved. Furthermore, these findings suggest a way of labelling the proteins that participate actively in nerve function (impulse propagation) and make possible their isolation and study.

I am indebted to Miss Ines Hoppe and Miss Silvia Rissetti for technical assistance, as well as to Miss

Emmy Wittig, who kindly carried out the nitrogen analyses. The experiments were made with equipment purchased by the Rockefeller Foundation, to which we are much in debt. I thank also Dr. Hodgson, who provided the mixture of labelled amino-acids.

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Hydroxyproline and the Shrinkage Temperature of Collagen

Dr. B. J. Rigby and Dr. J. D. Spikes[1] have quoted a value of 8·3 per cent for the hydroxyproline content of fibrinoid tissue as being taken from a paper by Bowes, Elliott and Moss[2]. The figure given in this paper is in fact 7·6 for the hydroxyproline-nitrogen expressed as per cent of the total nitrogen of the gelatin solution obtained on autoclaving fibrinoid tissue. Assuming a total nitrogen content of 18 per cent, this corresponds to 12·8 per cent hydroxyproline on protein weight which, according to Fig. 1 of Rigby and Spikes, should give a T_s of 60° or more. Their suggestion that rheumatic effects are the result of a structural breakdown due to temperature effects only is, therefore, not supported.

We would also like to direct the attention of the authors to certain exceptions to the argument that the T_s of collagen is related to its hydroxyproline content, for example, invertebrate collagens[3-5].

In the absence of any evidence that the preparation is homogeneous it seems more likely that variation in the hydroxyproline content of mammalian tissues is an indication of the collagen content, rather than of differences in the composition of the collagen itself.

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WE regret the error in our original publication[1], and thank Drs. Bowes and Moss for the correction. As they point out, the T_s corresponding to the correct value for the hydroxyproline in the example quoted is about 60° C. However, as was stated in the original article of Bowes, Elliott and Moss[2], fibrinoid tissue from patients suffering from rheumatic fever and rheumatoid arthritis contains less hydroxyproline than normal tissue, so that our statement was qualitatively correct. We reiterate our main theme, that since the denaturation and shrinkage of collagen is a time-dependent process[3], collagen will denature at temperatures below the instantaneous shrinkage temperature given a sufficiently long time, and that this time will be reduced (at any fixed temperature) if the percentage of hydroxyproline is also reduced. Gustavson[4] has presented experimental evidence along these lines showing that calf-skin begins to denature in water at 45° C. after one week. Stress relaxation studies[5] also show that rat-tail tendon slightly extended in 0·9 per cent saline begins to denature at about 40° C., although there is no tendency for the tendon to shrink when unloaded. We consider this to be the beginning of the structural breakdown which, however, only takes place on a large enough scale to cause instantaneous shrinkage at the higher temperature known as the shrinkage temperature.

With reference to invertebrate collagens we point out that our speculations applied only to vertebrates and were applicable only because of the similar chemical nature of these collagens. With invertebrate collagen the greater variability in chemical composition[6] means that differences in chemical properties cannot be related to one particular constituent.

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HÆMATOLOGY

Possible Origins of the Anti-Gm Sera

SINCE Grubb and Laurell discovered the Gm factor in 1956 (ref. 1), all those who have worked in this field have carried out the tests with sera from patients suffering from rheumatoid-arthritic diseases. Thus Harboe and Lundevall[2] and then Harboe[3] found and described the Gmx and Gmb factors in 1959. Also using a rheumatoid-arthritic serum, Steinberg[4] was able to demonstrate in the sera of Negroes the presence of a Gm-like factor, a factor which is not found in the white population. In 1959, however, Grubb found an anti-Gm factor in the serum of a young girl who was suffering from hepatitis with plasma cells[5].

Investigation of the Gm factor is based on the fact that a certain percentage of normal sera has the property of inhibiting the agglutinating power of some rheumatoid-arthritic sera. It is characteristic of this agglutinating power that the sera agglutinate O CDE red cells sensitized by an incomplete anti-D. Such agglutinating powers have been found and described by Milgrom *et al.* in the sera of clinical patients and by Unger *et al.* in the sera of healthy persons. But these authors have also noticed the non-inhibition of these agglutinating powers by the adjunction of human γ-globulins or normal sera.

From examination of more than 12,000 blood donors from the population of the Seine-Maritime, France[6,7], and also patients from different departments of our hospital, we have found this agglutinating power in some sera. But these sera could be inhibited by the adjunction of other normal sera[8]. Further investigations have shown that these sera were anti-Gm.

Hence, at the present time, we have been able to demonstrate the presence of anti-Gma in the sera of

Table 1

		Dilutions of the normal sera									
		1:2	1:4	1:8	1:16	1:32	1:64	1:128	1:256	1:512	1:1,024
Blood donor's sera	Gm + serum	−	−	−	−	−	−	−	++	++	
	Gm − serum	++	++	+++	+++	+++	++++	+++	+++	+++	
Rheumatoid-arthritic sera	Gm +	−	−	−	−	+	++	+++	+++	+++	
	Gm −	−	±	+	++	+++	++	+++	+++	+++	

9 apparently healthy blood donors, and one patient suffering from pulmonary tuberculosis. The Gmx has been found in one blood donor and in the serum of one patient treated for allergic reactions. Each time, the specificities of these anti-Gm sera were checked by testing on a panel of 50 normal sera which have been tested with anti-Gma and anti-Gmx rheumatoid-arthritic sera and furthermore by genetic control of matings involving about 100 children.

From the serological point of view, it is important to direct attention on the difference which seems to exist between the inhibitory tests[7,8]; with the rheumatoid-arthritic sera, the inhibition appears to be a quantitative phenomenon. Suitable dilutions of sera are necessary for the test, in order to demonstrate the presence or absence of the inhibitory factor. For that reason, Harboe[10] has set up his method of scores.

On the other hand, when anti-Gm sera from patients (tuberculosis, allergic diseases) or blood donors are used, inhibition appears as a qualitative phenomenon. It occurs with sera Gm +, employed undiluted as well as diluted to 1/128 or more (see Table 1).

It would be interesting to study these different agglutinating properties as regards their physico-chemical aspects and particularly to investigate whether or not the anti-Gm property of rheumatoid-arthritic sera is different from that found in patients suffering from other diseases or in healthy persons.

At present, contrary to the general opinion, we find that anti-Gm sera can be present in the rheumatoid diseases, in chronic and evolutional diseases and in healthy persons.

Note added in proof. Since this communication was submitted for publication, a new serum group has been found and called InV. The agglutinating power has been found in the serum of a healthy blood donor. This InV factor is independent of the Gma, Gmb and Gmx factors. It is present in the sera of Whites as well as Negroes. Also we have found an anti-Gmb in the sera of two other healthy blood donors.

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Thalassæmia in a Tibetan discovered during a Hæmoglobin Survey among the Sherpas

As a part of an investigation into the health of the Sherpas, undertaken during the course of the British Sola Khumba Expedition during the spring of 1959, venous blood samples were obtained from 129 inhabitants of Khumbu villages, out of an estimated population of 2,500 (von Fürer-Haimendorf, C., personal communication).

The blood samples were collected into sterile vacuum tubes ('Venules', Winthrop Laboratories, Ltd.), which were then sealed with adhesive wax ('Okeria Wax 1350/2', Astor Boisselier and Lawrence, Ltd.). The sealed tubes were stored on ice in large wide-mouthed vacuum flasks for protection from cold at high altitude and from heat during the return march to Katmandu in June. The flasks themselves, supplied by the British Vacuum Flask Co., were housed in stout wooden containers with hinged lids and packed with sawdust. These were wrapped in polythene foam sheeting which could be doused with water at frequent intervals during the hot stages of the march. By these means small pieces of ice were still preserved on arrival back at Katmandu on the eighth day after the last opportunity to recharge the flasks. The samples were flown back to London in ice-filled flasks, when they were taken at once to St. Bartholomew's Hospital.

All the samples were examined for hæmoglobin F by the 1′ alkali denaturation test[1]. In view of the presence of hæmoglobin H in Chinese and South-East Asian populations in general, and of the finding of hæmoglobin E in Malayans and occasionally in Ghurkas, all samples were tested by electrophoresis at alkaline *p*H using barbiturate buffer[2]. They were further examined by electrophoresis in *tris* buffer[3] to determine the level of hæmoglobin A_2. No abnormalities were discovered in 128 blood samples, but in one, 5·9 per cent alkali-resistant hæmoglobin was found, and the hæmoglobin A_2-level was seen to be raised above the normal 3·5 per cent (Fig. 1). The finding of a significant amount of hæmoglobin F, and of a raised hæmoglobin A_2-level is diagnostic of thalassæmia minor. The only other evidence of a thalassæmia gene in a Himalayan population was made in the Ghurkas[4], who, however, are racially quite distinct from the Sherpas.

The Sherpas live on the southern watershed of the main Himalayan range in north-eastern Nepal in villages lying mostly at altitudes between 10,000 and 12,000 ft. They are of pure Tibetan ancestry. The man in whom the evidence of thalassæmia was discovered was a servant in the Bhuddist monastery at Thyangboche, aged about seventy years, and he was born in Tibet. He was suffering from right-sided heart failure with generalized œdema, which was thought to be due to 'chronic mountain sickness' or so-called Monge's disease. The blood pressure was

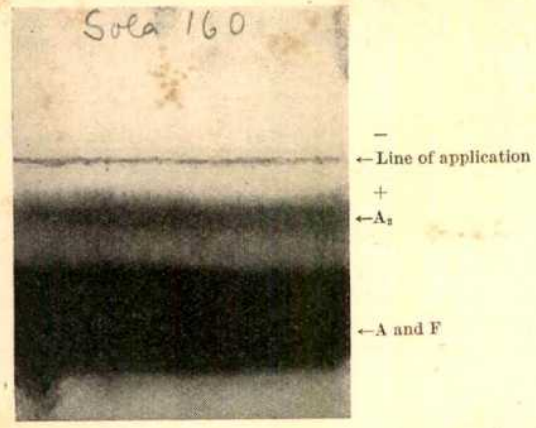

Fig. 1. Hanging paperstrip electrophoresis of hæmoglobin of Tibetan with 5·6 per cent F and 4·1 per cent A_2. *Tris* buffer, *p*H 8·9, stained with 'light-green'

135/95, and the serum cholesterol 119 mgm. per cent.

We are indebted to the Royal Nepalese Government for permission to make these observations, and to the Medical Research Council and Newcastle Regional Hospital Board for their generous support.

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HISTOLOGY

Neurokeratin Network of Myelin Sheaths

THE recent communication of Tewari and Bourne[1] on the neurokeratin network of peripheral nerve fibres is valuable not only for its intrinsic content but also because it validates the histological procedures, findings and arguments derived therefrom, by which it was concluded that neurokeratin formations are part of the architecture of the nerve fibres and not artefacts[2,3]. It is sad to think that Nageotte[4], who saw the structures in peripheral nerve fibres described by me[2,3] and by Tewari and Bourne, looked on them as artefacts. One of the strongest anatomical arguments against the notion of artefact is that the disposition of neurokeratin in spinal cord axons and in the preterminal axons found in spinal cord, in brain stem and in cerebral and cerebellar cortices is quite different from that characteristic of peripheral nerve trunks, even although the material examined was fixed and prepared for sectioning under strictly comparable conditions in all instances.

Work in progress shows that not only the disposition, but also the amount, of neurokeratin varies in different parts of the nervous system. This can be shown optically by using the falgic acid staining process described elsewhere[5]. In this process sections are stained first with acidified acid fuchsin and then with a very dilute solution of light green. Acid fuchsin can combine with one, two or three molecules of light green to form red, violet or blue compounds, respectively; these have been named the falgic acids. The red compound is formed where acid fuchsin is most abundant, the blue where it is least so. Thus the relative uptake of acid fuchsin (relative erythrophilia) of tissue elements can be determined by colour. Neurokeratin is erythrophilic and the falgic acid method shows that it is present in great density in spinal cord axons, somewhat less so in peripheral and least in the axons of the white matter of the cerebral and cerebellar cortices, and indeed in fine medullated fibres everywhere. These latter fibres are therefore difficult to display by the falgic acid technique.

Nevertheless, the essential feature of this technique can be used to make such fine fibres clearly visible as well as showing the markedly erythrophilic types of axon. The falgic acids are formed by the union of one or more molecules of light green with the amino-groups of acid fuchsin, one molecule of light green uniting with one of these amino-groups. The acid fuchsin, already attached to basic elements of the tissue by its sulphonic groups, behaves as a 'trivalent' base towards the acid light green. Other acid dyes can replace light green in this type of combination. In particular, violamine 3*B* can be used; the red, violet and blue colours produced by the falgic acid technique are then replaced by red, purple and deep violet, respectively. If sun yellow *G* be mixed with the violamine solution, the erythrophobic tissue elements are stained yellow, giving a very good contrast with the elements coloured by the 'faviolic acids', as we may call them. This shows the finest nerve fibres and is a very simple technique for the display of both dendrosomatic and axonic parts of neurones. It gives a picture equivalent in detail shown to that provided by MacConaill's acid fuchsin–lead hæmatoxylin method[2], but it is free from the risk of the formation of precipitates which that method entailed. By it the staining properties of neurokeratin can be used for a demonstration of the presence of medullated fibres, and for an assessment of the relative amounts of neurokeratin present in different fibres.

Details will be published elsewhere when the work has been completed. Meanwhile it would seem that the descriptions of the structure of myelinated fibres should be drastically revised in current text-books, notwithstanding the apparent discrepancy between the findings of optical and electrical microscopy.

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Structure of the Walls of the Bile 'Canaliculi' in Mammalian Liver Cells

THE structure of the walls of the bile canaliculi of the liver has long been of interest; the question of importance being whether the canaliculi had definite walls of their own, or whether they were formed from modifications of the walls of the hepatocytes themselves. Early workers[1-3] believed that the canaliculi had definite walls of their own; but Zimmermann[4] suggested that they were formed by modifications of the walls of the hepatocytes, and described dense structures at the edges of the canaliculi which he called "terminal bars". Morton[5] was able to show that the lining of the bile canaliculi was in the form of a 'brush border', and apart from Zimmermann's terminal bars he found a collection of basophilic material in the cell cytoplasm lying close to the bile ducts. Rouiller[6], in an electron microscope study of the rat liver bile canaliculi, showed that the cell membranes were closely opposed in the neighbourhood of the canaliculus, but with only osmium as an electron stain, he found no modification or thickenings of the cell wall in the proximity of the duct. In a study of normal and regenerating rat liver using 'Araldite' embedding followed by phosphotungstic acid staining, it was found that some parts of the cell walls related to the bile ducts took up this stain particularly well.

In liver cells stained with phosphotungstic acid, dense bands of materials are seen at various points on the plasma membrane. These bands are always exactly opposite a similar band of identical length on the membrane of an adjoining cell (Figs. 1 and 2). They cause a thickening of the plasma membrane from its usual 80–90 Å. to 500–600 Å., and are always present close to the points where the plasma membranes of two cells divide to form a bile canaliculus, although they are also to be found at other points on the cell membrane.

These structures, revealed by phosphotungstic acid staining in close relationship to the bile canaliculi of liver cells, seem in agreement with the previous work using the light microscope. Thus the dense phosphotungstic acid-positive bands on the cell membranes close to the bile canaliculi are in the same position as the "terminal bars" of Zimmermann, and are probably identical with these structures. Zimmermann's original term "Kittleisten" suggested a cementing substance, and it is therefore perhaps not surprising to find areas of phosphotungstic acid-positive material, scattered all along the cell membrane.

Similar material has been found on the plasma membranes of mouse pituitary cells by Barnes[7]. In this case the material is neatly laminated instead of being a single band on each membrane; but the same conclusion is reached, namely, that the function

Fig. 1. Part of an elongated bile canaliculus formed at the junction of the three liver cells. The cell membranes close to the canaliculus are much thicker than normal, being as much as 500 Å. thick, and stain very densely with phosphotungstic acid. (× c. 40,000)

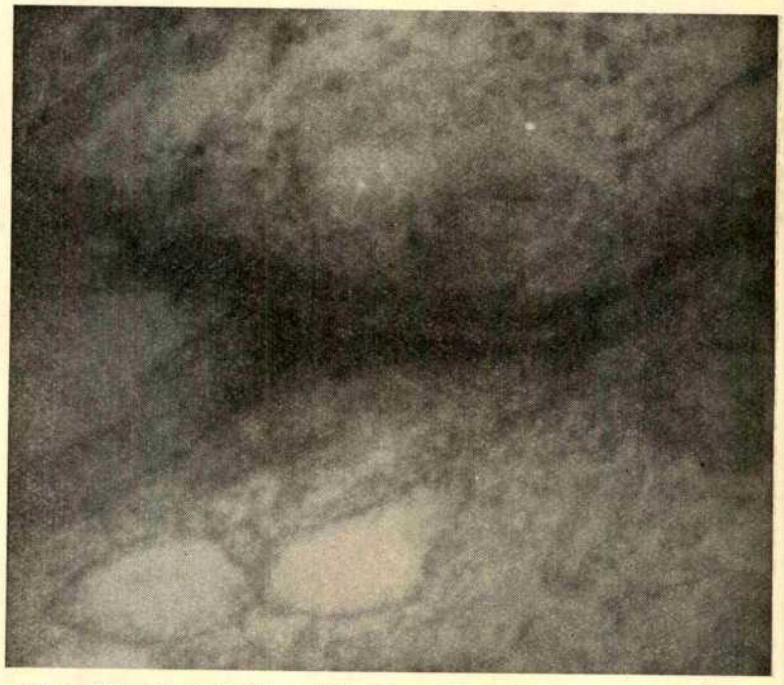

Fig. 2. A high-resolution picture of the cell membranes of two liver cells close to a bile canaliculus. The dense phosphotungstic acid-positive material is clearly visible. (× c. 128,500)

of this material may be to assist in the binding of cells together. The material for this work was obtained from normal adult Wistar rats. It was fixed by the method described by Barnes and Davis[8] and embedded in 'Araldite' as described by me[9].

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PATHOLOGY

Porphyrin Fluorescence of Experimentally produced Squamous Cell Carcinoma

ULCERATED squamous cell carcinomas of the human skin frequently show a red fluorescence when examined under ultra-violet radiation[1-3]. This red fluorescence is usually restricted to small areas of the necrotic surface. Hitherto the substance or substances responsible for this phenomena have not been identified. This is probably due to the fact that very small amounts of material are available for study in any single case. Recently, Ghadially[4] observed that experimentally produced squamous cell carcinomas of the skin of many animals show a similar red fluorescence. It seemed to us that by pooling material from a number of tumours, sufficient might be obtained for a chemical analysis. Six rabbits with large ulcerated carcinomas produced by repeated painting of the skin with a 2 per cent solution w/w of 9 : 10 dimethyl 1 : 2 benzanthracene in a mixture of equal parts of lanolin and paraffin were available for study. After many attempts, we were ultimately able to collect one large (5 gm.) pooled sample for analysis. Another large sample was obtained from a single rabbit which died as a result of a very large fungating carcinoma of the ear. Here about 5 gm. of red fluorescent debris had collected on the carcinoma and within the ear over a prolonged period of time. The results obtained in each case were essentially similar.

Red fluorescence has been attributed to the presence of porphyrins in a chloroma[5], a fungating adenocarcinoma of the breast[3] and a hepatic adenoma[6] of man. Therefore it seemed reasonable to suppose that similar material might be associated with the red fluorescent squamous carcinomas.

An ethyl acetate (75 ml.) – acetic acid (25 ml.) extract of red fluorescent debris (5 gm.) from the rabbit carcinoma was examined for protoporphyrin, coproporphyrin, and uroporphyrin by the methods of Schwartz and Wikoff[7] and Dresel and Falk[8]. The absorption spectrum of a fraction corresponding to protoporphyrin was measured in ethyl acetate solution with a Unicam spectrophotometer *SP* 500 in the range 350–800 mμ (in 5-mμ steps) in 1-cm. cells versus an ethyl acetate blank. Table 1 gives wave-lengths and optical density values of the maxima and minima exhibited by this porphyrin solution, and, for comparison, the corresponding values are quoted for the spectrum of an authentic sample of protoporphyrin (Light and Co.) in ethyl acetate. These spectra were closely similar, and it may be concluded that protoporphyrin occurs in the carcinoma debris.

Table 1

Material from carcinoma debris			Authentic protoporphyrin		
400 mμ	max.	1·750	400 mμ	max.	2·520
460	min.	0·025	465	min.	0·030
505	max.	0·135	505	max.	0·197
525	min.	0·048	525	min.	0·058
540	max.	0·077	540	max.	0·123
565	min.	0·019	560	min.	0·019
585	max.	0·052	580	max.	0·073
615	min.	0·008	615	min.	0·007
635	max.	0·027	635	max.	0·049

The fraction which should contain coproporphyrin fluoresced red in ultra-violet light, but the porphyrin content was so low that only a very feeble Soret band was detected at 400 mμ in the most concentrated extract we could obtain.

Finally, the fraction which should contain uroporphyrin according to Dresel and Falk failed to fluoresce in ultra-violet light.

Thus the material responsible for the fluorescence of rabbit ear carcinoma seems to consist mainly of protoporphyrin with perhaps a trace of coproporphyrin.

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Phenylketonuria in Infant Monkeys

WE had previously established[1] that the characteristic aberrations found in human phenylketonuria, namely, high plasma phenylalanine, phenylketones in the urine, and characteristic odour were observed in adolescent monkeys fed excessive amounts of L-phenylalanine in their diet. From the results of behavioural tests utilizing discrimination and maze performance, as well as poor adaptability to the test situation, these monkeys appeared to be retarded in their learning ability. It seemed important to determine whether phenylketonuria could be produced in infant monkeys when the brain is apparently more sensitive to chemical insult. Long-term observation could then be made throughout the period of development and it might be possible to correlate the biochemical changes with behavioural patterns.

Four infant macaques born in this laboratory were separated from their mothers at birth and were given a high phenylalanine milk diet from the second day of life. Whole cow's milk or powdered milk formula containing 0·25 gm. L-phenylalanine per 100 ml. in final dilution was fed for the first two weeks. Later,

increasing quantities of the amino-acid were included to a maximum of 0·5 gm. of L-phenylalanine per 100 ml. The average infant monkey consumed enough milk to make the daily intake approximately 2·75 gm. of phenylalanine per kgm. body-weight. The infant monkeys were bottle-fed by hand every 2 hr. for the first 2 weeks, then fed by means of an infant feeding bottle placed in a mother surrogate so that the infant could crawl on to this false mother for the nipple feedings in the usual position. Plasma phenylalanine was determined[2,3] at weekly intervals for the first six months, then at bi-weekly intervals up to the first year. The urine was tested daily during the first year and revealed strongly positive phenylketones as determined by the 'Phenistix' (Ames Co., Elkhart, Indiana) or ferric chloride methods, and it had the peculiar musty odour typical of that of children with this disease. Quantitative blood and urine analyses are shown in Table 1. The fasting plasma phenylalanine of normal infant monkeys ranged from 1·0 to 1·5 mgm. per cent, while the monkeys which received L-phenylalanine ranged from 8·8 to 47·5 mgm. per cent. These high plasma phenylalanine-levels are comparable to that of phenylketonuric patients. The urine collected from male monkeys indicated that normal animals excreted negligible amounts of phenylpyruvic acid as determined by the method of Berry and Woolf[4], while the monkeys which received L-phenylalanine excreted 79–465 mgm. phenylpyruvic acid in 24 hr.

Table 1

Monkey	Mgm. phenylalanine/ 100 ml. plasma	Mgm. phenylpyruvic acid/24 hr. urine
A 8 ♂	16·6–39·0	113–257
A 18 ♂	8·8–32·9	79–465
A 23 ♀	10·9–46·1	—
A 24 ♀	10·4–47·5	—
Controls	1·0–1·5	0

The monkeys receiving the high phenylalanine milk grew nearly as well as monkeys fed a normal laboratory diet. Those animals which consumed very high amounts of phenylalanine because they were better milk drinkers usually showed less gain in weight than the monkeys the milk intake of which was not as great. This may be a clue that the phenylalanine was near toxic levels at 2·75 gm. of amino-acid per kgm. body-weight per day. The fur coat of the animals was in all respects normal in colour and in quantity, and no abnormal skin lesions or delay in dentition were noted. Neurological examination revealed no sensory or motor abnormalities in these animals up to one year of age. Two of the four animals had typical grand mal convulsions at widely spaced intervals, and the monkeys usually slept for a short period following the seizure, but promptly recovered with no residual effects.

The psychological testing of each animal was begun shortly after the first week of life and consisted of: (1) delayed response tests; (2) discrimination learning set tests; (3) object discrimination tests; (4) Hebb-Williamson maze test, according to methods performed in this laboratory by Harlow[5] and his associates. The total performance of the phenylketonuric animals was much below that of normal animals of the same age in all tests. It was quite clear that the retarded animals could not learn delayed response and discrimination learning set tests. These monkeys demonstrated motivational defects, inappropriate behaviour, subnormal learning, and sub-optimal intellectual performance.

An unusual opportunity for obtaining additional information on certain aspects of brain metabolism in mental retardation is thus provided by the production of phenylketonuria in a sub-human species. Work is now in progress to obtain information from monkey experiments so that treatment of phenylketonuria in human infants might be more satisfactory. The role of liver hydroxylase and brain decarboxylases on amino-acid metabolism can be thoroughly investigated in these animals. Further experiments designed to produce other types of retardation in monkeys are now under way.

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RADIOBIOLOGY

Early Incorporation of Sulphur-35 Sodium Sulphate into Plasma Proteins of Man

IN investigating the fate of radiosulphate in multiple myeloma[1], the incorporation of sulphur-35 in human plasma protein fractions was investigated.

Carrier-free sulphur-35 as sodium sulphate in doses ranging from 0·867 to 2·07 mc. was administered intravenously to 10 patients with multiple myeloma and 14 patients with other neoplastic diseases. A patient with chondrosarcoma received labelled sulphate in three intravenous doses at weekly intervals of 505 mc., 391 mc., and 322 mc., respectively. (We wish to express our gratitude to Dr. C. Botstein, head of the Radiotherapy Dept., Montefiore Hospital, for making this patient available for study. The sulphur-35 for this patient was supplied by Abbott Laboratories.)

Sulphur-35 assays were made with a calibrated gas-flow counter and corrected for back-scatter and self-absorption. Blood samples were obtained at intervals during the initial 24 hr. and daily thereafter for the next 6 days.

Analysis of plasma proteins was performed with electrophoretic and staining techniques previously described[2]. Simultaneously run filter paper strips were scanned for radioactivity in a suitably adapted gas-flow counter and exposed for 90 days to Kodak No-screen double-coated X-ray film for radioautography. Continuous curtain electrophoresis was performed on 1- to 3-ml. samples of plasma with standard techniques[3].

In none of the plasma samples obtained from the myeloma patients and subjects with other neoplastic diseases was radioactivity demonstrable by scanning of the electrophoretic strips, radioautography, or continuous electrophoresis.

For the subject with chondrosarcoma, given more than 1 c. of sulphur-35 in 3 doses, however, progressive incorporation of sulphur-35 into the plasma protein fractions was readily detected after each dose by the assay of the electrophoretically separated proteins on the filter paper strips (Fig. 1). The relative distribution of sulphur-35 for the various protein moieties as a function of time is presented in detail for the initial therapeutic dose of 505 mc. (Fig. 2). Similar patterns were observed after each therapeutic dose. The albumin fraction promptly incorporated sulphur-35 with the maximum value reached in 4 hr. and thereafter showed a more gradual decline during 48 hr. Little further change was observed during the next 4 days. A slower incorporation of sulphur-35 with the maximum peak occurring in 18 hr. was noted for fibrinogen. The degradation was also slower than that of albumin, taking 4 days to reach minimum values. The α- + β-globulin fraction paralleled the fibrinogen curve at a lower level of radioactivity. Its peak-level was also reached in 18 hr. Little incorporation of sulphur-35 into γ-globulin was observed. However, it should be noted that this patient had a low concentration of γ-globulin. The highest level for this fraction was attained in 8 hr. and fell to base-line levels in 24 hr.

Sulphur-35 administered as sodium sulphate has been shown to be incorporated into the plasma proteins of animals[4], but such incorporation has not been demonstrated in man. Reasons for this failure include: (1) Most of the sulphur-35 administered is excreted in the urine within 48 hr.[1,5]. (2) The fraction of the dose remaining within the body is widely distributed in the sulphomucopolysaccharides of cartilage, aorta, sclera, cornea and intestinal mucosa[6]. (3) The maximum permissible dose of 2 mc. for this work was insufficient for the detection of radio-

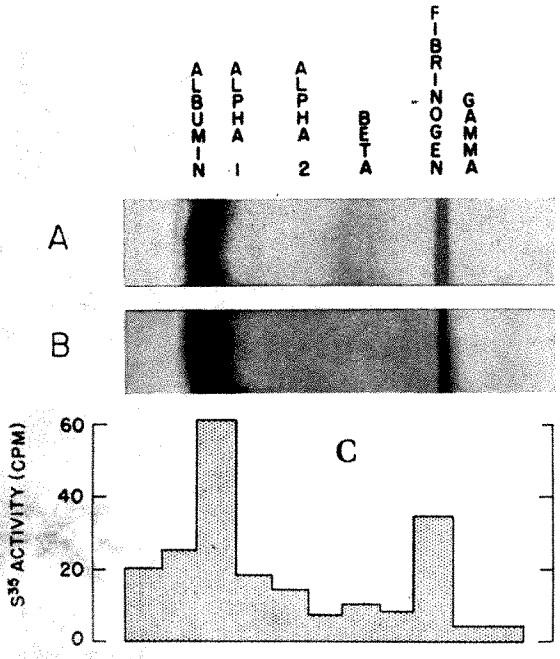

Fig. 1. *A*, Paper electrophoretic strip stained for protein prepared from plasma obtained from chondrosarcoma patient 1 hr. following administration of 505 mc. labelled sulphate. *B*, Radioautograph of strip (94-day exposure); density corresponds to sulphur-35 activity. *C*, Relative distribution of activity along a strip determined by scanning with collimated gas-flow counter; adequate counts collected to assure 5–10 per cent accuracy

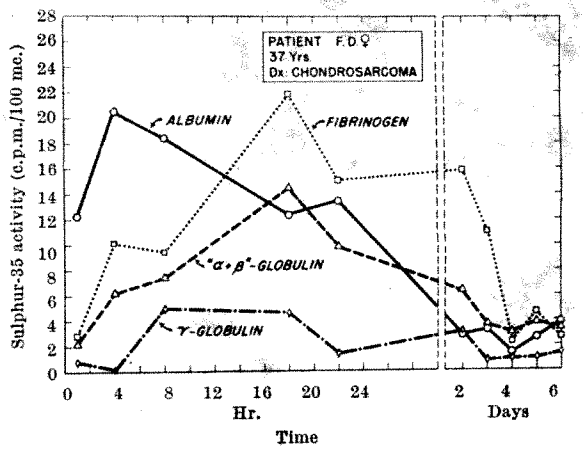

Fig. 2. Variation of sulphur-35 activity in plasma protein fractions with time as derived from scans of corresponding electrophoretic strips

activity in human plasma protein fractions, although even smaller amounts were found adequate for the rat[4].

In the patient with chondrosarcoma, sulphur-35 was readily detected in all the plasma protein fractions after each therapeutic dose. The problem then arises as to how the sulphur-35 is bound to protein. One possibility is that the sulphur-35 is incorporated only into the protein-bound sulphated mucopolysaccharides. If this were so, the radioactivity would be distributed in the plasma protein fractions in proportion to the distribution of protein-bound polysaccharides. Indeed, this was found to be the case in the rat, where about 40 per cent of administered sulphur-35 sulphate activity was bound to a serum constituent having the electrophoretic mobility of α-1-globulin, suggesting that the binding occurs in a protein-bound sulphomucopolysaccharide[7]. However, the distribution of sulphur-35 in the plasma protein of the patient herein reported was not that of mucopolysaccharides. The greatest concentration of sulphur-35 was found in albumin and fibrinogen, indicating that the sulphur-35 was incorporated into the sulphur-containing amino-acids of the protein rather than the protein-bound mucopolysaccharides. This, of course, does not rule out some tagging of the sulphated mucopolysaccharides.

After oral administration of sulphur-35 labelled cysteine to man, the incorporation of the label into serum protein fractions has been shown to occur with great rapidity[8]. A striking similarity between our results using sulphur-35 labelled sulphate and those using the labelled amino-acid is noted. Thus, the albumin peak for sulphur-35 cysteine also occurred in 4 hr. and the α- + β-globulin peak at a time similar to ours. Of interest is the fact that the maximum for γ-globulin after labelled cysteine was low in a nutritionally normal patient, so the low values we observed may not be related necessarily to the hypogammaglobulinæmia of our patient with chondrosarcoma. Furthermore, the ratios of the respective maxima to each other are almost identical for both studies. It would appear then that inorganic sulphate is rapidly bound to the various plasma protein fractions, presumably after first being incorporated into an amino-acid precursor. Also, the fact that our findings with sulphate parallel those done by others with labelled cysteine supports the view that sulphate is incorporated into the protein fractions, rather than

non-specifically bound. This is confirmed by our unpublished work in which we failed to demonstrate labelling of the plasma protein fractions after incubation with sulphur-35 labelled sulphate.

Plasma proteins contain functional SS groups and SH groups which are probably part of the cystine and cysteine molecules. Although there is little evidence to suggest that animal tissues can synthesize sulphur-containing amino-acids, there is good evidence that it does occur in animals and that this requires the presence of micro-organisms in the alimentary tract[9]. The steps whereby the sulphur-35 of labelled sodium sulphate becomes incorporated into the sulphur-containing amino-acids of human plasma proteins are yet to be elucidated. This investigation demonstrates that it does occur. It is possible that in the human, as in lower animals, the activity of intestinal micro-organisms plays an important part. However, in the present work, one must postulate initial secretion of labelled sulphate into the bowel, directly or via bile, because all doses were given intravenously. The rapidity with which the incorporation of the inorganic sulphate into plasma protein occurs suggests that an alternative metabolic pathway may exist.

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BIOLOGY

Sun Navigation by Birds

C. J. PENNYCUICK[1], discussing the physical possibility of an estimate of the change in azimuth of a celestial object by a bird, says: "Birds very often fly round in circles whilst orienting, and therefore cannot have their eyes stabilized in azimuth. The change in azimuth can therefore be measured only by reference to a fixed object [*sic*], when the bird is stationary on the ground. Over the sea it is not physically possible to measure it at all without some kind of compass. However, birds do navigate over the sea. Hence Matthews' hypothesis as it stands is untenable". Again in his summary: "Matthews' hypothesis . . . is rejected on the grounds of physical impossibility of making one of the measurements ,. . .".

Assertions about the physical impossibility of animal activities have so often proved false that they should be closely scrutinized, and Pennycuick's argument appears to be fallacious. What the bird needs is not a fixed object (in parenthesis it may be pointed out that a compass needle is not a fixed object) but an indication of a direction—any direction—in the horizontal plane lasting long enough (not more than a few minutes on Matthews's[2] hypothesis) to allow the change of azimuth of the celestial object to be measured. My experience of flying at a moderate height over the open sea is strictly limited; but I have never known an occasion when the sea could not be seen at all and when the necessary stable indication of direction could not have been obtained from the pattern of waves on its surface; in the belief that occasions when this indication is not available are exceedingly rare, I am confirmed by an experienced pilot of aircraft. It is therefore fair to assume that a flying bird could always obtain the necessary information in flight over the sea and that Matthews's hypothesis has not, on this ground, been invalidated.

Pennycuick's own hypothesis, requiring only an appreciation of the Sun's elevation and of its rate of change, is attractive and economical, but it is surely unlikely that a bird should neglect information about the sign and magnitude of the Sun's rate of change of azimuth when this information, always available, could be used to increase the accuracy of estimate of its own position and to eliminate the ambiguity which can arise, according to Pennycuick, in certain circumstances.

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IT must be conceded that the rate of change of the Sun's azimuth could, in principle, be measured by reference to the orientation of the waves on the sea, but the possibility of using this method for navigation requires closer scrutiny. If it be assumed that the bird can use the maximum accuracy available, the problem falls into three parts:

(1) Within what limits can the direction of the waves be defined?

(2) Within what limits may its rate of change be deemed to be zero?

(3) To what distance on the ground does the minimum detectable change of rate of change of azimuth correspond?

It is to be hoped that someone better qualified than I will be able to produce definite information on the first two questions, but meanwhile some reasonable surmises may be made.

(1) The meaning of the "direction of orientation" of the pattern of waves on the sea would appear to be statistical in nature, the accuracy with which it could be defined increasing with the number of waves visible. The direction of the waves on a large stretch of sea seen from the air could clearly be defined within 10°, and probably usually within 1°. Whether it could be defined within 0·1° (1/5 of the diameter of the Sun's disk) is not so clear. In the following argument ± 0·01° accuracy will be assumed, which is perhaps optimistic.

Large errors would occur in shallow waters owing to refraction of the waves in water of varying depth, so the use of the method would probably be confined to the open ocean.

(2) The limits within which the rate of rotation of the wave-pattern may be deemed to be zero (even when it really is zero) will depend on the above accuracy with which the direction of the wave-pattern can be determined, and also on the length of time available for observation. It would be logical to choose for the latter that time during which rate of change of azimuth changes by, say, 5 per cent, but to avoid complication, an observation time of 1 min. will be assumed arbitrarily. This has the effect of making changes of navigational accuracy from place to place appear greater than they really are, since in those regions where rate of change of azimuth changes rapidly with distance (good navigational accuracy) it also changes rapidly with time (short time available for observation). Also the best accuracy on the present assumptions is obtained when the Sun is high in the sky, which makes azimuth and changes thereof more difficult to observe. For the sake of argument let it be assumed that the rate of change of the Sun's azimuth can be measured by reference to the waves on the sea within $\pm\ 0{\cdot}01°$/min. of time.

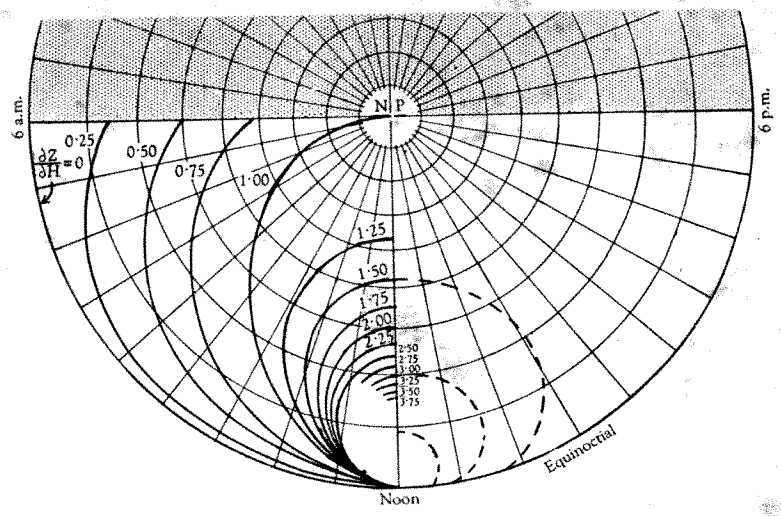

Fig. 1. Stereographic projection of the northern hemisphere, showing lines of equal rate of change of azimuth. The curves are approximate except that their intercepts on the noon and six o'clock lines are calculated. Dotted lines enclose zones in which particular accuracies of position finding could be obtained (see text)

Apart from the problem of measurement, it is likely that an accuracy of this order would only be obtainable in regions of rather constant weather, such as the trade wind zones: such stability could probably not be relied upon in the North Atlantic, for example.

(3) If Z is the Sun's azimuth, L the observer's latitude, and H the local hour angle, it may be shown that, in the special case of equinox:

$$\frac{\partial Z}{\partial H} = \frac{1}{\operatorname{cosec} L \sin^2 H + \sin L \cos^2 H} \qquad (1)$$

Fig. 1 is a diagram of lines of equal rate of change of azimuth, plotted for equinox. They form a family of closed curves meeting at the Sun's position. The points at which they cut the centre and edge of the diagram are calculated, but the shape in between is approximate.

The error of position for a given error of $\partial Z/\partial H$ is proportional to the spacing of these lines, that is, the rate of change of position with respect to $\partial Z/\partial H$. At noon ($H = 0$) we have:

$$\frac{\partial Z}{\partial H} = \operatorname{cosec} L$$

whence, differentiating up the Sun's meridian,

$$\frac{\partial}{\partial L}\left(\frac{\partial Z}{\partial H}\right) = -\operatorname{cosec} L \cot L \qquad (2)$$

If the permissible error of $\partial Z/\partial H$ is $\pm\ 0{\cdot}01°$/min. of time, or $\pm\ 0{\cdot}04°$/deg. of hour angle, and the required accuracy of position finding is arbitrarily taken as $\pm\ 0{\cdot}005$ radian (17 nautical miles), then:

$$\operatorname{cosec} L \cot L = \frac{0{\cdot}04}{0{\cdot}005} = 8$$

$$L = 20°$$

The middle dotted line in Fig. 1 encloses the zone within which the required accuracy can be obtained. It crosses the meridian at $L = 20°$, but the rest of it is drawn approximately. There is another mirror image zone south of the equator.

If the assumptions as to accuracy have been five times too optimistic, the zone comes up to 9° lat. (inner dotted line): if they have been five times too pessimistic, it comes up to 42° (outer dotted line). There is always a minute zone near the Sun within which any accuracy, however bad, will suffice.

It is hoped that the dubious assumptions in the above argument have been made explicit and will elicit informed comment. It seems likely that the method suggested by Prof. Pumphrey, while restricted in application, might very well provide navigational information to pelagic birds living in the trade wind zones. However, it would work best in roughly the same region where maximum accuracy can be obtained from rate of change of altitude, so it will not fill in any deficiencies in the system previously suggested.

It may be worth noting that observing the direction and speed at which the Sun moves across the sky, is equivalent to measuring the rates of change of altitude and azimuth, and no reduction in the accuracy requirements can be made by describing the process in one form rather than the other.

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Reactions of Soil Nematodes to Coal-Tar Dyes

TESTS with dilute aqueous solutions of coal-tar dyes on soil nematodes reveal that reactions to 19 basic dyes of varied chemistry are of three classes.

Class I (absorption reaction), observed in many genera of the Enoplida, typically involves entry of the dye first at the anterior and then almost simultaneously at the posterior end of the nematode, with staining progressing toward the centre. Minimum

solution thresholds of this reaction range from 100 to 10 p.p.m. in 24 hr. Death occurs commonly; and in the stronger solutions is accompanied by intense accumulation of dye throughout the nematode corpus, obscuring internal structures. The reactions of all groups of soil nematodes to iodine fall into Class I. Minimum thresholds for iodine of both staining and toxicity in *Tylenchorhynchus martini* Fielding 1956 were between 10 and 1 p.p.m. in 24 hr.

Class II (basophilic reaction) has been observed in the genera *Tylenchorhynchus* (6 species), *Aphelenchoides* (2 species) and *Rhabditis* (2 species). This reaction manifests extreme sensitivity with minimum concentration thresholds ranging from 10 to 0·1 p.p.m. It is non-toxic, generally unaffected by solution *p*H and appears to be an adsorption phenomenon with staining intensities independent of dye concentrations. Each dye imparts a uniform tint of characteristic colour and intensity to the corpus, with the internal structures clearly visible. Staining occurs in 3–5 min. at dye concentrations between 10 and 1 p.p.m. and very rapidly at 100 p.p.m. The dyes appear to enter at all points on the nematode surface and the reaction is reversible in living nematodes. Stained specimens of *T. martini* placed in soil around rice plants for 7 days were re-isolated and examined. The dyes had disappeared from the corpus but were strongly retained by intestinal granules.

Class III (resistant reaction), in which there is little or no staining, has been observed in 9 known and 3 suspected phytophagous genera of the Tylenchida, in certain genera of the Rhabditida and in a *Plectus* sp. of the Chromadorida. Staining, when it occurs, is slight even at dye concentrations of 1,000 p.p.m. in 24 hr. and is largely confined to certain parts of the corpus, intestinal granules, sclerotized structures and inclusions of the body cavity.

The integrity of each class of reactions to basic dyes is maintained essentially in heat-killed and formalin-preserved nematodes, although breaking of resistance (Class III reaction) has been observed in some instances. Tests with 13 acid dyes on mixed populations of nematodes extracted from soils revealed, in comparisons with basic dyes, a more restricted spectrum of activity. Typical results, after 24 hr. in dye solutions of 200 p.p.m., show that approximately 10-fold more nematodes are stained by basic than by acid dyes.

Details of this work will be submitted for publication elsewhere.

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Toxicity of Aluminium to Black Pepper (*Piper nigrum* L.) in Sarawak

SYMPTOMS of an unknown disorder have been increasingly observed on pepper vines since 1956; no pathogen seemed to be involved. Affected vines show an overall bright green to yellow colour and their leaves a pronounced droop. Individual leaves first show symptoms of a speckled necrosis mostly along the main veins, each brown spot having a surrounding yellow halo. Afterwards the necrotic areas spread and become more serious so that finally the leaves fall. These vines have a greatly reduced root system, which dies off centripetally. Different stages of the leaf symptoms are shown in Fig. 1.

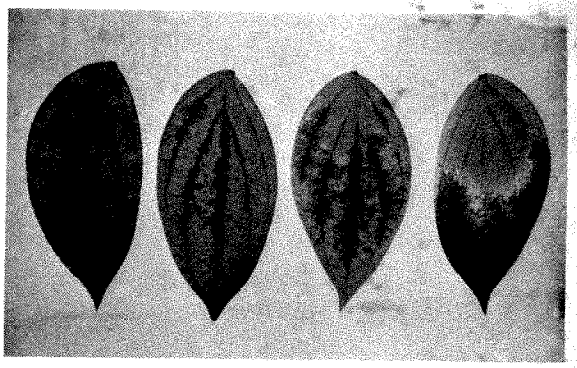

Fig. 1. The under-surface of detached pepper leaves showing a healthy leaf on the left and symptoms of increasing severity towards the right

Pepper vines are grown on low mounds in latosolic soils, which are poor in bases, particularly magnesium. The soil from mounds of affected vines was found always to be low in *p*H, generally below *p*H 4·5, and some mounds were as low as *p*H 3·5. Vines grown in soils of above *p*H 5·5 were unaffected. Analysis of soil from mounds of healthy and affected vines are given in Table 1.

Table 1. BASE AND ALUMINIUM CONTENT IN P.P.M. AND *p*H-LEVELS OF SOILS WITH AFFECTED AND UNAFFECTED VINES

	*p*H	Calcium	Magnesium	Aluminium
Unaffected vines (mean of 12)	5·6 (0·59)	2,529 (61·2)	84 (5·88)	91 (22·72)
Affected vines (mean of 25)	3·9 (0·39)	195 (91·7)	29 (3·91)	330 (15·21)

All differences are significant at $P = 0·001$. *S.E.* given in brackets

The cause of this disorder is apparently a toxicity of aluminium ions at low *p*H. These ions prevent the uptake of calcium and magnesium, leading to the deficiency symptoms of these elements, the yellowing and necrosis which appear in the pepper leaves. This free aluminium also causes the root systems to die, so that the foliage wilts, producing the characteristic droop. With the reduced uptake of calcium and magnesium, and a presumed reduction in the cation exchange capacity of the affected root system, the amount of potassium taken up actually increases, so that the ratio of K/(Ca + Mg) can be used as a diagnostic index. The critical value appeared to be approximately 1·00. These effects are illustrated in the leaf analyses presented in Table 2.

Table 2. BASE CONTENT IN PERCENTAGE DRY MATTER, AND RATIO OF MONO- TO DI-VALENT CATIONS IN PEPPER LEAVES

Condition of vines	Calcium	Magnesium	Potassium	(K/Ca + Mg)
Unaffected (mean of 23)	1 1·363 (0·053)	4 0·231 (0·010)	7 1·450 (0·240)	10 0·930 (0·071)
Affected (mean of 18)	2 1·046 (0·060)	5 0·179 (0·013)	8 1·568 (0·270)	11 1·290 (0·081)
Seriously affected (mean of 12)	3 0·523 (0·082)	6 0·142 (0·014)	9 1·829 (0·310)	12 3·390 (0·029)

S.E. are given in brackets.
Differences significant at $P = 0·001$: 1 and 2, 1 and 3, 4 and 6, and 10 and 12.
Differences significant at $P = 0·01$: 4 and 5, 7 and 9, 10 and 11.

The recent apparent increase in this toxicity can be accounted for historically. After 1945 there was a tendency to abandon the traditional method of manuring pepper. This was to apply large quantities of burnt earth, supplying adequate bases to the mound. Gradually, relatively small quantities of processed organic manures and cheaper inorganic fertilizers have replaced the burnt earth. Presumably, therefore, the continual loss of bases and their inadequate replacement have led to a steady increase in soil acidity, which has now apparently reached a critical level.

Steps are being taken to continue this work and to provide remedial measures. Preliminary results indicate that the incorporation of magnesium limestone into the mound will prevent this toxicity.

The permission of the Director of Agriculture to publish these results is gratefully acknowledged.

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Digestion of the Alga, *Macrocystis pyrifera*, by the Sea Urchin, *Strongylocentrotus purpuratus*

IT has been known for some time[1] that sea urchins when fed and then starved seem to retain for long periods the food present in the intestine. Furthermore, *in vitro* experiments have shown that a battery of digestive enzymes exist, some of which can digest complex polysaccharides such as iridophycin[1] and algin[2]. During a series of experiments on the digestion of various substrates by sea urchins we had occasion to feed and afterwards starve an adult urchin and then recover all the material remaining after digestion. So far as we are aware no evidence exists on the percentage of algal food that can be completely degraded to assimilable products by a sea urchin. An urchin was prestarved until no fæcal pellets were passed. The animal, a female, weighing 99·3 gm., test height and test diameter measuring 26·5 mm. and 63·1 mm. respectively, was then fed a 33·3 mgm. (dry weight) piece of *Macrocystis pyrifera*, a food for which the sea urchin exhibits a high degree of preference[3], and fed no further food for 18 days. The algal piece was consumed within 8 hr. No fæcal pellets were passed during the observation time, and the animal was killed at the end of this time.

We removed the complete intestine of the urchin and recovered all the undigested materials. By comparison of the dry weight of the undigested residue with the dry weight of the food eaten, it is possible to determine the percentage of the alga that was digested, and, presumably, assimilated. 8·5 mgm. of undigested material was recovered, hence more than 76 per cent dry material of the alga was removed by the digestive processes of the urchin.

This completeness of digestion by a sea urchin supports the cited study on alginase since *Macrocystis* is known to contain at least 14·5–36 per cent dry weight of algin[4]. The extensive digestion of a meal when another is not forthcoming, coupled with the urchin's ability to resorb its gonads during starvation (Boolootian and Giese, unpublished work), may account for the urchin's ability to adapt itself to environments where food might become restricted.

This work forms part of a programme of investigation supported by funds from the National Science Foundation Grant 9561 to one of us (R. A. B.).

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Biosynthesis of Arbutin from Some Phenylpropanoid Compounds in *Pyrus communis*

HIGHER plants are capable of synthesizing aromatic compounds from shikimic acid, possibly through a pathway similar to that described by Davis *et al.*[1]. Certain benzene rings, however, are formed from acetate in accordance with the hypothesis of Birch and Donovan[2]. Thus the *B* ring of quercitin is synthesized from shikimic acid[3] whereas the *A* ring is an acetate-formed ring[4].

Arbutin or hydroquinone-β-D-glucoside occurs in many plants, such as members of the Ericaceae, and accumulates to the extent of 0·05–0·17 per cent of the fresh weight of pear (*Pyrus communis* L.) leaves[5]. So far as we know there has been no report on the origin of the ring of hydroquinone. Gloor and Wiss[6] have shown that mevalonic acid labelled with carbon-14 is incorporated by the rat into ubiquinone (a 2,3-dimethoxy-5-methyl benzoquinone with an isoprene side-chain of 50 carbon atoms). They have suggested that, whereas the isoprene side-chain is built up from mevalonic acid, the ring component is not synthesized by animals.

We have found that arbutin is synthesized in young leaves of pear from shikimic acid and more readily from phenylpropanoid compounds, whereas activity from acetate-^{14}C, pyruvate-^{14}C, and succinate-1,4-^{14}C is not incorporated into arbutin under the same conditions of administration.

The methods used were as follows: ten leaf disks (diameter 1·2 cm.) were vacuum infiltrated with tap water, blotted and floated in a Petri dish in 1·2 ml. of a solution containing 1–2 μc. of a radioactive compound. The covered Petri dish was placed under fluorescent lights for approximately 17 hr., after which the leaf disks were rinsed in tap water and extracted with boiling 80 per cent ethanol. The ethanol extract was concentrated, and chromatographed two-directionally in 80 : 20 phenol/water followed by 4 : 1 : 5 butanol / acetic acid / water. Radioactive spots were located by radioautography, and activity measurements were made by direct counting on the chromatograms. Arbutin, which is detected by its colour reactions with diazotized *p*-nitroaniline or diazotized sulphanilic acid, is well separated on chromatograms from chlorogenic acid and the other phenolics present in extracts.

Results of some of the feedings to pear tissue are given in Table 1.

Arbutin-^{14}C obtained from a phenylalanine-U-^{14}C feeding was hydrolysed with 2 *N* hydrochloric acid,

Table 1. INCORPORATION OF COMPOUNDS LABELLED WITH CARBON-14 INTO ARBUTIN IN LEAF DISKS OF *Pyrus communis*

Compound administered	Age of tissue (leaf disks)	Percentage of ethanol soluble activity in arbutin
Pyruvate-1-^{14}C	young	0
Pyruvate 2-^{14}C	young	0
Pyruvate-3-^{14}C	young	0
Succinate-1,4-^{14}C	young	0
Acetate-1-^{14}C	young	0
Acetate-2-^{14}C	young	0
Glucose-U-^{14}C	young	0·8
Shikimic acid-U-^{14}C	young	5
Phenylalanine-U-^{14}C	young	12
Phenylalanine-U-^{14}C	young	21
Phenylalanine-U-^{14}C	mature	0
Phenylalanine-U-^{14}C	dormant leaf buds	12
Phenylalanine-3-^{14}C	young	0
Tyrosine-U-^{14}C	mature	0
Tyrosine-U-^{14}C	young	8
Cinnamic-ring, 3-^{14}C	mature	0
Cinnamic-ring, 3-^{14}C	young	29
Benzoic acid-1-^{14}C (ring labelled)	young	0

after elution from the chromatogram with cold ethanol, and the products chromatographed in the butanol/acetic acid/water solvent. Hydroquinone-^{14}C was identified by its R_F value and colour reaction, which were the same as those of standard hydroquinone. Arbutin-^{14}C obtained from the feeding of glucose-U-^{14}C was hydrolysed in the same way to give non-radioactive hydroquinone together with glucose-^{14}C.

Phenylalanine-U-^{14}C fed to *Grevillea robusta* A. Cunn. was also incorporated into arbutin, confirming the results obtained with pear. In this species, however, the age of the leaf did not appear to be an important factor. In pear, chlorogenic acid was the major compound labelled with carbon-14 obtained when phenylalanine-U-^{14}C was fed, but no radioactive chlorogenic acid was obtained with *Grevillea*. According to Bate-Smith, chlorogenic acid does not occur in *Grevillea* (personal communication).

It is not known at present whether tyrosine gives rise to the hydroquinone or the glucose moiety of arbutin or both. It is known to form sugars readily when fed to pear leaves maintained in light.

It is evident, therefore, that hydroquinone may be formed in young pear leaves by the removal of the C_3 side-chain of certain phenylpropanoid compounds such as cinnamic acid, phenylalanine, and possibly tyrosine. This, together with the fact that it is not formed from acetate, indicates that it is an aromatic compound formed via the shikimic acid route.

This work is to be published in detail elsewhere.

We wish to thank the National Research Council of Canada for financial support of this project. We also thank Dr. E. E. Conn of the University of California, Berkeley, for a generous gift of ring and 3, carbon-14-labelled cinnamic acid.

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ENTOMOLOGY

A Tick infesting the Nostrils of Man

AN interesting example of the necessity for co-operation in the solution of complex problems of tick bionomics was recently brought to my notice by Dr. V. G. L. Van Someren of Nairobi and concerns infestation of the nostrils of man by the immature nymph stage of a tick belonging to the genus *Amblyomma*. These nymphs are white and were removed from the nostrils of three different persons, namely, Mr. D. Van Someren, Dr. V. G. L. Van Someren and Mr. T. H. E. Jackson, during visits to the depths of primary tropical rain forest in Uganda. The two former-mentioned persons were infested while in the Budongo Forest of Bunyoro during July 1952; the two latter while in the Kayonza Forest of Kigezi (known also as the Impenetrable Forest) during May and June 1957. A single example of the same tick was also found by Dr. Van Someren as it crawled up his neck when in the Kibali Forest of Toro.

It is of interest to note that these highly experienced entomologists were never aware of the ticks crawling across their faces or entering their nostrils. The first indication of infestation was tenderness of the nose when touched or when blown. Equally interesting was the absence of irritation or epistaxis and the disappearance of tenderness within a few hours of removal of the ticks. This almost complete absence of reaction to the presence of the parasite in man when acting as alternative host might suggest that nymphs of these ticks normally infest the nasal passages of anthropoid apes (Pongidae). The chimpanzee (*Pan troglodytes* sub. sp.) is in fact common in these Uganda forests.

Examples of these nymphs removed from human nostrils in the Kayonza Forest were examined and compared with all known African *Amblyomma* nymphæ by Dr. Gertrude Theiler of the Veterinary Research Laboratory, Onderstepoort, Transvaal, Union of South Africa, Miss Jane Walker of the East African Veterinary Research Organization, Muguga, Kenya, and by Dr. Harry Hoogstraal, head of the Department of Medical Zoology, U.S. Naval Medical Research Unit No. 3, Cairo, Egypt. Although all three specialists were unable to identify these nostril ticks, it is suggested by Miss Walker that they may be the nymph stage of *Amblyomma paulopunctatum* Neumann, 1899, which in the mature stage is known to be a parasite of the giant forest hog (*Hylochoerus meinertzhageni*) in western Uganda and distributed in equatorial Africa from French Guinea to Uganda.

Anyone hunting in or visiting the Uganda or West African forests could assist the identification of these ticks by examining the nasal passages of mammals, watching for any white ticks falling from the nose of captured chimpanzees or, when aware of nasal tenderness, allowing the ticks to remain *in situ* until engorged with blood and approximately the size of a small pea, when they may become detached and be blown out into a handkerchief or gently removed with forceps. The ticks should not be killed or put in spirit, but should be kept alive in a tin or tube stuffed with moss or moist tissue paper with a piece of rag tied over the top and posted to one of the specialists mentioned above. In man these ticks become attached to the nasal septum or upper anterior recess of the anterior nasal chamber.

I am indebted to Dr. Van Someren for his detailed observations and wish to thank Dr. G. Theiler, Miss J. Walker and Dr. Harry Hoogstraal for examining Dr. Van Someren's specimens.

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Atypical Spermiogenesis in *Thermobia domestica*, a Thysanuran Insect

SPERM formation of a thysanuran, *Lepisma domestica*, has been repeatedly investigated by a number of workers[1-5]. Unfortunately, diverse opinion prevails on the basic morphology of this sperm.

It is pertinent to recall that Bowen[2] and Nath and Bhatia[5] find *Lepisma* sperm to be unique inasmuch as the funnel-shaped acrosome lies at the posterior and centriole at the anterior end of the elongated nucleus. Nath and Bhatia add further that the mature sperm is devoid of mitochondrial material. On the other hand, Gatenby and his associates, in a number of earlier publications on *Lepisma* and a recent study[6] on another thysanuran, *Pterobius maritimus*, disagree with the interpretation of Bowen, Nath and Bhatia. In view of these contradictory reports, the present work[7] was undertaken to investigate, employing classical and modern cytological techniques, not only the morphology but also cytochemistry of spermiogenesis in another genus, *Thermobia domestica*. I agree with the assumption of Gatenby and Mathur that the insects (*Lepisma domestica*, *Pterobius maritimus*) and *Thermobia domestica* so closely allied could not have spermatozoa basically different in construction.

The investigations on *Thermobia domestica* confirm the view that thysanuran sperm is atypical in having a funnel-like acrosome in an unusual position behind the nucleus and the centriole at the anterior end of the latter. The identification of the acrosome as a 'post-nuclear' funnel is further strengthened by the observations that it is periodic acid–Schiff positive and that it arises in connexion with the fusion of the dictyosomes. The mitochondrial development is of the usual insect type. Unlike *Pterobius maritimus*, a single rod-like centriole, as observed in the living cells under the phase-contrast microscope, moves around the nucleus, and the acrosome, once deposited on the latter, continues to occupy the basal end of the metamorphosing spermatozoon. Electron microscope study (Fig. 1) reveals, apart from many new features, that the tail flagellum (*AF*) along with the mitochondrial sheath (*MN*) runs adjacent to the nucleus (*N*). This situation can only be interpreted if the centriole from which the tail is always considered to emerge lies at the head end of the developing spermatozoon. The 'lateral fold' of the nucleus in *Pterobius*[6] is most probably the backward continuation of the flagellum.

Fig. 1. × 6,000

Most of this work was done as a Boese Post-Doctoral Fellow, Department of Zoology, Columbia University, New York, 27.

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BACTERIOLOGY

Germination of Bacterial Spores by Long-Chain Alkyl Amines

SURFACE-ACTIVE agents induce striking changes in the physical, chemical and biological properties of bacterial spores[1,2]. The alterations caused by selected quaternary ammonium compounds are relatively minor at room temperature, but rapid and large at 50–100° C. The changes in spores of *Bacillus megaterium* brought about by combinations of mild heat and the quaternary ammonium compounds studied were practically identical with germinative changes induced by L-alanine and inosine[3,4] except that the cells treated with surfactants were non-viable[2]. In all probability this class of surfactants induced germination, the germinated spores being hypersensitive to the concentrations of surfactants required for germination and being killed immediately on germination.

Germinative changes in spores brought about by non-metabolites has been called 'chemical germination' in contradistinction to 'physiological germination'[2,5] effected by amino-acids and ribosides, etc. Germinative changes in spores accompanied by loss of viability (loss of ability to form colonies on agar media) may be regarded as 'lethal germination'.

Chemical germination of spores of *B. megaterium*, whereby germinative changes are accompanied by retention of viability, has now been achieved with long-chain alkyl primary amine surfactants.

L-Alanine, inosine or other physiological germinants are not essential in this system, nor is heat shock[6]. For optimal physiological germination of these spores heat shock combined with L-alanine and inosine or adenosine were found to be essential.

n-Dodecylamine [$CH_3(CH_2)_{10}CH_2NH_2$] was added to a suspension of spores of *B. megaterium* (approximately 6×10^7 spores per ml.) in 0·067 *M* phosphate buffer, *p*H 8·0. Final concentration of the dodecylamine was 0·00006 *M*. The following changes took place within a few minutes at 42° C.: (1) The normally refractile spores lost their refractility as determined by phase-contrast microscopy. (2) The spores became readily stainable with crystal (gentian) violet. (3) The spores were somewhat enlarged. (4) There was a marked reduction in the optical density (at 500–570 mμ) of the spore suspension (Fig. 1). (5) The majority of the cells in the suspension were capable of forming colonies (Fig. 1) on a complete agar medium[2] after neutralization of the dodecylamine with cephalin as described by Baker *et al.*[7]. (6) The surviving cells were not resistant to heat (Table 1). Likewise, they were killed by a variety of physical and chemical stresses which were lethal to spores germinated physiologically, but which were essentially innocuous to normal ungerminated spores (Table 1). (7) The spores lost more than 30 per cent of their dry weight. (8) The spores discharged their dipicolinic acid which appeared in the suspending liquid (Fig. 1). An excretion of calcium and of a peptide which contained hexosamine was also observed. (9) Finally, the spores treated with dodecylamine exhibited an increased respiration at the expense of added glucose; they also had a definite low endogenous respiration. Ungerminated spores had a negligible respiration either in the presence or absence of glucose.

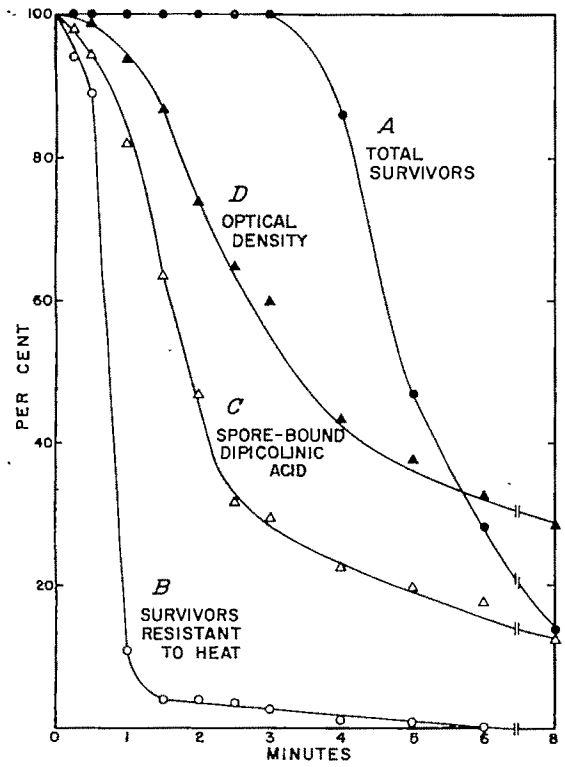

Fig. 1. Chemical germination of spores of *B. megaterium* with 0·00006 *M* dodecylamine, temperature 42° C. Curve *A* denotes survivors which formed colonies on a complex agar medium. Curve *B* denotes survivors which were able to tolerate heating at 65° C. for 20 min. Note that after 1-min. exposure to dodecylamine 90 per cent of the total viable survivors had become sensitive to heat. The dodecylamine was not lethal to the spores until after 3 min. Curve *C* shows that dipicolinic acid was released from the spores by dodecylamine prior to loss of viability but at a rate slower than the rate of labilization to heat. Curve *D* shows the typical reduction in optical density which accompanies germinative changes in bacterial spores

Table 1. SURVIVAL OF SPORES OF *B. megaterium* GERMINATED WITH DODECYLAMINE

Stress	Viability (per cent)		
	Spores germinated with dodecylamine	Spores germinated with L-alanine and inosine	Ungerminated spores
None	100	100	100
Heated, 20 min. at 65° C.	1	12	97
Ultra-violet light, 80 sec.*	48	17	89
Freeze–thaw†	53	39	98
Ethyl alcohol, 50 per cent‡	11	12	93
Phenol, 1 per cent‡	3	16	95
Hydrogen peroxide, 5 per cent‡	18	27	97
Sodium lauryl sulphate, 0·1 per cent‡	8	15	100
Mercuric chloride, 0·01 per cent‡	2	14	100
Sodium hypochlorite, 0·0005 per cent‡	0	6	96
*p*H 3·3 (HCl)‡	35	20	100
*p*H 11·0 (NaOH)‡	38	100	100

* 60 ergs/sec./mm.^{2}.

† Cells were frozen with a mixture of dry ice and acetone and thawed with running tap water in rapid sequence a total of eight times.

‡ Cells were exposed for 2 min. to aqueous solutions of these chemicals, then diluted rapidly and plated to recovery medium.

Since all the above features are characteristic of spores which have been germinated either physiologically or mechanically[8], it seems logical to conclude that true germination took place in the presence of dodecylamine and that this represents chemical germination in the sense described above. Other straight-cham primary amines displayed the germinative properties to varying degrees.

Some preliminary experiments were undertaken to determine whether germination by dodecylamine involves enzymes. Dodecylamine induced a germination-like decrease in optical density, a loss of refractility, a conversion to stainability and a release of dipicolinic acid under the following unphysiological conditions: at an incubation temperature of 70° C., at a *p*H of 11, in a solution containing 10 per cent ethyl alcohol, 15 per cent hydrogen peroxide, 1 per cent phenol or 1 per cent sodium cyanide, respectively. Presumably, any enzymes which might be activated by dodecylamine to elicit the germinative changes would be located near or at the surface of the spore, hence would not only have to persist throughout dormancy of the spore but also would have to be active in all the physiological extremes mentioned above.

The non-enzymatic evidence presented here extends the support[5] for the concept[8] that the prime event in germination is a breaching of a permeability barrier in the dormant spore which permits an ingress of water and attendant rehydration of the vital spore constituents.

A point of major interest now is to determine how the physiological germinants L-alanine and inosine fit into the picture and whether or not they have a function in a non-enzymatic or enzymatic mechanism for rehydrating the bacterial spore.

This work has been supported in part by a grant from the Office of Naval Research.

An extended account of these and related experiments will be published elsewhere.

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VIROLOGY

Polyoma Virus in Syrian Hamsters: a Non-communicable Infection

EPIZOOTICS caused by polyoma virus have been reported[1,2] in mouse colonies maintained in proximity to mice infected experimentally with this virus. Establishments without facilities to house infected and uninfected mice in separate buildings run the risk of contaminating their polyoma-free stock. It was of interest to determine, therefore, whether similar problems would be encountered when the Syrian hamster was used as the experimental animal to study this disease. Our experience indicates that infected hamsters rarely transmit polyoma virus to other hamsters or mice. The evidence that polyoma infection is a much less contagious disease of hamsters than of mice is shown by the following experiments.

(1) Hamsters less than 24 hr. old were divided into three groups and injected subcutaneously in the interscapular region with either $10^{5.5}$ mouse embryo tissue culture doses ($1\ CID_{50}$) of polyoma virus, $10^{2.5}\ TCID_{50}$, or sterile diluent fluid. The hamsters were appropriately marked and distributed among 13 mothers so that each litter contained 2–4 animals from each group. The hamsters were weaned and placed in separate cages when they reached 21 days of age. Approximately half the hamsters were bled between 41 and 59 days of age. Autopsies were performed on all hamsters dying during the experiment. At 98 days of age the surviving animals were bled, killed and autopsied. The sera were tested by hæmagglutination-inhibition and complement fixation for the presence of antibody to polyoma virus as described elsewhere[3]. As shown in Table 1, there is no evidence that any of the litter-mates injected with sterile diluent fluid contracted infection with polyoma virus.

(2) During assays of tumour-inducing capacity of polyoma virus in hamsters, approximately 200 suckling animals and more than 400 weaned animals were housed at the same time in nursing or individual cages in a single room with a floor area of 900 sq. ft. The hamster cages were arranged in series on long tables according to the age of the animals. To test whether the virus could spread from hamsters to mice, 7 cages each containing 5 young (8–10 gm.) mice were distributed in the room, some adjacent to cages occupied by suckling hamsters recently injected with polyoma virus, some among 21–50-day-old infected hamsters, and others among cages containing infected animals older than 90 days of age. The mice were bled twice, at 40 and 96 days, after being placed in the environment with infected hamsters. During this time all cages were cleaned and changed as needed, and all other usual activities permitted in the room. All the sera of the mice were negative when tested by hæmagglutination-inhibition and complement fixation. Careful gross inspection of the mice killed at 96 days after exposure to infected hamsters failed to reveal the presence of tumours.

Table 1

Inoculum	No. injected	No. cannibalized before 21 days of age	No. with tumours	No. dead of unknown causes*	No. of animals with antibody . total tested
$10^{2.5}\ TCID_{50}$	45	2	24	6	19/21
$10^{2.5}\ TCID_{50}$	37	1	10	6	16/21
Sterile diluent fluid	35	1	0	4	0/20

* 14 of the 16 animals dead of unknown causes were dwarfs.

(3) To achieve randomization in experiments with polyoma virus in new-born hamsters, we have distributed our inoculated hamsters so that each litter contained animals injected only with control diluent fluid as well as animals injected with various test dilutions of virus. To date, we have studied nearly 2,500 animals of which 320 were injected at birth with non-infectious materials. From autopsies and serological tests on individual sera it became apparent that only two hamsters injected with non-infectious material at birth showed evidence of infection at the time the experiments were terminated. Although we suspect that they contracted the infection from their litter-mates, we cannot exclude the possibility of error made at the time the inoculum was administered.

Several factors probably account for the non-contagious nature of polyoma infection in hamsters as compared with mice. Mice infected with polyoma virus excrete virus in urine, and cross-infection probably takes place through inhalation of aerosols[1,2]. Hamster urine is considerably less copious, and because of their habits they are less prone to create aerosols. Moreover, virus might be lacking in their urine since polyoma virus multiplies poorly in hamsters albeit tumours are readily induced. This is evident from the finding that only a fraction of tumours induced by cell-free filtrates contain demonstrable virus[3]. Occasionally, hamsters with tumours lack demonstrable antibody[3].

The results indicate that, with minimal care, laboratories doing research with polyoma virus in Syrian hamsters should not have much difficulty in keeping their small animal stock from becoming infected.

This investigation was aided by a grant from the U.S. Public Health Service (*C*-4204).

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FORTHCOMING EVENT

Thursday, December 29

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 3 p.m.—Dr. V. E. Cosslett: "Seeing the Very Small". (The One Hundred and Thirty-first Course of six lectures adapted to a Juvenile Auditory. Further lectures on December 31, January 3, 5, 7 and 10.)

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

ASSISTANT LECTURER IN ASTRONOMY—The Registrar, The University, Manchester 13 (December 31).

GRADUATE CHEMIST or PHYSICIST at the Houldsworth School of Applied Science, for a two-year programme of research on the physical and chemical properties of clays, particularly those used in the manufacture of building brick and heavy clayware—The Registrar, The University, Leeds 2 (December 31).

LECTURER (suitably qualified science graduate) IN DENTAL MATERIALS, to assist in the teaching of dental students and to undertake research in the physical, chemical and mechanical properties of plastics, elastomers, ceramics, alloys and other materials used in restorative dentistry—The Secretary, The London Hospital Medical College (University of London), Turner Street, London, E.1 (December 31).

RESEARCH WORKER (with some training in physics and mathematics) IN THE DEPARTMENT OF GEOGRAPHY, to assist the Lecturer in Polar Studies in a project concerned with the analysis of heat and water transfer in a river and a glacier basin—The Registrar and Secretary, King's College (University of Durham), Newcastle upon Tyne (December 31).

SENIOR LECTURER IN MATHEMATICS; a LECTURER IN OPHTHALMIC OPTICS; and a LECTURER IN MATHEMATICS OR STATISTICS—The Bursar, College of Advanced Technology, Gosta Green, Birmingham 4, quoting "N" (December 31).

EXPERIMENTAL OFFICER (graduate) IN THE DEPARTMENT OF CHEMISTRY, with responsibility for the maintenance of electronics apparatus—The Registrar, The University, Leicester (January 7).

ASSISTANT (medically qualified for at least three years and interested in human genetics and epidemiology)—The Director, Population Genetics Research Unit, Medical Research Council, Old Road, Headington, Oxford (January 14).

TUTOR (graduate in physics or chemistry or mathematics) IN THE INSTITUTE OF EDUCATION—The Registrar, The University, Hull (January 14).

LECTURER IN COAL PREPARATION IN THE DEPARTMENT OF MINING AND MINERALS ENGINEERING—The Registrar, The University, Edgbaston, Birmingham 15 (January 15).

PSYCHOLOGIST (with an honours degree in psychology or its equivalent) IN THE DEPARTMENT OF SOCIAL ANTHROPOLOGY, to assist in a study of urbanization and the effects of industrialization which the Department is conducting in Sierra Leone, West Africa—Dr. Kenneth Little, Department of Social Anthropology, University of Edinburgh, 3 Buccleuch Place, Edinburgh (January 15).

SCIENTIFIC OFFICER (with at least a good honours degree in geography, with subsidiary zoology and/or botany, or in zoology, with subsidiary geography, and preferably some experience in biogeographical, bioclimatic or ecological research) IN THE GEOGRAPHICAL SECTION, for research in the biogeography and ecology of economically important locusts and grasshoppers—The Director, Anti-Locust Research Centre, 1 Princes Gate, London, S.W.7 (January 16).

PROFESSOR OF MICROBIOLOGY, to take charge of the Department of Microbiology within the School of Biological Sciences, The University of New South Wales—The Agent-General for New South Wales, 56–57 Strand, London, W.C.2 and The Bursar, University of New South Wales, Box 1, Post Office, Kensington, N.S.W., Australia, marking envelope "University Appointment" (January 23).

LECTURER or ASSISTANT LECTURER IN APPLIED MATHEMATICS—The Registrar, The University, Leeds (January 24).

ASSOCIATE PROFESSOR (with a higher degree and preferably specialized in the field of feedback control systems) IN ELECTRICAL ENGINEERING at the University of New South Wales—The Agent-General for New South Wales, 56–57 Strand, London, W.C.2, and the Appointments Section, The University of New South Wales, Box 1, Post Office, Kensington, N.S.W., Australia, marking envelope "University Appointment" (January 27).

SENIOR LECTURER, and a LECTURER IN GEOLOGY at the University College of the West Indies—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (January 27).

BRITISH COKE RESEARCH ASSOCIATION FELLOW (honours graduate in chemistry, physics or applied science relating to fuel technology), to work on the physical chemistry of carbon under the direction of Prof. W. F. K. Wynne-Jones—The Registrar and Secretary, King's College (University of Durham), Newcastle upon Tyne (January 31).

ELDER CHAIR OF PHYSICS in the University of Adelaide, Adelaide, South Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, January 31).

LECTURERS (2) IN PHYSICS at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, January 31).

LECTURERS (2) IN ZOOLOGY at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, January 31).

CHAIR OF LOGIC—The Secretary of University Court, The University, Glasgow (February 3).

SENIOR LECTURER (with a higher degree or equivalent qualifications) IN PHYSICS at the Newcastle University College, The University of New South Wales—The Agent-General for New South Wales (Dept. HH), 56–57 Strand, London, W.C.2, and the Appointments Section, The University of New South Wales, Box 1, Post Office Kensington, N.S.W., Australia (February 3).

LECTURER IN THE SCHOOL OF MINERALS ENGINEERING—The Registrar, The University, Edgbaston, Birmingham 15 (February 15).

SENIOR LECTURER or LECTURER IN STATISTICS at the University of Otago, Dunedin, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand and London, February 15).

CHAIR OF APPLIED MECHANICS tenable in the Newcastle Division—The Registrar, University Office, 46 North Bailey, Durham (February 18).

CHAIR OF PHYSICS tenable in the Newcastle Division—The Registrar, University Office, 46 North Bailey, Durham (February 18).

LECTURER IN PHILOSOPHY at the University of Western Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, February 18).

IMPERIAL CHEMICAL INDUSTRIES FELLOW IN ONE OF THE FOLLOWING SUBJECTS: CHEMISTRY, BIOCHEMISTRY, PHYSICS, ENGINEERING, CHEMOTHERAPY and related subjects—The Secretary, Academic Council, The Queen's University, Belfast (March 1).

ELECTRONICS TECHNICIAN, to undertake the construction, development and maintenance of electronic and electrical equipment used in the physiological and radiological fields of medical research—The Secretary, Nuffield Institute for Medical Research, 48 Woodstock Road, Oxford.

LECTURER (single man) IN AGRICULTURAL BOTANY (AND ASSISTANT WARDEN)—The Clerk to the Governors, Essex Institute of Agriculture, Writtle, near Chelmsford, Essex.

LECTURER (well qualified, with industrial and teaching experience) IN ELECTRICAL ENGINEERING at the Norwich City College and Art School, Ipswich Road, Norwich—The Director of Education, City Hall, Norwich, NOR 01 A.

LECTURER (with an honours degree and teaching experience, and preferably with higher degrees and evidence of research ability), TO TEACH PHYSICAL CHEMISTRY to B.Sc. General (New Regulations), Grad.R.I.C. and H.N.C. standards—The Clerk to the Governors, South-West Essex Technical College and School of Art, Forest Road, Walthamstow, London, E.17.

LECTURER (with good academic qualifications in mathematics, and either experience of or an interest in numerical analysis) IN MATHEMATICS in the Department of Science, Bournemouth Municipal College of Technology and Commerce—The Chief Education Officer, Town Hall, Bournemouth.

MARINE BIOLOGIST (with a good honours degree in natural science, and preferably experience in marine research) with the Fisheries Development and Research Unit, Sierra Leone, for research into problems connected with the development of the marine and freshwater resources of Sierra Leone and biological investigations designed to assist in the conservation of the trawl fishery—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.65/15/01.

POSTDOCTORAL RESEARCH FELLOWS IN THEORETICAL PHYSICS—L. E. H. Trainor, Physics Department, University of Alberta, Edmonton, Alberta, Canada.

READER (with the qualifications and experience to direct research and postgraduate work, and to take a leading part in advanced teaching) IN PHARMACEUTICS—The Registrar, Bradford Institute of Technology, Bradford 7.

RESEARCH ASSISTANT (suitably qualified in biochemistry, pharmacology or zoology) IN THE WELLCOME LABORATORIES OF PHARMACOLOGY The Gatty Marine Laboratory, St. Andrews, for work on thyroid metabolism of lower vertebrates—The Joint Clerk to the University Court, College Gate, St. Andrews.

RESEARCH FELLOWS and RESEARCH ASSISTANTS (with an honours degree in pharmacy or other allied subjects) IN THE DEPARTMENT OF PHARMACY—The Registrar, Bradford Institute of Technology, Bradford 7.

SCIENTIFIC ASSISTANT (with an honours degree or its equivalent in biological sciences, preferably including physiology; a knowledge of languages, especially Spanish; and the ability to write correct English), to work on literature for *Nutrition Abstracts and Reviews*—The Director, Commonwealth Bureau of Animal Nutrition, Rowett Research Institute, Bucksburn, Aberdeen.

SCIENTIFIC OFFICER (CHEMIST), and an ASSISTANT EXPERIMENTAL OFFICER (CHEMIST)—The Secretary, Room 165(L), New Scotland Yard, London, S.W.1.

SENIOR LABORATORY TECHNICIAN (Grade I)—The Hospital Secretary, Harefield Hospital, Harefield, Middlesex.

TEACHING ASSISTANTS IN THE DEPARTMENT OF CHEMISTRY—Prof. Harry E. Gunning, Head, Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada.

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COLLEGES OF ADVANCED TECHNOLOGY

THE Advisory Council on Scientific Policy in its last report expressed the opinion that the development of colleges of advanced technology in Britain and the expansion of the smaller or medium-sized universities, which have hitherto included only faculties of arts or pure science, afforded an opportunity unlikely to recur for promoting studies in fields where there is little or no tradition of research and its application, and where there is little interaction between the universities and the industries which are the customers for the resulting technological skills. In the subsequent debate on the Council's report in the House of Lords, the question of research in the colleges of technology was scarcely mentioned, but in speaking on educational policy in the House of Commons on November 7, the Minister of Education, Sir David Eccles, after referring to the steady growth of postgraduate work in these colleges which the Government proposes to encourage as much as possible, said that he is very keen that these colleges should vigorously develop applied research.

Sir David expressed the view that the colleges of advanced technology are excellently placed to do so, because of their close links with industry; and those links would undoubtedly assist in the selection of projects for research that are really worth while. This appears to be what the Advisory Council on Scientific Policy also has in mind, but it is not here that the real difficulties in encouraging research in technical colleges lie. They are to be found in relation to staff, to problems of administration and status, and to a certain extent in finance. These difficulties, however, were not considered in the debate, though Mr. A. Albu doubtless had them in mind when he urged that the colleges of advanced technology should have independent governing bodies and should not come under the local authorities.

How small is the comparative contribution from the colleges of advanced technology may be seen from some figures quoted by Dr. D. C. Freshwater in *Technology*. Against an estimated 6,000 postgraduate workers in science and technology in the universities, there are only some 200 scientists and technologists on full-time postgraduate research in these colleges, of whom 40 are financed by Government grants, 20 by awards through the Department of Scientific and Industrial Research and 140 by the local education authorities. Of these 200, some 120 are in colleges in the London area and only about 80 in the remainder of the country, including those industrial areas of the Midlands and the North where it might be expected that close contact with local industry would be most conducive to stimulating exactly the type of technological research that the Advisory Council on Scientific Policy suggested in its last report.

Any advantage that the colleges of technology may enjoy through closer relations with local industry in the selection of projects for research, and possibly for the conduct of such research, can be more than offset if the conditions these colleges offer are not such as to attract staff of the requisite quality or to retain competent postgraduate students. The function of the colleges of technology in advancing knowledge, especially knowledge of value to industry, is still insufficiently recognized, and not all local authorities responsible for such colleges appreciate that research can make an important contribution in the teaching of advanced students, the vitality it imparts to the instruction being as important here as in a university. There are still local education authorities which do not acknowledge research as a normal and indeed an important function of the technical colleges. In consequence, there is no general pattern to the scope and practice of research in progress at the present time; and even where it is formally recognized, lack of facilities and equipment is an obstacle to the postgraduate research student, and the lecturer may find difficulties in giving time to research as distinct from teaching.

In a recent article in the *Journal of the Royal Institute of Chemistry* (84, 235; 1960), Dr. D. E. Chisman describes the position more particularly with regard to chemical research, which is believed to be in progress to some extent in at least forty colleges, or about half the technical colleges recognized by the Institute for training candidates for the graduate membership examination. In two of these there are more than fifty research workers in the chemistry department; but this includes part-time and full-time workers, both for the teaching staff and research students. In a further five colleges there are between 25 and 50 research workers; but in most of the colleges there are fewer than ten research workers, sometimes just one or two members of the staff who are endeavouring to complete research projects started elsewhere. Altogether, Dr. Chisman suggests that in the technical colleges in 1959–60 there were more than 300 chemistry research projects under way.

Again, the facilities available for research vary widely. Sometimes the only space available is in a corner or at one end of a teaching laboratory. Elsewhere small rooms have been partitioned off from large laboratories; but in a few colleges the facilities have been appropriately designed, and an area up to 3,500 sq. ft. is available, though the usual area specifically available where a research laboratory is provided seems to be about 1,000 sq. ft. Especially in the smaller colleges, research in chemistry is at present undertaken only by members of the teaching staff, and their research interests have to be integrated with their teaching duties. If the latter are particularly onerous, the time for research is naturally curtailed, and the research project at best is protracted, if indeed it is ever completed.

To help members of staff who have genuine research projects in train, many local education authorities are prepared to allow some time for research in lieu of teaching duties, and according to Dr. Chisman this usually amounts to 3–6 hr. a week, although for a reader or principal lecturer it may be 12 hr. per week. Not all local authorities, however, appreciate the desirability of allowing teaching staff time for research, and Sir David Eccles's observation in the House of Commons should induce some improvement here, though it is reasonable to expect that the teaching staff concerned should display some initiative and enthusiasm, and disclose the nature of their projects. The brochure issued by the London and Home Counties Regional Advisory Council for Higher Technological Education on research in progress in technical colleges of the region, for, or in collaboration with, industry, Government departments and research associations indicates the range and value of such projects even in 1956.

One disappointing feature of the present situation to which Dr. Chisman refers is the comparatively small number of students of research calibre, to whom research studentships in science and technology have been awarded through the Department of Scientific and Industrial Research, who elect to receive their training in technical colleges. There are at present more than 2,000 such awards held in universities and technical colleges in Britain, and it is expected that about a further 1,000 awards will be made this year. Less than 2 per cent of such research studentships in 1958 were for tenure in technical colleges, mostly in chemistry.

Some, but not all, research in colleges of technology is undertaken for the purpose of obtaining a higher degree or equivalent qualification, and the new award of membership of the College of Technology, introduced by the National Council for Technological Awards, which will normally be made for a programme of work (not necessarily research) carried out jointly in industry and at a college, should assist in removing any difficulties which research workers at the colleges of technology may experience in obtaining a higher qualification. While the College of Technologists will expect a high standard of candidates, the award will not be restricted to holders of the diploma in technology. Here there is, of course, a time factor: the award has to establish its merits, and this might perhaps be the easier if there were less readiness to blur the distinction between colleges of technology and the technical colleges. To say the least, it is debatable how far postgraduate work is really practicable in an institution which is not devoted to instruction at university-level.

Dr. Chisman expresses the opinion that there are probably in the colleges of technology more *ad hoc* short-term research projects in progress at any given time than research designed specifically for a higher degree or equivalent. Local industrial needs often lead to the initiation of short-term special research problems, thus effecting a valuable link between industry and technical education. Moreover, industry can, and does, assist by giving expensive equipment, and some colleges have thus been able to develop useful specialized research facilities. This is obviously a step towards the co-operation in the attack on major technological problems which the Advisory Council on Scientific Policy had in mind in its last report. If the major colleges of technology are to develop schools of research in particular technological fields, it will be just as essential that the immensely expensive equipment, which technological research no less than scientific research requires, shall be used on an agreed co-operative basis—perhaps between such colleges themselves, or between a particular college or group of colleges and industry—as it has now become for the universities.

Developments along such lines are likely to provide one of the surest ways of winning the prestige that will enable the colleges to attract—and keep—all the research workers they are able to accommodate. They will also help to solve the problem of status; but it must be realized that the question of status and autonomy cannot be left to chance. They must be tackled simultaneously and urgently. Research workers of the requisite calibre will not be drawn to the colleges of technology unless they are assured of a status comparable with that which they would enjoy in a university institution, and have the freedom to teach and investigate which it is a primary function of academic autonomy to ensure. The independence of the colleges of technology is a problem which needs urgent consideration, and local interest should not be allowed to overrule the national interest. Given goodwill and understanding and sense, the reconciliation of a live interest in local institutions with the larger national concern should prove no more difficult than in the creation of new university institutions.

One final aspect of research noted by Dr. Chisman might well make a valuable contribution to this problem, as well as to the prestige of the colleges Dr. Chisman refers to the need for investigations into methods of presenting the subject-matter used by lecturers in the technical colleges. As he rightly points out, the rapid developments of the past few years in the understanding of many phenomena through modern theories of atomic and sub-atomic structure have spurred the abler teachers to re-appraise their systems of teaching and to introduce substantial modifications, leading to more logical and co-ordinated presentation and to a more comprehensible and sound basis for further study. The whole content of university science courses as well as of school courses is under challenge and re-examination. There are also numerous ways in which standard experimental techniques may be improved and new demonstration techniques devised to illustrate theoretical topics. The colleges of technology may, in fact, enjoy more flexibility to take advantage of the considerable scope for such work, especially in the field of small-scale equipment; and in the measure to which they seize the opportunity, their prestige both as teaching and research institutions should be enhanced.

GEOGRAPHICAL DISTRIBUTION OF EUROPEAN BIRDS

Atlas of European Birds

By Prof. K. H. Voous. Pp. 284 (419 maps and 355 gravure plates). (Edinburgh and London: Thomas Nelson and Sons, Ltd., 1960.) 70*s*. net.

THIS splendidly produced volume fills a long-felt need in ornithology. A map is given showing the full breeding range of every species of bird that nests in Europe. For this purpose two basic maps have been used, one extending to the equator and the other covering the world, and so planned that one occupies half the space of the other, thus simplifying the arrangement. On each map the land is left uncoloured, the sea is shown in blue and the range of the bird is over-printed in red, which makes for extremely clear presentation. The author has used question-marks wherever there is doubt as to the range concerned.

The author's text is clear, concise and sound. He has in each case detailed the geographical range and habitat, and wherever these present problems of biological interest he has discussed them, so that the book is both a reliable summary of the known and a valuable guide to questions of zoo-geography and species-formation that would profitably repay further research. He has not discussed sub-specific variation except in a few cases where the allocation of species is difficult, but, while I think that it was fully justifiable to omit sub-specific names, I am sorry that he did not give a little more attention to the main trends of sub-specific variation. This is not, however, a serious omission. The author's treatment of the taxonomic limits of each species is very sound, and while it would be impossible to please all authorities, he has given his reasons where he differs from what may be found in other standard works. He has added short notes on food, nest-site and migration. Perhaps it is ungenerous to ask for more, but a second series of maps illustrating the range of each migratory species in winter is needed for proper evaluation of distributional problems, and such maps are not included.

The third section of the book is, in my view, irrelevant to the others. A black-and-white photograph is given of almost every species, providing a unique assemblage of fine photographs, even though many are already familiar from other bird-books. As a guide to identification, photographs can be misleading, particularly as there is no indication of the size of the bird. For example, in the double page featuring all the acrocephaline warblers, the smallest of all, to judge from the photographs, is the great reed warbler, which is in fact the largest of those shown. Anyway such photographs, being essentially bird portraits and not habitat pictures, are inappropriate to a bird atlas. There was, indeed, a strong case for two separate books, the first dealing with zoo-geography and the second with photographs, and omission of the latter from the atlas would, I imagine, have reduced its cost to less than half, and would have permitted printing on pages of half the present size, thus making it an even more valuable reference book than it is now. The photographs appeal to a different type of ornithologist and could have been issued separately with, perhaps, a brief description of each bird.

D. LACK

SEA BIRDS

Sea Birds

By Charles Vaucher. Translated by James Hogarth. Pp. 254 (255 photographs). (Edinburgh and London: Oliver and Boyd, Ltd., 1960.) 105*s*. net.

THIS is a sumptuous volume, beautifully produced, and its 255 photographs, 15 of which are in colour, are fine examples of the art of the camera. Charles Vaucher, their author, is to be congratulated on them. They include close-up bird portraits, snapshots of birds on the wing, some seascapes, among them an excellent picture of a four-mast sailing ship becalmed on a placid sea, and two or three shots of grey seals on the Farne Islands by way of contrast. Despite the seals, this is a bird book dealing with the birds to be found on or near the sea, particularly on the coasts of northern Europe, especially those of Britain and Scandinavia.

As indicated, this is primarily a picture book; but the literary matter is far from negligible or unimportant. The author amplifies the plates with chapters on the different species illustrated, their habits and habitats. He writes of what he has seen, with many interesting observations on bird conduct and behaviour, he gives us facts concerning distribution, breeding places, etc., and tells about his visits to many of the great seabird haunts in England, Scotland, Sweden, Finland and so on, his delight being the spectacular species that may be found on cliff, shore and island.

The author's style is concise but pleasant, and he has the gift of vivid description. We must not forget this is a translation from the French in which it was written and first published; however, it does not read as if it has lost anything in the process.

The latter part of the book is devoted to "Descriptive Summaries" in which the facts concerning each bird are set out concisely so that they may be seen at a glance.

Reverting to the pictures, which are all good, it is difficult to pick out one for special mention, but the photograph of an arctic tern on p. 189 is a remarkable study of a bird in flight, every detail, every feather, being depicted of the spread wings and spread tail.

A parent or other person wishing to give a boy or girl a present could not do better than choose this book, for it will surely fire youthful enthusiasm.

FRANCES PITT

CRYSTALLOGRAPHY CONDENSED

General Crystallography

A Brief Compendium. By W. F. de Jong, with the collaboration of J. Bouman. (Series of Books in Geology). Pp. ix+281. (San Francisco: W. H. Freeman and Company, 1959.) 38*s*.

ORIGINALLY published in Dutch in 1951, this work has now been enlarged and partially re-written for an English language edition. The primary object was to provide a review of the whole subject of crystallography; in the preface the author suggests that his book may also be used as a guide in private study, and by undergraduates as a summary of modern ideas on the subject. The book is in four parts, the first and longest (92 pages), on geometrical crystallography, being followed by sections on

structure theory and determination (43 pages), crystal chemistry (53 pages) and crystal physics (79 pages).

To review a whole science in a small space is a task calling for the most careful selection and presentation. The author has chosen to make his book reasonably encyclopædic, keeping down the length by a terse style of writing, by the use of numerous excellent diagrams, and by a multitude of references to more specialized works. The selection has, in fact, been a local, as against a regional, one. Considered as a compendium rather than a text-book and in view of its length, this is a successful book, remarkably complete and accurate. The brevity of the presentation has many drawbacks, of course; thus results are often stated without proper derivation, and the mathematical sections inevitably make dull reading. In the more descriptive chemical and physical sections the *hors d'œuvres* presentation certainly whets the appetite, but for the main course one is referred to other books. The section devoted to the explanation of crystal properties in terms of atoms is the most original and interesting one with a wide scope, including such topics as Frank–Read sources of dislocations, Raman radiation and transistors. Even the granitization theory gets a brief mention, one of the few reminders that this book is part of a geological series.

The proper balance for a work of this kind is a matter of opinion, but probably most English-speaking crystallographers will feel that the theoretical side here outweighs the experimental one, and that the geometrical section in particular is far too heavy for the rest.

A few detailed criticisms may be made. The author goes against well-established nomenclature in certain places. For example, he uses 'solid solution' for what would normally be called an interstitial structure, the usual solid solution becoming a 'substitutional structure'. Again, (*hkxl*) is used in place of (*hkil*) for four-axis Miller–Bravais indices with no real justification. Whatever the reasons for such changes, it is a mistake to introduce them in a reference book.

For the professional crystallographer this book will have some value for reference, particularly for the geometric part, as this is otherwise mostly treated in German texts. As a guide to private work it would be hard going without advice on selection. Parts of the book will be valuable to the undergraduate for revision or summary, while others are too advanced.

M. G. Bown

GEOLOGY IN THE UNITED STATES

Geological Survey Research 1960

Professional Paper 400, U.S. Geological Survey. Vol. A, Synopsis of Geologic Results. Pp. xii+136, 1 dollar. Vol. B, Short Papers in the Geological Sciences. Pp. viii+515. 4.25 dollars. (Washington, D.C.: Government Printing Office, 1960.)

FOR many years the United States Geological Survey has had a greater output of research in the Earth sciences than any other organization in the world. The immense mass of its publications, embracing the work of close on a thousand geologists, coupled with the inevitable delays in printing long detailed reports, has, however, resulted in some of its work not being known as widely or as speedily as it deserves to be; and to provide a more prompt and succinct release of new information the Survey has now issued this summary of progress which, if found useful, will henceforth be published annually. The publication is in two quarto volumes. The first presents a narrative synopsis of the technical activities of the Geologic Division during the fiscal year ended June 30, 1960. The second comprises 232 papers, most of them less than 1,000 words in length, which are either announcements of new discoveries on problems of limited scope or reviews of the results of extensive investigations that have been in progress for some time.

In his preface Dr. T. B. Nolan, director of the U.S. Geological Survey, states that "This report is frankly an experiment". The experiment is a highly successful one, for all but the most parochial workers in the geological sciences will find in these columns contributions within their fields of interest. The short papers are concerned with economic geology (42 contributions), exploration and mapping techniques (20), geology applied to engineering and public health (11), regional geology mainly of the United States (101), palæontology (6), geophysics (14), mineralogy, chemistry, and petrology (20), and analytical or petrographic methods (18). Notwithstanding the remarkable rapidity in publication a high editorial standard is maintained throughout; and Dr. V. E. McKelvey, who planned and directed the preparation of the volumes, is to be congratulated on the overall lucidity of presentation. Undoubtedly this review of progress will henceforth be one of the high-lights of the geological year; and by setting an example it should do much to improve and speed up the annual reports of other national surveys.

C. F. Davidson

COAL SCIENCE: AN INDIAN VENTURE

Proceedings of the Symposium on the Nature of Coal

Held at the Central Fuel Research Institute, Jealgora, 7th–9th February, 1959. (Organized by the Central Fuel Research Institute in collaboration with the Institute of Fuel, Indian Section.) Pp. viii+321. (Jealgora: The Central Fuel Research Institute, undated.) n.p.

A REPORT of the symposium on "The Nature of Coal", held at the Central Fuel Research Institute, Jealgora, has already appeared in these pages (*Nature*, 183, 1438; 1959); now the proceedings have become available.

The volume is well produced and I have come across few typographical errors; all papers are written in English. As often with such collections, more than a year has elapsed between conference and publication of the proceedings; as a result, some sections, especially that on the rapidly developing subject of coal chemistry, no longer represent the latest views on all aspects considered.

The conference was divided into six sessions as follows: origin and systematics of coal; petrographic and X-ray studies on coal; ultra-fine structure of coal; coal constitution, physical methods; coal constitution, chemical methods; physico-chemical properties of coal.

The attendance from Western European countries, North America and Australia was unfortunately small, and most of the papers from these areas, for example those by H. Barking and C. Eymann, N. Berkowitz, J. D. Brooks, I. G. C. Dryden, R. A. Durie and S. Sternhell, C. Kröger and Dobmaier, and M. Samec, could not therefore receive adequate discussion. A paper from the Canadian Bureau of Mines and Technical Surveys was presented by one of the authors, B. N. Nandi. To judge from the printed discussion, similar difficulties limited the consideration given to papers from the U.S.S.R. and eastern Europe, of which there were nine distributed over the first five sessions, mainly in the first, and of those from Japan (three). Half the forty papers presented originated outside India.

The selection of papers with especial interest is invidious and must be to some extent personal to the reviewer. However, I would mention three: "Carbon-bound Methyl Groups and the Mechanism of Coalification", by Kaiser, Rao and Lahiri in particular; "Pyrolysis and its Relation to the Structural Parameters of Coal", by Mazumdar, Chakrabartty and Lahiri; and "Relation between Chemical Constitution and Pyrolysis of Coal", by Biswas, Sarkar, Kini, Das Gupta and Lahiri. Less personal perhaps is surprise at the widespread tendency to record chemical analyses to two places of decimals when only one is justified by the available analytical techniques. It is disappointing to find only eight pages of discussion on three hundred pages of papers presented. Despite the title of the symposium, the technology of the applications of coal is not unrepresented. The whole volume is of considerable interest both for reading and reference.

I. G. C. DRYDEN

PESTS AND THEIR CONTROL

Horticultural Pests

Detection and Control. By G. Fox Wilson. New edition, revised by Dr. P. Becker. (Agricultural and Horticultural Series.) Pp. xix+240+4 plates. (London: Crosby Lockwood and Son, Ltd., 1960.) 25*s*. net.

Chemical and Natural Control of Pests

By E. R. de Ong. Pp. viii+244. (New York: Reinhold Publishing Corporation; London: Chapman and Hall, Ltd., 1960.) 60*s*. net.

Ten Little Housemates

By Karl von Frisch. Pp. 146. (London and New York: Pergamon Press, 1960.) 17*s*. 6*d*. net.

THE late George Fox Wilson was a garden lover and economic entomologist with profound experience of the pest problems that beset the gardener, and the rare gift of being able to write clearly, accurately and interestingly for the layman. His book, "The Detection and Control of Garden Pests", was therefore well received by all. In agreeing to revise it, Dr. Paul Becker not only had to stand the test of comparison with his predecessor, but also to bring the book up to date with recent rapid developments. He has been outstandingly successful.

The book has a new title, but retains its original form and content. Additions have had to be made: many new chemicals have come into use, and perhaps as a result of their misuse we have been forcibly reminded of the existence and importance of the natural enemies of insects. Thus Dr. Becker has rewritten the section on biological control and very sensibly continued to stress the importance of cultural and other practices that reduce the need to use insecticides.

There are more illustrations and the excellent quality of the paper used has made the most of them. The colour photographs, mostly provided by the Shell Photographic Unit, are exquisite.

Except for the few who correctly foresaw the problems that might arise, the dawn of the synthetic insecticide era seemed to be heralded by many economic entomologists as the beginning of the end of our insect competitors. Within a few years, however, it appeared likely that insecticides were creating as many problems as they solved, and we became only too familiar with such things as pest resurgence and resistance to insecticides. Such things were not really new, but in the excitement of new chemical discoveries they were often forgotten. Perhaps the most important by-product of this era was the stimulus it gave to ecological and other studies of pests, and to thoughts about the rational use of insecticides. That is, to try to put it briefly, how these undoubtedly valuable chemicals can best be used in combination with cultural and other practices to minimize pest damage without interfering with the benefits that may be derived from the activity of beneficial insects, or of inducing other undesirable side-effects. This approach is clearly reflected in Dr. Becker's book, and a great deal of fascinating work has been done along these lines in North America and in Europe.

If the title of Dr. E. R. de Ong's book leads the reader to expect a balanced account of recent work on rational pest control he will be disappointed. This book deals mainly with the control of pests (insects, diseases and weeds) of crops and livestock, of the household and of storage in the United States. There is little doubt that the recommended measures are sound, and that the quite well-arranged information will be of use to the American extension worker, but of much less value in the United Kingdom.

In "Ten Little Housemates" Prof. Karl von Frisch has written a series of essays that give the impression that he enjoyed writing them. If the purist is prepared to tolerate a work that makes no pretence of being a scientific treatise, no doubt he will be able to enjoy them too. It is written for the layman who takes an intelligent interest in what he sees around him, and for him this little book can be recommended.

F. H. JACOB

GROWING POINTS IN PLANTS

Gründzuge der Histogenese Höherer Pflanzen

Von Prof. Dr. Hermann von Guttenberg. 1: Die Angiospermen. (Handbuch der Pflanzenanatomie, Band VIII, Teil 3. Zweite, völlig neubearbeitete Auflage herausgegeben von Prof. Dr. W. Zimmermann und Prof. P. G. Ozenda.) Pp. viii+315. (Berlin-Nikolassee: Gebrüder Borntraeger, 1960.) 110 D.M.

THIS book is about the patterns of cells in the apical meristems of roots and shoots although its title may lead us to expect something else. It falls into three main parts, dealing with roots, shoots

and leaves, and there is a short section on a few anatomical aspects of differentiation. Prof. Guttenberg is well known for his work on root apices, and, for some people, the most useful part of the book will be the summary of his views on these, but the other two main sections are useful, painstaking accounts of developmental anatomy of the comparative kind. The book is profusely illustrated with modern line drawings and a few badly reproduced photographs.

It is marred by an almost total exclusion of any work which is not a simple consideration of cell patterns and by a dogmatic assertion of the author's views on these. He has not appreciated that merely putting some arrows on a diagram is not good evidence that cells behave in the way he says they do. Prof. Guttenberg does not like my interpretation of root meristems, and, to attack this, he ascribes to me views which I do not hold and does not try to explain the facts which, in spite of his protestations, are inconsistent with his own interpretation. Similarly, he has missed the significance of Thielke's important work on chimeras and of some American work on shoot apices. There are also some extraordinary gaps in some of the work presented and quite a lot of minor errors. There are, however, adequate indexes.

The book is likely to find a place in reference libraries partly because it is one of a reputable series of volumes on plant anatomy and partly because of its value as a comparative account of apical structure. Its price is likely to keep it out of personal libraries in Great Britain. Its old-fashioned approach is not likely to inspire a young biologist to study apices, and this is a pity to-day when there are so many opportunities for useful work on the behaviour of meristems. F. A. L. CLOWES

FLORA OF TROPICAL EAST AFRICA

Loganiaceae

By E. A. Bruce and J. Lewis. Edited by C. E. Hubbard and E. Milne-Redhead. Pp. 47. (London: Crown Agents for Overseas Governments and Administrations, 1960.) 4*s*.

THE "Flora of Tropical East Africa", of which the parts dealing with the families Loganiaceae by Mr. J. Lewis and the late Miss E. A. Bruce, Rosaceae by the late Mr. R. A. Graham, and Alismataceae and Butomaceae by Miss S. Carter have been published this year, covers the territories of Kenya, Uganda, Tanganyika and Zanzibar, an area of about 707,000 square miles in all. The Flora, which is being prepared under the editorship of Dr. C. E. Hubbard and Mr. E. Milne-Redhead, is being published family by family in separate parts with individual paging and pricing. So far 30 parts, including an introductory part and a glossary, have been published. Although the work is centred at Kew, much of it has been carried out by staff appointed by the Colonial Office for work on this Flora.

The Flora itself contains keys both to the genera and species, and also where necessary to sub-species and varieties; in addition, there are descriptions which are not intended to be exhaustive, but sufficient to indicate the main features of importance in identification of the entities keyed. References to the most important literature, particularly that of concern in East Africa, are also given, and representative specimens from the territories in which each species occurs are cited, usually only a limited selection of the total number seen. There are, in addition, brief notes on the habitat of each species in East Africa and its distribution both in East Africa and elsewhere. As a great deal of new taxonomic research has been involved, many specific names hitherto accounted distinct are here reduced to synonymy for the first time, and the lists of synonyms (primarily those relating to East Africa) will be found to contain much otherwise unpublished information. Each part of the Flora is illustrated with black-and-white figures so as to represent the habit of at least the majority of the genera described. There are also comparative figures bringing together for comparison diagnostically important organs of a series of species. As the total number of species in the area is probably in the neighbourhood of eleven thousand, it will be realized that the labour involved in working out this Flora will be both massive and lengthy.

The area covered by this Flora is, at least for Africa, unusually varied both in climate and altitude, including different sorts of vegetation ranging from the rain-forest, found here and there in Uganda and north-western Tanganyika and still more rarely and locally elsewhere, to the semi-desert scrub of the northern parts of Kenya, and the wonderful afro-alpine vegetation of the high mountains of East Africa. Perhaps the majority of the area is covered by the different aspects of the grassland, wooded grassland and woodland that clothe such huge tracts of tropical Africa. On this variety of vegetation, which often reflects differences in climate, there is superimposed a variety of different floristic elements: the rain-forest flora the species of which are mostly typical of the Congo and West Africa, the rich and remarkable flora, often containing numerous endemics, in the patches of forest scattered near the coast, the Somalian flora in northern Kenya, which though perhaps not rich in species, contains, however, many found nowhere else but in north-eastern Africa, the remarkable mountain flora so well represented in East Africa, and the generalized woodland and grassland flora so typical of much of east and south-tropical Africa may be taken as examples.

One of the interesting results coming from the taxonomic research involved in this Flora is that many species are being shown to occupy unexpectedly wide areas in tropical Africa, and to display ranges of variation which may frequently be far-reaching and complicated. What is now shown to be a single, perhaps polymorphic species may in the past have been known under several different names, each corresponding to a different part of its total geographical range. This has often given rise to false and misleading ideas about endemism and the size of genera. The patterns of variation take many different forms, and may have originated in various ways, perhaps through the intrinsic variability of certain species, or perhaps through the swamping of originally distinct and separate species which have come into contact with one another for some cause, giving rise to numerous hybrids destined to outnumber their parent species. The presence of such problems is obvious enough, but the evidence is usually insufficient for more than guessing at their cause.

J. P. M. BRENAN

Nuclear Radiation Measurement

By J. Sharpe. (Nuclear Engineering Monographs.) Pp. vii+71. (London: Temple Press, Ltd., 1960.) 12*s*. 6*d*. net.

THIS book is one of a series of short monographs on nuclear engineering subjects intended for university and technical college students, research assistants and qualified technicians. With only sixty-six pages of text the author has concentrated on outlining the physical principles by which the various detectors operate, and there is little practical information on their design and construction. Each of the four main chapters has a useful list of references, and there is a short index.

The first main chapter, which occupies one-third of the book, discusses the way by which charged and uncharged particles and electro-magnetic radiations interact with matter. The various processes of energy absorption are mentioned, and some relevant data are presented in tabular form. Emphasis is placed on the scintillation phosphor as a detector, and the properties of different types of phosphor are examined in some detail.

The next chapter describes the operating mechanism of different types of detector, including a mention of such specialized devices as cloud- and bubble-chambers and photographic emulsions. Perhaps inevitably, the treatment of the more common gas-ionization detectors (ion chambers, proportional counters and Geiger–Müller counters) is somewhat incomplete; there is a short section on multiplier photo-cells. There follows a small section listing the ancillary equipment necessary for the working of the detectors, such as power supplies, amplifiers, scalers, etc., and then the last main chapter considers the types of detector best suited for a number of specific applications. Mention is made of α-particle assay using a zinc sulphide phosphor or a flow proportional-counter, and the absolute and relative measurement of β-particles.

The measurement of the energy of gamma radiation by scintillation counters is described, and the use of X-ray proportional counters for low-energy X-radiation is mentioned. Detectors employing the boron-10 (n,α) reaction for thermal neutron measurement are described, and some techniques for the detection of fast neutrons are noted.

The book is clearly written and produced, and fulfils its aim of introducing the very wide subject to technical students and research assistants.

W. R. LOOSEMORE

Anorganische Chemie

Band 1. Von István Náray-Szabo. Pp. 664. (Budapest: Verlag der Ungarischen Akademie der Wissenschaften (Akadémiai Kiado), 1959.) n.p.

PROF. SZABO'S book is planned to extend to three volumes. It begins with a good, concise account of atomic structure, radioactivity, and the theory of valency. The author believes that a book on inorganic chemistry of this size should confine itself to its subject and not branch off into disquisitions on physical chemistry or organic chemistry. The elements are dealt with systematically in the order of the Periodic Table, the compounds being in a systematic order. There are tables of physical properties, an arrangement which saves space and is useful for reference. In a few places the treatment requires revision, for example, in the description of non-existent substances such as FO. The translation from Hungarian into German makes the book accessible to a large class of readers, and it deserves to be successful.

J. R. PARTINGTON

Chemical Instrumentation

A Systematic Approach to Instrumental Analysis. By Dr. Howard A. Strobel. (Addison-Wesley Series in Chemistry.) Pp. xviii+654. (Reading, Mass. and London: Addison-Wesley Publishing Company, 1960.) 74*s*.

THIS is a volume of 653 pages, printed legibly on excellent paper, and it presents, in small compass, an extensive store-house of information on the theoretical and practical aspects of most known fields of instrumental analysis. Its range of topics is so incredibly wide that, from the practical laboratory point of view, some useful detail has, of necessity, been omitted. Nevertheless, as a book for the undergraduate or honours degree student it has much to commend it.

The theoretical approaches are excellently described; the compilation of methods has been admirably done, and the many diagrammatic illustrations are clear and singularly helpful.

Most fields of spectroscopy are succinctly described: radioactive techniques, polarography, gas chromatography, polarimetry, electrometric methods, etc., all find their place in the various chapters. Scientific fundamentals are never ignored; there are two chapters on basic electronics, including transistor circuitry, and the information contained therein materially assists the student in the real understanding of the instrumental methods covered in the text. Another interesting chapter deals with "Errors of Measurement". The book concludes with a suggested series of detailed laboratory experiments which parallel in diversity the topics covered by the author.

It is not often that the student can purchase so much scientific information at such a modest price.

D. T. LEWIS

The Bridal Bed

By Joseph Braddock. Pp. 189+8 plates. (London: Robert Hale, Ltd., 1960.) 18*s*. net.

THIS book is really an anthology, culled from a great variety of authors, some reliable and some otherwise, concerning marriage ceremonies in many parts of the world.

The book is divided into six parts. In the first the choice of the marriage partner is described, while in the second courtship as seen in both civilized and primitive communities is described in some detail. From these preliminaries spring naturally accounts of the wedding itself; and finally some consideration is given to what various writers have said about consummation and customs relating to the various human relationships within the marriage state.

For those who wish to gain a general idea of what has been said about marriage customs in both Western and Oriental countries this anthology would provide an excellent introduction, although it would have been much improved had more trouble been taken to verify references and avoid relying on authors whose inaccuracy must surely have been apparent. The book is well printed and arranged, although it is not easy to understand why the bibliography is not arranged in correct alphabetical order.

E. J. DINGWALL

LOW-TEMPERATURE FORMS OF ICE AS STUDIED BY X-RAY DIFFRACTION

By L. G. DOWELL and A. P. RINFRET

Tonawanda Research Laboratory, Linde Company, Division of Union Carbide Corporation, New York

IN recent years a number of investigators have studied the low-temperature, low-pressure structures of ice, using such techniques as thermal analysis (Pryde and Jones[1]), electron diffraction (Konig[2]), and X-ray diffraction (Barnes[3]). A comprehensive treatment of the literature is given by Blackman and Lisgarten[4]. General agreement exists that there are three possible phases of ice at low temperatures and pressures, namely, hexagonal or ice I, diamond cubic, and vitreous. There is, however, wide divergence of opinion as to the details of formation of these phases and to the conditions for their existence. We have determined the temperature-ranges in which the various phases exist and the rates of transformation from one phase to another. We have been able to produce vitreous ice only by condensing water vapour on a surface maintained below − 160° C. This vitreous ice undergoes a partial and irreversible change to cubic ice at temperatures above − 160° C., the rate of transformation being strongly dependent on temperature. The mixed cubic-vitreous phase undergoes an irreversible transformation to hexagonal ice I at temperatures above − 130° C., the rate also being dependent on temperature.

The basic X-ray equipment consisted of a water-cooled diffraction unit (Norelco Type 12045), a copper target X-ray tube, a scaler-ratemeter (Norelco Electronic Circuit Panel, Type 12096), a linear amplifier (Norelco Main Amplifier Chassis, Type 42234) and pulse-height analyser (Atomic Model 510). The diffractometer was built in our own shops but closely resembled the Norelco Type 42266. It was equipped with a flow-type proportional counter using an argon–methane (90 : 10) gas mixture.

A low-temperature vacuum chamber attachment was constructed as a replacement for the regular sample holder. It consisted of a hollow copper tank (Fig. 1) containing a depression for the sample plate and was attached to a phenolic block which was in turn attached to the sample shaft. An O-ring provided a vacuum seal between the vacuum chamber back-plate and the phenolic block. The back-plate carried Kovar seals for the thermocouple leads and also carried the refrigerant lines. The vacuum cover was sealed to the back-plate with an O-ring and contained slots covered with polystyrene sheets as the X-ray windows. The vacuum connexion was also in the cover. The copper–constantan thermocouple was cemented to the sample plate with silver paint and was located just outside the area irradiated by the X-ray beam. A vapour inlet tube was inserted into the vacuum cover, and its tip was located 1 in. above the centre of the sample plate. Finally, a 0·00035-in. nickel foil sheet was placed over the depression in the tank and served both as a thermal radiation shield and as an X-ray filter.

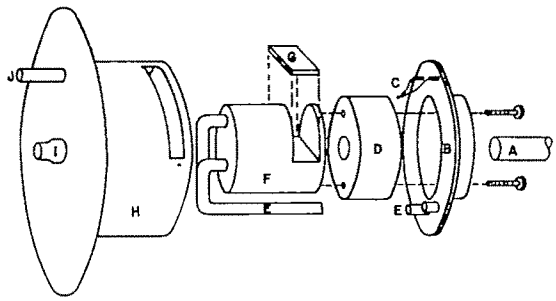

Fig 1. Low-temperature cell for the X-ray diffractometer *A*, diffractometer sample shaft; *B*, vacuum chamber base plate; *C*, thermocouple; *D*, phenolic block; *E*, refrigerant lines; *F*, hollow cold cell; *G*, specimen plate; *H*, vacuum chamber cover; *I*, vacuum connexion; *J*, water vapour inlet

The vacuum system consisted of a rotary oil-sealed pump which maintained a vacuum estimated at about 5μ except during sample preparation. This pressure provided adequate thermal insulation yet did not cause noticeable sublimation of the sample except at temperatures above −30° C The total heat leak was such that the rate of warming was about 3 deg. C. per min. at − 160° C. and less than 2 deg. C. per min. at − 90° C. when the refrigerant supply was discontinued.

Two refrigerant systems were used. For investigations near − 190° C., liquid nitrogen was forced through the refrigerant lines directly into the cold cell. The minimum temperature obtained was − 192° C. For most of this work, however, the various temperatures were maintained by means of a stream of nitrogen gas which first passed through a copper coil immersed in a Dewar flask of liquid nitrogen before moving into the cold cell. By controlling the rate of flow of the gaseous nitrogen, any temperature down to − 175° C. could be maintained as long as needed.

Ice Structures

Hexagonal phase. Much has been published concerning the structure of ordinary hexagonal ice (usually called ice I), and the reader is referred to Owston[5] for an excellent review of this literature. We will discuss the simple Barnes model of ice which shows only the oxygen arrangement in the lattice, since the hydrogen atoms contribute so little to the X-ray diffraction pattern.

One may conveniently consider the hexagonal model as being built up of layers of oxygen atoms, each layer consisting of a network of open puckered hexagonal rings. Each additional layer is a mirror image of the preceding layer, so that the stacking is of the $A \cdot B \cdot A \cdot B \cdot \cdots$ sequence. It can be shown that this leads to the tetrahedral arrangement of atoms of oxygen known to exist in ice I. The c_0 parameter is twice the layer spacing and was found to be 7·338 ± 0·004 Å. at − 175° C., while the a_0 parameter was 4·498 ± 0·002 Å. There are four

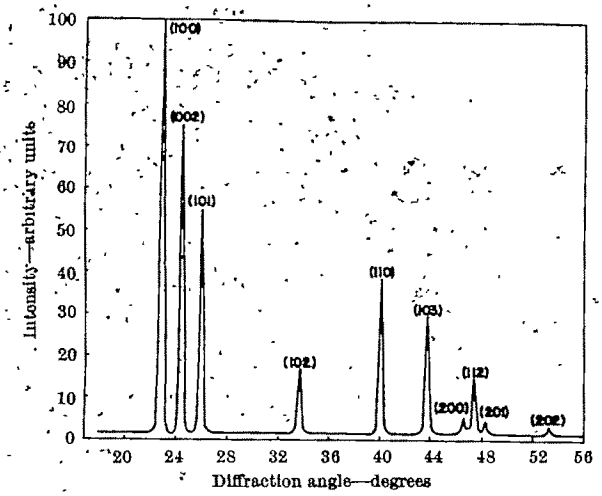

Fig. 2. X-ray diffraction pattern of hexagonal ice (Ice I)

molecules per unit cell, leading to a computed density of 0·924 gm./c.c. A typical X-ray diffraction pattern of this phase is shown in Fig. 2, and Table 1 shows the d values and relative intensities of all lines observed up to an angle of 56° (2θ). The lines are quite sharp, indicating no line broadening due to small particle size. The variation of intensity ratios from experiment to experiment indicates either the presence of large particles or of preferred orientation of somewhat smaller particles. The relative intensities listed in Table 1 are the averages of several typical patterns of this phase.

Table 1. X-RAY DIFFRACTION DATA FOR HEXAGONAL ICE AT − 175°C.

hkl	2θ (deg.)	d (Å.)	I/I_0
100	22·82	3·897	100
002	24·26	3·669	75
101	25·89	3·441	53
102	33·55	2·671	17
110	40·09	2·249	39
103	43·70	2·072	30
200	46·62	1·948	4
112	47·41	1·918	18
201	48·84	1·883	3
202	53·24	1·721	2

Diamond cubic phase. König[2] was probably the first to recognize and deduce the structure of cubic ice. Shallcross and Carpenter[4] confirmed the identity of this structure, describing the conditions for its formation as well as its properties. The oxygen atoms are located in a diamond cubic lattice, but the structure may also be considered as being built up in layers of oxygen, each layer identical with that of the hexagonal phase. However, each successive layer is shifted one-half the diameter of the hexagonal ring, leading to the $A \cdot B \cdot C \cdot A \cdot B \cdot C \cdot \cdots$ stacking sequence typical of the diamond cubic system.

We have found the cubic parameter to be $a_0 = 6{\cdot}358 \pm 0{\cdot}004$ Å. at − 185° C., leading to a computed density of 0·923 gm./c.c. This density is identical with that of the hexagonal phase within experimental error. The similarity of the structures of the two phases is more easily seen by deducing the pseudohexagonal cell of the cubic phase and comparing it with the hexagonal phase (Table 2). It will be noticed that the a_0 parameters are the same, but the c_0 parameter of the pseudohexagonal cell is 50 per cent greater, leading to the same layer spacing for both phases.

Table 2. CRYSTAL PARAMETERS FOR HEXAGONAL AND CUBIC ICE

	Hexagonal	Cubic	
		Diamond cubic cell	Pseudohexagonal cell
a_0	4·498 Å.	6 358 Å	4·495 Å.
c_0	7·338 Å.	—	11 012 Å.
c_0/a_0	1·631	—	2 450
Layer spacing	3·669 Å.	—	3 671 Å.
Density	0 924 gm./cm.³	0·923 gm./cm.³	0·923 gm./cm.³

A typical X-ray diffraction pattern of the cubic phase is shown in Fig. 3, and Table 3 lists the d values and intensities of all lines appearing up to 56° (2θ). The small peak appearing to the left of the (111) peak is partly due to a trace of hexagonal ice and partly to the maximum of the residual vitreous ice. The intensity ratios are quite reproducible and the lines show considerable broadening. Application of the Scherer law gives an average particle size of about 400 Å. This same result is obtained regardless of the rate or temperature of transformation from the vitreous phase.

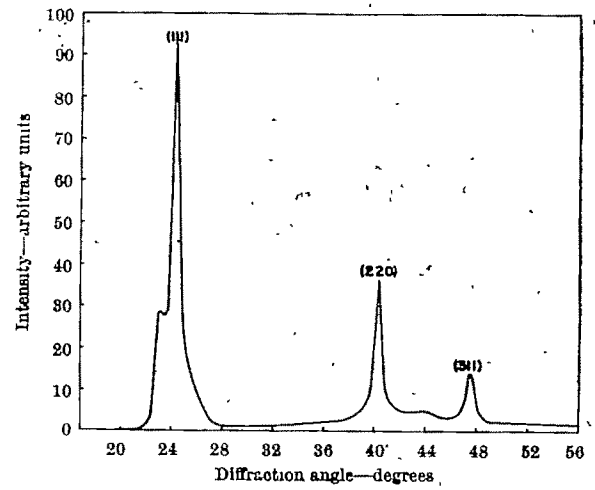

Fig. 3. X-ray diffraction pattern of diamond-cubic ice in the presence of vitreous ice

It should be pointed out that we have never observed the cubic phase in a pure state, but always with what has been considered as a modification of the original vitreous phase. This aspect of the problem is examined in the following section.

Vitreous phase. Fig. 4 shows a typical X-ray diffraction pattern of vitreous ice. It is characterized by two intensity maxima, one at 24° (2θ) corresponding to a Bragg spacing of 3·71 Å. and having a half-width of 5·0°, and the second at 42° (2θ) corresponding to 2·15 Å. Dorsey[7] has compiled a list of X-ray diffraction patterns of liquid water reported by a number of investigators. These data indicate periodicities in the structure having values of 3·20 Å, 2·11 Å. and 1·35 Å. Although our observed value of 2·15 Å. and the reported value of 2·11 Å. are in

Table 3. X-RAY DIFFRACTION DATA FOR CUBIC ICE AT −185° C.

hkl	2θ (deg.)	d (Å.)	I/I_0
111	24·25	3 670	100
220	40·11	2·248	40
311	47·43	1·917	15

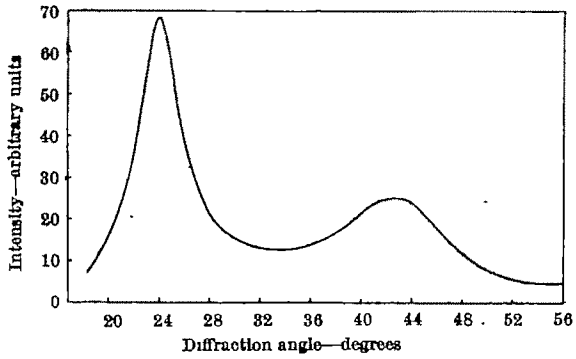

Fig. 4. X-ray diffraction pattern of vitreous ice

agreement, the 3·71 Å. observed value is unique. It is therefore evident that the structure of vitreous ice is different from that of water at ordinary temperatures. Further discussion of the structure of this phase is found in the final section of this article.

The portion of the original vitreous ice which remains after the cubic transformation is complete has also been altered. If the shape of the vitreous diffraction curve near 24° (2θ) is observed during the transformation to the cubic phase, it is found that the centre of the curve remains virtually unchanged, whereas the intensity gradually diminishes on the high-angle side and more abruptly on the low-angle side. At the same time, the relatively sharp cubic (111) line appears on the crest of the vitreous maximum. When an estimated 30 per cent of the vitreous ice has been transformed to the cubic phase, the conversion ceases regardless of the time or temperature involved. In addition, this same pattern is observed when the original condensation is carried out at temperatures sufficiently high to form the cubic phase directly.

Production of Vitreous Ice

Several attempts were made to produce vitreous ice from liquid water, but none was successful. They included spraying water on a substrate held at − 190° C., and plunging films of water on metal foils into liquid nitrogen. Only normal hexagonal ice resulted, as might be expected from Luyet's[8] prediction that a cooling-rate of 20,000 deg. C. per sec. would be required to vitrify liquid water.

In another method, atmospheric moisture was collected on the refrigerated sample plate. Small amounts of vitreous ice were obtained; but, as the deposit formed, the surface temperature rose due to the insulating effect of the ice layer and the crystalline forms of ice appeared, as did solid carbon dioxide.

The condensation of pure water vapour is the most reliable and practical method of producing vitreous ice. Although the direct condensation of vapour from a liquid or solid source has been used by most investigators, we have found that greater control can be exercised by using a stream of wet gas. We caused a small stream of nitrogen gas to pass through a spiral gas-washing bottle containing distilled water and then through a needle valve into the vapour inlet tube built into the vacuum cover of the low-temperature cell. The wet gas impinged on the centre of the cold sample plate, where the water vapour was condensed and the nitrogen was continuously pumped off. The thickness of the ice film was computed by measuring the decrease in intensity of the diffraction pattern of the silver sample plate. At a rate of flow of 75 c.c. per min. of wet nitrogen, a layer of ice 60μ thick was deposited in 30 min.

No attempt was made to determine accurately the conditions for the formation of the various phases from the vapour state. However, we found that vitreous ice could be formed at any temperature below − 160° C., while various amounts of cubic ice appeared if condensation occurred at higher temperatures. Above − 120° C. a very highly oriented film of hexagonal ice formed. We also found 60μ to be the maximum thickness of vitreous ice obtainable. This was also probably due to the high surface temperature acquired as the deposit thickened.

Most of the work reported here was carried out using a polycrystalline silver plate for the substrate. To test the substrate effect several trial experiments were made using a glass plate, but in no part of the entire procedure was any difference noted. It is concluded that our results are free of any substrate effects.

Phase Transformations

Vitreous to cubic. This irreversible phase change was observed to be strongly dependent on temperature and took place in the temperature range − 130° to − 160° C. At higher temperatures, the conversion is very rapid and no measurements of rate were made. The rate of transformation was measured by setting the X-ray diffractometer at the correct angle for the cubic (111) line and observing the increase in intensity as a function of time at various temperatures. The transformation appears to proceed linearly with time, until it nears completion, when it suddenly slows. The conversion times were obtained by extrapolating the main part of the time – intensity curves to the maximum intensities when equilibrium was reached. It should be noted that this occurs when about 30 per cent of the original ice has been converted, as estimated from the area under the vitreous curve and the peak heights of the crystalline phases. For the lower temperatures the scaler and timer were used periodically to determine the increase in counting-rate with increasing time. The temperature was then raised to − 120° C. for a short time to ensure the maximum conversion, the counting rate was measured, and the transformation time was computed. Equation 1 relates conversion time and sample temperature in the range of − 135° C. to − 160° C.:

$$t = 2{\cdot}04 \times 10^{26} \times \exp(-\,0{\cdot}465T) \qquad (1)$$

where t is the time in minutes for the conversion and T is the absolute temperature in degrees Kelvin. A graph of observed values is shown in Fig. 5. The transformation occurs rapidly above − 135° C., and if the temperature of a specimen of vitreous ice is raised at a rate of 5 deg. per min., the conversion appears to take place suddenly near − 130° C.

A single determination of rate was carried out at − 160° C., but since the 12-hr. observation period was a small fraction of the computed transformation time of 205 days, we do not consider that observations at this temperature are reliable. One approach to this problem is to store a specimen for weeks at − 160° C. and lower, and to examine it periodically by X-ray diffraction methods to determine whether our equation is valid for lower temperatures.

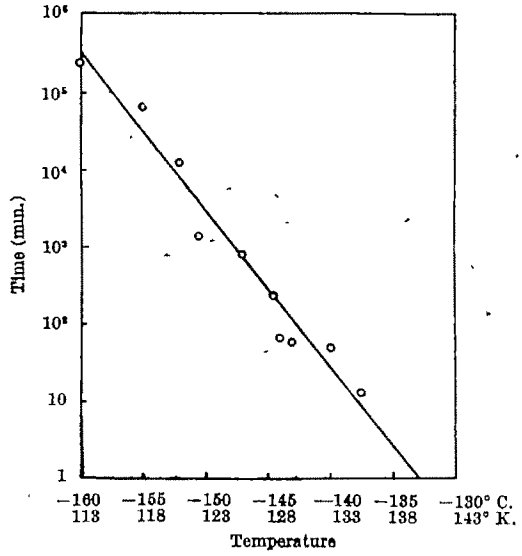

Fig. 5. The time necessary for the conversion of vitreous to cubic ice

Cubic to hexagonal. A further increase in temperature above − 130° C. allows transformation to the hexagonal phase. Although it is certain that the residual vitreous ice becomes converted to hexagonal ice, the evidence that the cubic phase is also converted is indirect. All three diamond cubic lines exactly coincide with hexagonal lines, and the large particle size and possible orientation effects of the hexagonal phase make the analysis of intensity ratios a poor guide to the presence of the cubic phase. However, the sharpness of the hexagonal lines and the lack of broadness near the base of the lines show that the cubic ice, if present, has appreciably increased in particle size. We conclude that probably both the vitreous and the cubic forms are converted to the hexagonal phase, and we will call it the cubic–hexagonal transformation.

The rate of this transformation is also dependent on temperature, although much less sensitive in this respect than is the vitreous–cubic change. The rate was measured with the same procedure described earlier, except that the diffractometer was set at the angle for the (100) line of hexagonal ice. Equation 2 relates time of conversion and sample temperature in the range of − 65° to − 120° C.:

$$t = 2{\cdot}58 \times 10^{12} \times \exp(-\,0{\cdot}126T) \qquad (2)$$

with t in minutes and T in degrees Kelvin. The observed values are shown in Fig. 6. This transformation occurs rapidly above − 70° C., and if the temperature of a specimen of vitreous and cubic ice is raised at a rate of 5 deg. C. per min. the conversion takes place rather quickly near − 60° C.

A single determination of rate was carried out at − 120° C., but here also the time of observation was too short for us to obtain reliable results.

Discussion and Conclusion

The results presented require consideration of alternatives with respect to the actual structure of the vitreous phase. Of two possible interpretations of the observed diffraction pattern, one is that the 'vitreous' ice obtained by our procedure is composed of small particles of crystalline ice, so small that the diffraction maxima are greatly broadened. Supporting this view is the fact that the 3·71 Å. spacing is very close to the 3·67 Å. value of the (111) line of cubic ice. Further, the 2·15 Å. value is between those of the (220) and (311) lines of cubic ice, and could be due to the overlapping of these two lines. However, application of the Scherer formula to the 3·71 Å. peak gives a particle size of about 20 Å., or about 3 unit cells in length. Since ordering is even less in the other directions and since the very essence of the crystalline state is the regular repetition of the unit cell, we consider it without significance to refer to this as a microcrystalline phase.

The second interpretation of this type of pattern is that 'vitreous' ice really has a typical vitreous or random network type of structure. In agreement with this theory are the following facts:

(1) No sharp conversion temperature from the vitreous phase was observed. This is consistent with the slow development of a crystalline lattice from a disordered array of molecules as the temperature is raised.

(2) Below − 160° C., substrate temperature and the rate of deposition of vapour produced no change in the X-ray diffraction pattern. Since crystal size is directly related to temperature, changes in the sharpness of the maxima could reasonably be expected between −190° and −160° C. if a microcrystalline structure were characteristic of vitreous ice.

(3) During the vitreous – cubic transformation (− 160° to − 130° C.) the intensity of the cubic peaks changed but their half-widths remained unaltered. This supports the interpretation of phase change (to a structure of constant particle diameter) rather than crystal growth.

(4) An exotherm near − 130° C. was reported by Pryde and Jones[1]. This observation would be expected if associated with a change in order, but would not be expected if associated with the growth of larger crystals at the expense of their smaller neighbours.

The foregoing observations predict that if a sample of vitreous ice is rapidly warmed, for example, 5 deg. C. per min., the vitreous–cubic transformation should

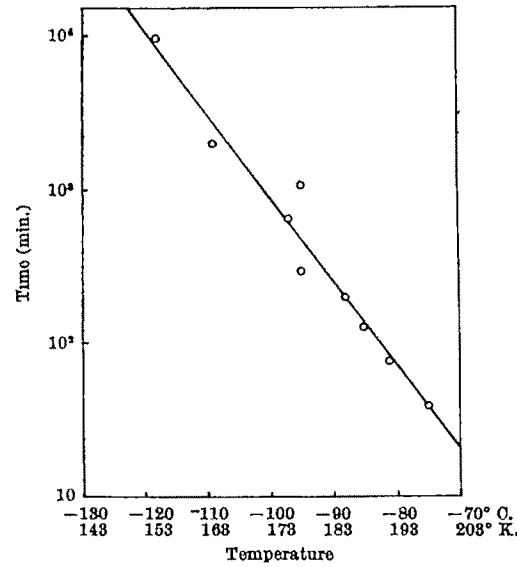

Fig. 6. The time necessary for the conversion of cubic to hexagonal ice

appear suddenly at about − 130° C. In a number of such experiments we have observed a sudden increase in the intensity of the cubic (111) line in the range −126° to −130° C., depending on the rate of increase of temperature. There can be little doubt that the exotherm reported by Pryde and Jones is due to this particular transformation and not to the vitreous–hexagonal one they have assumed. That we have observed only a partial transformation to the cubic structure is in agreement with their observation of a smaller amount of heat evolution during the phase transition than was expected on theoretical grounds.

If the fraction of the original vitreous ice that did not become converted to cubic ice is in fact vitreous, a second exotherm should be observed when it is converted to hexagonal ice. It is assumed that because of the structural similarity between the two crystalline phases very little heat will be evolved if or when the portion having the cubic structure is converted to the hexagonal. On the basis of the results presented for the cubic–hexagonal transformation, if the temperature is raised at about 5 deg. C. per min. through the − 90° to − 50° C. range, the second exotherm should appear at about − 60° C. Pryde and Jones, however, state that no thermal change (other than that at − 129° C.) occurred until the temperature reached 0° C. They did not include in their report the rate of warming of the specimen; but if, through the range −90° to −50° C., it was not greater than that near −130° C., it is likely that the exotherm would not have been observed. This is due to the relatively slow rate of crystallization to the hexagonal phase, a change which is far less sensitive to temperature than the vitreous–cubic transition. Slow crystallization would occur over a wide temperature-range making it difficult to observe an exotherm. To define more clearly the structure of the vitreous state, precise thermal measurements should be carried out on samples shown by X-ray diffraction techniques to be in that state.

We conclude that in vitreous ice domains exist in which there is a tendency toward the same layer structure present in the crystalline phases, although with random distribution of molecules within the layers. Those domains having very nearly the same layer spacing as the crystalline phases are apparently quite stable, but those having greater disorder are unstable. At temperatures above − 160° C., crystallization to the cubic phase begins spontaneously at a few sites in the unstable zones, and the crystallites at each site quickly grow to about 400 Å., where further growth is hindered by the more stable zones. Further crystallization takes place at new sites in the unstable domains, the process continuing until all such areas have crystallized. This state is now stable at all temperatures below − 130° C.

Above − 130° C. both the cubic and the remaining vitreous ice begin to show conversion to the stable hexagonal phase, the individual crystallites growing to moderate size, probably near 10μ. In view of the abundant evidence showing that ice crystals can grow in size at temperatures many degrees below the freezing point, it is reasonable to suppose that the ultimate size of the crystallites will depend on the highest temperature to which the sample is exposed for a given time.

[1] Pryde, J. A., and Jones, G. O., *Nature*, **170**, 685 (1952).
[2] König, H., *Z. Kristallog.*, **105**, 279 (1944).
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THE COLE LIBRARY OF ZOOLOGY AND EARLY MEDICINE, UNIVERSITY OF READING

IT has often been stated that the scientist is lacking in literary and artistic merit, yet this is far from the truth. Its complete falsity is demonstrated by the example of the renowned biologist, artist and historian of the evolution of biological knowledge and thought, the late Prof. F. J. Cole, who died in 1959 at the age of eighty-six. Whatever he did he made as perfect as possible, and his achievements in research, in the Department of Zoology which he founded at the University of Reading, the Museum which he built up, and the Library which he collected in his home, all testify to his greatness as a man of learning. When he retired from the professorship of zoology in 1939, the Council of the University resolved that the museum should be known as the Cole Museum (*Nature*, **177**, 555; 1956). This article deals with his library, henceforth to be known as the Cole Library.

Prof. Cole was a confirmed bibliophile. He collected books from his school-days onwards, throughout his long life. At first he bought the great monographs of biology, then turned more and more to the earlier works, so that at the end of his life he had built up a library of about eight thousand volumes, illustrating the history of early medicine and zoology from the fifteenth century to the present day. In 1932 he had a house built on the Chilterns, literally around the bookcases, and after his retirement from the professorship of zoology in the University of Reading in 1939, he compiled author, title and subject catalogues, before writing his major historical work, "A History of Comparative Anatomy from Aristotle to the Eighteenth Century" (ref. 1).

This Library, the most exhaustive one of its kind in private hands in the country, has recently been acquired by the University of Reading. For the present the books will remain in the late Prof. Cole's house, where they will be available to scholars as heretofore; but when the new University Library building, to be erected in Whiteknights Park, is completed, they will be transferred to a room set apart for the books and the catalogues, as the Cole Library, a fitting complement to the Department of Zoology and the Cole Museum at the University of Reading.

The two earliest books in the library are incunabula. Pliny's "Natural History" ("Caii Plynii Secundi Naturalis Historiae Libri Tricesimiseptimi") was printed in Venice in 1472. Although rebound in

vellum, it is in perfect condition, and has thirty-five coloured illuminated capitals and one full-page illumination. Aristotle's "De Historia Animalium, De Partibus Animalium, De Generatione Animalium" (Venice, 1476) is the first edition of the Latin translation by Theodorus Gaza. That doodling was an ancient habit is evident from the contemporary patterns made in the margins by one Angelus Calydonius, who signed his name on p. 110, September 17, 1491.

It is noteworthy that nearly all the authors of biological books in the sixteenth and seventeenth centuries were medical men. Their works, for reasons that may be inferred, were frequently dedicated to dignitaries of the Church—cardinals and popes. Their subject was primarily the human body, though with references, not always acknowledged, to the bodies of animals. A beautiful copy of Galen's works in six volumes ("Omnia Quae Extant Opera ex Secunda Juntarum Editione") is in the Library. It was printed at Venice in 1550. But Galen's day was passing, and the professor no longer would read chapters from his works to his students. Independent accounts of the human body, based on dissection, were appearing. The first of these, and the most valuable book in the library, is "De Humani Corporis Fabrica" by Andreas Vesalius, first edition, printed at Basle in 1543. The second edition, 1555, is in its original tooled leather binding, with metal clasps, by Johannes Mechler, 1557. Prof. Cole never tired of showing these two magnificent folios to his visitors.

A valuable French book of the period is Estienne's "La Dissection des Parties du Corps Humain" (Paris, 1546). Its beautiful binding is in red morocco, tooled gold. Thomas Vicary's "The English Man's Treasure, with the true Anatomie of Man's Bodie" (Black Letter, London, 1596) is a transcript of a fourteenth-century manuscript, and is therefore pre-Vesalian. Only two other copies of this edition were known to Prof. Cole—one in the Bodleian and the other in the Surgeon-General's Library in Washington. The first Englishman to make a systematic study of natural history was the physician Edward Wotton, who graduated, as Harvey did, at Padua. His book "De differentiis Animalium" (Lutetiae Parisiorum, 1552) is a fine copy bound in limp vellum.

The chair of anatomy at Padua was filled during the sixteenth and seventeenth centuries by Vesalius, Columbus, Fallopius, Fabricius, Casserius, Spigelius and Veslingius. Vesalius has already been mentioned, and works by Columbus, Fabricius, Casserius and Veslingius are represented. Of the three works of Fabricius (Harvey's teacher) the most important is "Tractatus Quatuor" (Francofurti, 1624) which contains the section "De Venarum Ostiolis", and describes, without understanding of their function, the valves of the veins. The beautiful publications of Casserius, the pupil and understudy of Fabricius, include a fine copy, with portrait, of his "De Vocis Auditusque Organis Historia Anatomica", bound up with "De Auris Auditus Organi Historia Anatomica" (Ferrariae, 1601, 1600) and by his "Pentaestheseion, hoc est De Quinque Sensibus Liber" (Venetiis, 1609). Both works describe the sense organs of animals as well as those of the human subject.

Giulio Casserio (1552–1616)

The study of aquatic animals interested physicians at this period. Pierre Belon, called by Casey Wood "the founder of modern ichthyology", published "L'Histoire Naturelle des Estranges Poissons Marins, avec la Vraie Peincture et Description du Dauphin" (Paris, 1551). This, the first edition, is very rare. But the finest early work on fishes is Salviani's "Aquatilium Animalium Historiae" (Romae, 1554), famous for its eighty-one full-page copper-plate engravings of fishes and marine creatures by Nicolas Béatrizet. Rondelet's "Libri de Piscibus Marinis" (Lugduni, 1554–55), with its cruder but more numerous woodcuts of all kinds of marine creatures, is in its original tooled leather binding, with metal clasps.

An interesting, rare and beautiful volume, the provenance of which was described by Prof. Cole in his "Obiter Dicta Bibliographica"[2], is Carlo Ruini's "Dell'Anotomia et dell'Infirmita del Cavallo" (Bologna, 1598). This is the first complete work on the anatomy of an animal, and was plagiarized by Snape and others.

We come now to the seventeenth century, "the most constructive and significant period in the history of modern biology". The whole animal kingdom is reviewed in the eleven publications of Aldrovandus, ranging from 1613 to 1668. Four books by Severino include a fine copy of his "Zootomia Democritaea", with portrait (Noribergae, 1645). Six works of Walter Charleton, with a copy of the first edition of his "Onomastikon Zoicon" (Londini, 1668). Eight works by Redi, who in his "Esperienze intorno alla Generatione degl' Insetti" (Firenze, 1668), "successfully attacked by experiment the universal belief in

spontaneous generation". Nine works by Jan Swammerdam, whose "Ephemeri Vita of afbeeldingh van's Menschen Leven" (t'Amsterdam, 1675), is the first edition of a superb monograph on the may-fly. Two volumes of Samuel Collins's "Systeme of Anatomy, treating of the Body of Man, Beasts, Birds, Fish, Insects and Plants" (London, 1685), the first treatise on comparative anatomy by an Englishman, and with an extremely fine engraved portrait by Faithorne. Edward Tyson's "Orang-outang [that is, chimpanzee], sive Homo sylvestris, or the Anatomy of a Pygmie compared with that of a Monkey, an Ape and a Man" (first edition, London, 1699) is signed "The Author's gift, June 9, 1699".

The seventeenth century was the century of William Harvey. Prof. Cole did not possess a first edition of Harvey's "De Motu Cordis et Sanguinis Circulatione"; but he had copies of all the facsimile productions and translations down to Dr. Franklin's translation of 1958. In this work Harvey put the last stone on an edifice, the foundations of which had been built by many other workers, but in his work on generation in animals ("Exercitationes de Generatione Animalium"; first edition, Londini, 1651) he was a pioneer, and the book was described by Prof. Cole as the "work of a sadly puzzled human being". The Elzevir edition (Amstelodami, 1651) was T. H. Huxley's copy.

A remarkable feature of the seventeenth century was the foundation of learned societies in the great capitals of Europe, and the participation of groups of investigators in research. Though the series of the *Philosophical Transactions of the Royal Society* is not complete, the earliest and rarest volumes and also long runs are in the library. The fifteen volumes of the German "Academia Naturae Curiosorum" (Frankfurt und Leipzig, 1670–90) is a fine series, bound in the original vellum. Of the Danish publication, "Acta Medica et Philosophica Hafniensia", associated with Thomas Bartholin, 1671–79 (all issued), published 1673–80, only two other complete copies were known to Prof. Cole. Vol. 1 bears the signature of Clopton Havers, M.D. The Amsterdam Society was short-lived, and Prof. Cole was unable to purchase a copy of its *Proceedings*, so he had a facsimile edition of a hundred copies of "Observationes anatomicae selectiores Collegii privati Amstelodamensis" (Amstelodami, 1667–73), printed in the Typography Department of the University of Reading in 1938. Of the "Académie des Sciences" in Paris, there are the two volumes, large folio, of C. Perrault's "Mémoire pour servir à l'histoire naturelle des Animaux" (Paris, 1671 and 1676), and a magnificent copy of the 1676 volume, handsomely bound in red morocco, with the royal fleur-de-lis tooled in gold, and showing on the title-page Louis XIV and his minister Colbert attending a meeting of the Academy in the Royal Library at Versailles in 1671. The Italian Society, Accademia del Cimento, is in Richard Waller's English translation, entitled "Essayes of Natural Experiments made in the Academie del Cimento" (London, 1684).

Returning to the Royal Society, there are the works of many of the original Fellows. Robert Boyle's six works include the complete works in five volumes printed in 1744; this set was formerly the property of the Boyle family, and bears the bookplate of the Earl of Cork and Orrery. Thomas Willis is represented by six works, including the first edition of "Cerebri Anatome", 1664, Robert Hooke by seven works, including the first and second editions of the "Micrographica" (1665 and 1667 respectively), Nehemiah Grew by six works, including his "Anatomy of Vegetables Begun" (1672), "The Anatomy of Plants" (1682) and "The Comparative Anatomy of Stomachs and Guts Begun" (1681) and Marcello Malpighi by seven works, a most valuable and complete set, including the "Opera Omnia", which Prof. Cole made perfect by buying three copies and binding the three volumes in one, with the portrait and the life (Londini, 1687, 1686 and 1697). There are fine copies of "Dissertatio epistolica de Bombyce" (first edition, Londini, 1669) and "Dissertatio epistolica de Formatione Pulli in Ovo" (first edition, Londini, 1673). Among the eight works of Antoni van Leeuwenhoek, the Dutch draper who, working in isolation, had to trust to his own observation and judgment, are the Dutch edition of his works in four volumes (Leyden and Delft, 1684–1718), the Latin edition (Lugd. Bat., 1722), the select works in four volumes (1798–99 and 1800–07) and the current "Collected Letters of Antoni van Leeuwenhoek, vols. 1–5 (all published to date) (1939–57).

The eighteenth century was a period of great activity by numerous major and minor investigators in all branches of biology, particularly in the attempt to understand the functions of the organs of animals. So physiology went side by side with anatomy. The microscope, too, was coming into use, thus enabling the minutest parts of animals to be examined. Museums were founded, and great skill was shown in preserving, injecting and otherwise exhibiting whole animals or their parts. There was a great accumulation of factual knowledge in preparation for the Darwinian era in the following century. Only a few of the outstanding works can be mentioned, chosen to illustrate the diversity of treatment and subject. "Oeuvres anatomiques de M. Duverney" (two volumes, Paris, 1761) contains reprints of his beautiful and detailed studies on the sinuses of the dura mater, on the structure, function and diseases of the ear, and the first accurate account of the solar plexus. Spallanzani's seventeen works include his "Essay on Animal Reproductions", translated from the Italian of 1768 (London, 1769), the forerunner to his conclusive experiments on the origin of life, described in his "Opuscula di Fisica Animale et Vegetabile" (first edition, two volumes, Modena, 1776). Comprehensive faunistic works were beginning to appear, one of the earliest being O. F. Müller's "Zoologica Danica" (third edition, Havniae, 1788–1806) with many illustrations of marine animals. It was published posthumously. The learned Swiss Albrecht von Haller, physician, physiologist, bibliographer and poet, has twenty-one entries in the catalogue. As a bibliographer his work is indispensable to a historian of biology, and the library contains his "Bibliotheca Botanica" (2 vols., Tiguri, 1771–72), "Bibliotheca Chirurgica" (2 vols., Bernae, 1774–75), "Bibliotheca Anatomica" (2 vols., Tiguri, 1774–77) and "Bibliotheca Medicinae Practicae" (4 vols., Bernae and Basiliae, 1776–88). It is said that Haller's library contained 13,500 volumes and that he wrote more than five hundred scientific papers. Prof. Cole was a great admirer of John Hunter, and his famous Museum, on which he planned his own Museum at the University of Reading. Hunter was not a diligent writer, and there are only six books of his in the Library; but there are nearly forty entries of references to him and his work. A complete publication of John Hunter's works in four volumes was published in London, 1835–37. John's elegant brother

William was a renowned lecturer. Prof. Cole had two sets of manuscript notes of his lectures (*c.* 1770), one of 280 pages, testifying to the appreciation and diligence of two of his students.

The nineteenth and twentieth centuries have produced a voluminous literature in every branch of zoology. The Library contains beautiful monographs in many languages. It is also rich in biographical and bibliographical works. Among the latter may be mentioned the Index Catalogue of the Library of the Surgeon General's Office, U.S. Army, Washington, which Prof. Cole used constantly. The first, second and third series, in 16, 21 and 10 volumes respectively, are present. Of the modern transcriptions and translations there are the works of Leonardo da Vinci, namely, "Codice sul volo degli Ucelli" (first edition, Rouveyre, Parigi, 1893), with the perfect facsimile of the original, "Dell'Anatomia, Fogli A" (Parigi, 1898), "I Manoscritti di Leonardo da Vinci, della Reale Bibliotheca di Windsor. Dell'Anatomia, Fogli B" (Torino, 1901), half the series (13 volumes) of the "Feuillets inédits" (Paris, 1901) and "Quaderni d'Anatomia", six volumes (Christiania, 1911–16), a truly noble collection, as most of these are limited editions.

The above selection can give only a meagre idea of the richness and scope of this wonderful library. Prof. Cole's wishes were that it should not be dispersed, but should be available *in toto*, as it has been in the past, to scholars in the history of biological thought. This happy outcome has, we believe, been achieved by its acquisition by the University of Reading.

[1] Macmillan and Co., Ltd., 1944; reprinted with corrections, 1949.
[2] *J. Hist. Med. Yale*, 13, 1 (1958).

OBITUARIES

Prof. W. N. Thomas, C.B.E.

Prof. W. N. Thomas, professor of engineering in University College, Cardiff, during 1928–50, died on November 24.

His initial engineering training was as pupil and assistant of the Borough Engineer at Crewe.

During 1910–15 he lectured at the Universities of Nottingham and Birmingham. He then saw war service with the Royal Engineers in France and Flanders. He returned to university life at Birmingham and afterwards at Oxford, where he was chief assistant to Prof. Jenkin for five years and received the degrees of M.A. and D.Phil. He left Oxford to become principal assistant at the Building Research Station at Garston, and three years later, in 1928, he was appointed professor of engineering at Cardiff, a post in which he remained until his retirement in 1950.

His time at Cardiff was broken by war service. In 1939 he became scientific adviser to the Ministry of Home Security, and an expert on the effects of bombs on structures. He visited Moscow in 1941 and led a team of specialists to Japan in 1945 to report on the atom-bomb damage at Nagasaki and Hiroshima. In 1946 his war work was recognized by the award of the American Medal of Freedom and he was made C.B.E.

On retirement from the University of Wales, Norman Thomas became president of the South Wales Institute of Engineers, and presided over the difficult negotiations which led to its amalgamation with the South Western Society of Mining Engineers. He continued his association with the Home Office and became chief scientific adviser for Wales on civil defence. He relinquished this appointment only a year ago. He was also active in the affairs of the Institution of Civil Engineers and made a number of journeys abroad on its behalf.

His academic interests were well spread. Norman Thomas was an authority on the effect of frost on materials, and he published many papers on the mechanical properties of materials. He was author of a well-known text-book on surveying, and completed a further revision within a year of his death. He also wrote a book on bridges and was interested in military bridging. While at Cardiff he succeeded in having constructed an addition to his somewhat modest laboratories, and he lived long enough to take part in a token demolition of the wooden walls which were his academic inheritance; and to see the demolition proper commence. His colleagues greatly regret that he did not survive a few more years to see the splendid new laboratories which will replace them.

In personal characteristics, Norman Thomas was modest and retiring, but his quietly expressed opinions were well received by his colleagues, and he had an unusual capacity for inspiring other people's affection.

C. Gurney

Dr. Pierre A. Chappuis

The Swiss zoologist Dr. P. A. Chappuis, who died at Zurich on July 9, 1960, was for many years assistant director of the Institut de Spéologie at Cluj, Rumania, where he also acted as Swiss Consul. At the time of his death he was attached to the Centre National de la Recherche Scientifique as director of research and assistant director of the Laboratoire Souterrain de Moulis (Ariège), France.

He was born on September 5, 1891, at Saint-Cloud, Seine-et-Oise, France, where his father was assistant director of the International Bureau of Weights and Measures. Educated in Switzerland, he obtained his doctorate at the University of Basle in 1920; his thesis on the fauna of the subterranean waters in the neighbourhood of Basle was prepared under Prof. F. Zschokke. The following year he joined the staff of the recently created Institut de Spéologie at Cluj and in 1927 he succeeded R. Jeannel as assistant director. He remained at his post when, following the Treaty of Vienna, a large part of Transylvania was ceded to Hungary and his Rumanian colleagues went into exile (1940–45). E. Racovitza, the founder and first director of the Institut, died in 1947, and political events compelled Chappuis to leave Rumania in 1948.

Until serious thyroid trouble put an end to strenuous activity, he was a great traveller. In 1921 he and A. David explored the region of the White Nile. In 1929 he joined R. Jeannel and Ch. Alluaud in an expedition to the Sahara. In 1931 he and Alluaud crossed the Sahara and collected extensively in the regions of the Upper Volta and Ivory Coast.

In 1932–33 he accompanied Jeannel and Arambourg on their expedition to the River Omo and climbed Mt. Elgon. He and his colleagues visited hundreds of caves in little-known or unexplored parts of Transylvania, notably in the Bihar Mountains, and in old Serbia.

A fuller account of his life, together with a complete list of his numerous scientific publications, will appear in a memorial part of the *Annales de Spéléologie*. He wrote the third volume of Thienemann's "Die Binnengewässer", entitled "Die Tierwelt der unterirdischen Gewässer" (Stuttgart, 1927). In the same year he also contributed the section on Anaspidacea to Kükenthal and Krumbach's "Handbuch de Zoologie". He was an authority on various groups of freshwater and subterranean Crustacea, especially harpacticids, bathynellids and isopods. His discovery, in 1942, of the true habitat of *Bathynella* and other minute animals that occur sporadically in wells, springs or caves opened a new field of investigation. Since then numerous new or little-known interstitial animals, freshwater and marine, have been discovered in many parts of the world. Many of the Crustacea, including a European species of Mystacocarida, were described by Chappuis and his collaborators and his last years in France were exceedingly productive ones.

In 1922 he married Heidie Spinnler, of Basle; their son, Pierre, resides in Basle, and their daughter is married to an English architect.

ISABELLA GORDON

Dr. Gertrude L. Elles, M.B.E.

THE doyen of women geologists, Dr. Gertrude L. Elles, emeritus reader in the University of Cambridge and honorary Fellow of Newnham College, died at Helensburgh on November 18, in her eighty-ninth year. She entered Newnham as a scholar in 1891 and remained, with few interruptions, resident in Cambridge until a few weeks before her death.

She obtained first-class honours in Part II of the Natural Sciences Tripos (Geology) in 1895 and for the next few years was associated with Lapworth at Birmingham and with Törnquist and others in Sweden. This initiated the work on graptolites for which she is so widely known, and she soon commenced with Dame Ethel Shakespeare the preparation of the Palæontographical Society's monograph on British graptolites under the editorship of Prof. Lapworth. The ten descriptive parts of this classic work appeared with extraordinary regularity between 1901 and 1914 and established her position as a world authority on these fossils. Of a dozen or so smaller publications on them, the most significant was her "Graptolite Faunas of the British Isles" (Geologists' Association, 1922), which has exercised a profound influence on subsequent work on their faunal succession and evolution.

Nevertheless, Dr. Elles's interest in fossils was pre-eminently that of the field geologist and stratigrapher, and, concurrently with her work on the graptolites, her investigations on Lower Palæozoic stratigraphy in Wales and the Welsh Borderland resulted in several papers on the geology of areas around Ludlow, Conway, Bala and Builth. Relatively late in her career, she turned to a completely new field in 'hard-rock geology', and jointly with Prof. C. E. Tilley published a notable contribution on metamorphism in relation to structure in the Scottish Highlands.

Dr. Elles was closely associated with the Sedgwick Museum (or its forerunner, the Woodwardian Museum) for nearly seventy years. Her standing in the Department of Geology was formalized by her appointment, under the new statutes, to a University lectureship in 1926; ten years later, she became the first woman reader in the University. Few who have graduated in the Cambridge Department of Geology during this long period but were influenced by her enthusiasm as lecturer or supervisor; and many were drawn to Cambridge as postgraduate students to work under her direction. She inspired great affection among her colleagues, and as a teacher she will be remembered for her vitality, forthright manner and clarity of exposition.

She held the degree of doctor of science of Dublin and of Cambridge. When the Geological Society of London extended its fellowship to women in 1919, she was one of the small but distinguished group at once admitted, and she was in the same year the first woman to receive the Society's Murchison Medal. She was president of Section C (Geology) of the British Association in 1923.

O. M. B. BULMAN

NEWS and VIEWS

Royal Society: New Gold Medal

THE Council of the Royal Society has accepted an offer by the Trustees of the Leverhulme Trust Fund to mark the occasion of the Royal Society's Tercentenary by the award of a gold medal. Under the terms of the offer, the medal is "for award by the Society, every three years, to the individual who in the opinion of its Council shall have made the most significant contribution in the field of pure or applied chemistry or engineering including chemical engineering. The medal, which will be in gold, will be accompanied by a monetary award of five hundred pounds". The Council has made the first award of the medal to Sir Cyril Hinshelwood, who retired as president of the Royal Society on November 30, for his outstanding contributions to physical chemistry.

Officers

SIR HOWARD FLOREY, president of the Royal Society, has appointed the following vice-presidents for the year ending November 30, 1961: Sir Alexander Fleck, treasurer of the Royal Society, formerly chairman of Imperial Chemical Industries, Ltd.; Sir Lindor Brown, biological secretary of the Royal Society, Waynflete professor of physiology in the University of Oxford; Sir William Hodge, physical secretary of the Royal Society, Lowndean professor of geometry and astronomy in the University of Cambridge; Sir Patrick Linstead, foreign secretary of the Royal Society, rector of the Imperial College of Science and Technology, London; Prof. T. M. Harris, professor of botany in the University of Reading; Dame Kathleen Lonsdale, professor of chemistry at University College, London.

The Gas Council's London Research Station : Mr. G. U. Hopton

MR. G. U. HOPTON has been appointed the new director of the Gas Council's London Research Station at the Fulham Laboratories. He was senior research chemist of the North Thames Gas Board from 1952, until the retirement of Dr. R. H. Griffith last August, when he became acting director. Mr. Hopton gained a first-class honours degree in chemistry at Oxford and the same year joined the Gas Light and Coke Company. In 1936 he was awarded the MacNab Medal of the Institution of Chemical Engineers and in 1945 gained the H. E. Jones Medal of the Institution of Gas Engineers. From 1950 until this year he was chairman of the board of examiners of the Institution of Chemical Engineers. Mr. Hopton has also been vice-president of the Institution. He is a member of the board of studies in engineering of the National Council for Technological Awards.

British Museum (Natural History) : Appointments

THE Principal Trustees of the British Museum have appointed Dr. F. C. Fraser, keeper of zoology, and Mr. J. E. Dandy, keeper of botany, to be deputy chief scientific officers in the British Museum (Natural History). They have also appointed Mr. J. P. Doncaster to be keeper of the Department of Entomology in the British Museum (Natural History), in succession to Dr. W. E. China, who will retire on January 31; and Dr. J. P. Harding and Mr. J. F. Perkins to be deputy keepers in the Departments of Zoology and Entomology, respectively.

Mr. Doncaster, who has been a deputy keeper in the Department of Entomology since December 1955, was educated at Leighton Park School, Reading, and St. Catharine's College, Cambridge. After some years on entomological work at the Plant Virus Research Station, Cambridge, he entered the British Museum (Natural History) in 1937, to take charge of the newly formed Exhibition Section. During the War he was seconded to the Agricultural Research Council to work on the aphid vectors of potato viruses, returning to the Museum in 1945 to begin the re-designing and reconstruction of war-damaged exhibits. In 1951 he joined the staff of the Department of Entomology to take charge of the collections of Homoptera (Sternorhyncha) and Thysanoptera, and to reorganize the collections of Aphididae. His published works have dealt mainly with the systematics of aphids and their role as virus vectors.

Dr. Harding was educated at Torquay Grammar School, University College, Exeter, the University of Cincinnati, and King's College, Cambridge. Prior to joining the staff of the British Museum (Natural History) in 1937, Dr. Harding worked for a year as assistant naturalist in the Ministry of Agriculture and Fisheries. Dr. Harding is a carcinologist specializing in the Entomostraca, on which he has published many papers in journals of learned societies.

Mr. Perkins was educated at Newton College and the Imperial College of Science and Technology (Royal College of Science), London, graduating in 1932 and being awarded the Forbes Medal. He entered the British Museum (Natural History) in 1933, where he has worked on the parasitic Hymenoptera, and in particular Ichneumonidae. During the War he was seconded to the Ministry of Agriculture, where he was associated with some of the early trials of D.D.T. against crop pests. His published works have been concerned with the general classification of the Ichneumonidae, and revisions of groups of this family particularly in relation to the British fauna.

Exhibition of The Institute of Physics and The Physical Society

IF one function of science is to enable us to rationalize our sense perceptions, we need instruments and apparatus to help us perceive; the coincidence of the pointer and scale is of profound importance. As our scientific knowledge ramifies and increases in complexity, demands upon apparatus for precise measurement and manipulation become more exacting. The manner in which this demand has been met so far will be clearly demonstrated at the annual exhibition to be held by The Institute of Physics and The Physical Society at The Royal Horticultural Society's Halls, Westminster, London, S.W.1, from January 16 until 1 p.m. on January 20. Lectures will be given by: Mr. F. S. Burt (Admiralty Research Laboratory) on "Hydrodynamics Research", on January 17; Dr. G. E. R. Deacon (National Institute of Oceanography) on "The Physics of the Ocean", on January 18; and Dr. F. P. Bowden (Laboratory for the Physics and Chemistry of Solids, Cambridge) on "Some Physical Problems in Travelling at Supersonic Speed", on January 19. These lectures will be at 5.45 p.m. The prize-giving of the Craftsmanship Competition will take place in the lecture theatre on January 19 at 3 p.m. The Society has published a *Handbook of Scientific Instruments and Apparatus* (price 6*s*., plus 2*s*. postage), which is a guide to the exhibits. It is also a reference book on recent developments in the design of physical apparatus; it provides a list of manufacturers and of recent scientific books. As a means of planning one's visit to the Exhibition, the handbook seems indispensable. Further information can be obtained from The Institute of Physics and The Physical Society, 47 Belgrave Square, London, S.W.1.

Institute of Information Scientists

A FULL syllabus for education in information work has now been prepared by the Institute of Information Scientists; it has also been approved by Aslib. Courses on "Collecting and Communicating Scientific Information" based on this syllabus have been arranged at the Northampton College of Advanced Technology, St. John Street, London, E.C.1, to start on January 24, and will comprise evening classes twice a week during two years. The Institute will hold (external) examinations, based on the syllabus, for the Certificate of the Institute, and will be set in two groups, at the end of 1961 and 1962, respectively. Details of the course may be obtained from the College, and other information from the honorary secretary of the Institute, J. Farradane, "Torran", Crofton Road, Orpington, Kent.

Forest Research and Training Institute for Latin America

A FOCUS for forest research and training in Latin America has been acquired with the permanent establishment—following four years on a temporary basis—of the Latin American Forestry Institute for Research and Training at the Forestry School of the University of Los Andes, Merida, Venezuela. A multilateral agreement has been reached between the Food and Agriculture Organization, under the aus-

pices of which the Institute will operate, the Government of Venezuela, and other interested member nations of the Organization. So far, Venezuela, Guatemala, Nicaragua, Panama, Peru, Colombia, France and the Netherlands have become party to the agreement. Several other countries are expected to join in the near future. The aims and functions of the Institute are fourfold: it will carry out research projects, particularly those of broad interest and of an applied nature which would contribute to the conservation, utilization and development of Latin American forest resources; it will organize forestry training courses in line with future demands for both Government and private foresters in Latin America; it will gather, classify and disseminate forestry information; and it will promote regional co-ordination of research by informing member Governments of forest research being carried out in Latin America.

Health Science Man-power in the United States

A SURVEY of the man-power needs in health science for the United States is to be carried out by the Federation of American Societies for Experimental Biology. Objectives of the survey will include: (1) an assessment of the present supply and demand for scientists in each of about twelve basic health fields; (2) projections of such supply and demand for the next 10–20 years; and (3) recommendations as to how the increased demand for these scientists may be met. Dr. John T. Cowles, director of educational planning for the health professions at the University of Pittsburgh, is director of the project. Dr. Lowell S. Levin has joined Dr. Cowles's staff in Pittsburgh to serve as full-time associate director of it. Some of the data being sought include: number of persons now employed, salary-levels, space requirements, current student enrolments, research expenditures, training programme income, instructional costs and student aid. The over-all project, which will require three to five years to complete, will be expanded from microbiology to include most, if not all, of the health science fields. The experimental phase of the project is being supported by an 87,000 dollar grant from the National Institutes of Health. The University of Pittsburgh has been selected to carry out the survey because of its available personnel and electronic computer facilities which will be required.

Educational Film Centre, Ltd.

A NEW organization, the Educational Film Centre, Ltd., has recently been founded. Its directors are Maurice Goldsmith, formerly science editor at Unesco, John Halas and Joy Batchelor, animation film producers, and Dr. Roger Manvell, formerly director of the British Film Academy. The objects of the Centre include promoting the production of educational films, and specially of science-teaching films, sponsorship of research into the most useful forms and techniques for instructional films and their best use in the class-room, and publication of pamphlets and film-strips associated with the films produced and with the research projects undertaken by the Centre. The Centre is in close consultation with the Educational Foundation for Visual Aids. The initial aim is the production of a planned series of science-teaching films designed specifically for use in secondary modern schools. These films will be made in collaboration with representatives from science teachers' associations, who have already undertaken to give advice and help. The Centre is to operate from Lysbeth House, 10*a* Soho Square, London, W.1.

Wallace and Darwin

MORE information about the theory of organic evolution put forward jointly by A. R. Wallace and Charles Darwin is contained in recent publications. In a recent issue of the *Proceedings of the Linnean Society of London* (171, Part 2, 139; 1960), Prof. C. F. A. Pantin introduces the essay prepared by Wallace in 1855 which served to stimulate Darwin to join him, and led to the publication of their famous paper of 1858. Mr. Tom Harrisson, curator of the Sarawak Museum, in a forthright article in the "Proceedings" of the Centenary and Bicentenary Congress of Biology held in Singapore during 1958, is concerned chiefly with Alfred Russel Wallace and a letter he wrote to Charles Darwin from Ternato in the Celebes in 1858. The author contrasts the background of these two men—Darwin, the son of wealthy parents, and Wallace, born of humble parentage. It was the Ternate letter, Mr. Harrisson claims, that forced Darwin's hand, for on its receipt "he had to speak or forever lose his place in the priorities of the new human thought".

In the fourth of his articles on Darwin's Notebooks on the Transmutation of Species, Sir Gavin de Beer deals with the Fourth Notebook, concerned with the period October 1838–July 10, 1839 (*Bulletin of the British Museum* (*Natural History*), Historical Series. Vol. 2, No. 5. Pp. 151–183. (London: British Museum (Natural History), 1960.) 15*s*.). Darwin's Fourth Notebook on Transmutation of Species was written after he had read Malthus's "Essay on the Principle of Population" on October 3, 1838. Considering the importance of the influence which Malthus's book was thought (even by Darwin himself in later life) to have exerted on Darwin's work and ideas, it is significant that he devoted so little space to Malthus in his Notebook which he wrote immediately after reading his essay. The reason is that Darwin had already and independently thought out the principle of selection of favourable variations and seen the possibility that the transmutation of species might be explained by its means. What Malthus gave Darwin was evidence of the rigorousness of selection and of the inevitability of widespread mortality. To this concept Darwin introduced the notion of extinction as the extreme case of depopulation and the notion of variation; and he showed that he was well aware that this would lead to results very different from those which Malthus thought he had achieved.

Darwin's Original Papers

IN 1942 the Pilgrim Trust and the Darwin family presented to the University Library, Cambridge, and to Down House, the original papers of Charles Darwin. Those intended for Cambridge arrived at the Library after the War and have been bound in volumes representing as closely as possible the papers in the order in which Darwin left them. A detailed hand-list of the papers was made in 1955 by Miss R. V. C. Bailey and Miss J. S. Gosse for the use of scholars working on the papers in the University Library. This hand-list has now been published in view of its general interest, together with a subject index and an index of correspondents compiled by Miss G. M. B. Tyrer (Pp. 72. Cambridge: At the University Press, 1960. 10*s*.).

Preservation of Wild Animals in Asia

MUCH has been written in recent years on the threat of extermination hanging over much of the fauna of Africa and on possible methods of averting it. Less has been heard about the equally pressing danger to the fauna of other parts of the world. The timely appearance of a report on some animals of the Middle East and southern Asia which are threatened with extermination entitled "A Look at Threatened Species", by L. M. Talbot (*Oryx*, the Journal of the Fauna Preservation Society, 5, Nos. 4 and 5, 157; May 1960), is therefore particularly welcome. The report is based on information collected during an extensive journey of reconnaissance in 1955 extending from Libya to Formosa. The investigation was concerned principally with the past and present status of the three species of Asiatic rhinoceros, the Indian lion, the Arabian oryx, and the Syrian wild ass; but the report also deals with many other species. It is a most interesting and well-written document that considers in some detail such matters as wild-life habitats and land-use, and gives an account of such reserves and parks as there are in the territories visited. One of the largest problems facing conservation is the lack of trained personnel. In most former 'Colonial' territories conservation and management were carried out by men from the colonizing country. When they departed, the country was left with very few people with any training at all in conservation matters. Nevertheless, although in many places there has been, and still is, much wanton destruction, a real effort is being made in others at conserving what is left. This report will strengthen the hand of the International Union for the Conservation of Nature in its efforts to help those concerned in preventing the final extermination of a number of interesting species of animals.

Geomorphological Abstracts

As a guide to the very scattered literature of interest to geomorphologists, a small journal of abstracts, in an attractive format, has recently been produced by a group of British geographers. In the first two numbers, for June and September 1960, abstracts are given of 136 recent papers, mainly works in English-language periodicals (No. 1; June 1960. Pp. 23. Published four times a year in March, June, September and December). At present some 120 journals are covered, and it is hoped to increase this number as circumstances permit. *Geomorphological Abstracts* will be published quarterly, and can be obtained from K. M. Clayton, Department of Geography, London School of Economics, Houghton Street, London, W.C.2, price 16*s*. per annum, post paid.

Canadian Museum Publications

THE National Museum of Canada has added to its guide-books two publications which should be well received by visitors to the Museum. The first, "Canadian Atlantic Sea Shells", by E. L. Bousfield, is an illustrated account in English of shell-bearing invertebrate animals commonly encountered on the beaches or in shallow waters of the Canadian Atlantic coast from the Strait of Belle Isle and the St. Lawrence estuary on the north to the ocean coasts of Newfoundland and Nova Scotia and the Bay of Fundy in the south. Altogether, 150 sea shells are described (Pp. v+72, 13 plates. Ottawa: Queen's Printer, 1960. 1 dollar). The second, "Les Mammifères du Canada", by Austin W. Cameron, contains descriptions in French of the mammals of Canada, each description being accompanied by a line drawing prepared by John Crosby (Pp. 89. Ottawa: Queen's Printer, 1960. 50 cents).

Scientific Instrument Manufacturers' Association

THE Scientific Instrument Manufacturers' Association has published a booklet, "Careers in the Scientific Instrument Industry", providing a well-illustrated summary of what a new entrant into the industry can expect to find and what his work and training may be like (Pp. 20. London: Scientific Instrument Manufacturers' Association of Great Britain, 1960). The launching of the booklet has been encouraged by the rapidly increasing number of apprenticeship certificates issued by the Association's members under their endorsement scheme in recent years. In 1958, 52 certificates were endorsed, 64 in 1959, and 82 in the first nine months of 1960, or at a rate double that of 1958. The endorsement ensures that certain standards of training with the appropriate equipment are the foundation of the apprentice's certificate, and provide him with the start to a career in the scientific instrument manufacturing industry. The booklet can be obtained from the Scientific Instrument Manufacturers' Association, 20 Queen Anne Street, London, W.1.

Information on Atomic Energy in Britain

UNDER the title "A Guide to Information on Atomic Energy in Britain", the Central Office of Information has issued an illustrated select list of British books, periodicals, reports, films, photographs and display materials, describing the latest nuclear developments in the United Kingdom, which was originally compiled for specialized and prestige distribution overseas (Pp. 64. London: H.M. Stationery Office, 1960. 5*s*. net). The list was prepared with the co-operation of the United Kingdom Atomic Energy Authority. The material is arranged under visual aids; general publications; serial publications; the power programme and nuclear engineering; radioisotopes; nuclear physics; and radiation hazards and protection. Books for the specialist and for the general reader are distinguished. There are also further lists of the Atomic Energy Authority's unclassified publications (including a list of depository libraries in the United Kingdom), and of publications covering legislation in the United Kingdom and co-operation with other countries.

Restoration of a Silk Flag

THE *Museums Journal* of November, in an article by Mr. Harry Wandrus, describes an economical method for the treatment of deteriorating silk flags. The flags were the property of the State of Ohio and most of them were of 'weighted' silk, that is, they contained chlorides or sulphates of magnesium, tin, iron or aluminium. Unfortunately, these chemicals have the effect of causing an early deterioration of the silk, which then crumbles and powders. The essence of the process is to soften the old flag with water and carefully assemble the parts in their correct positions on a flat table ready for a white silk chiffon backing. This backing should be neatly arranged over the flag and fastened with a 5 per cent solution of polyvinyl alcohol. The flag will then hang well in a vertical position. Full details of the process are given.

Atomic Weight of Silver

SILVER is an important secondary standard of atomic weights, the values of these for many elements having been determined with reference to silver. The natural element contains two isotopes, 107 and 109, and the average atomic weight has been accepted as 107·880, on the chemical scale. A mass-spectrometer investigation by W. R. Shields, D. N. Craig and V. H. Diebeler, of the Bureau of Standards, Washington, is reported in the October issue of the *Journal of the American Chemical Society* (p. 5033). It was found that no variation in abundance ratio occurred in six specimens of natural silver, but a seventh, from Cobalt, Ontario, showed a significant deviation. The values of the atomic weight found were, on the physical scale ($^{16}O = 16$) 107·9028 ± 0·0013, on the chemical scale (O = 16) 107·8731 ± 0·0020, and on the proposed unified scale ($^{12}C = 12$) 107·8685 ± 0·0013. It is seen that the chemical value differs appreciably from 107·880.

Binocular Depth Perception

ONE of the difficulties in studying depth perception is to isolate the different factors that contribute to the three-dimensional effect, and in particular to separate the binocular from the monocular cues. A highly original method of achieving this separation has been developed at the Bell Telephone Laboratories by B. Julesz, and, under the heading "Binocular Depth Perception of Computer-Generated Patterns", the subject is discussed in a recent issue of *The Bell System Technical Journal* (39, 1125; 1960). In this method the two pictures to be viewed in a stereoscope consist of a random arrangement of black, white and grey dots. These two micropatterns are similar in dot distribution except for a central area where, for example, a square-shaped region is given a uniform horizontal displacement. Each pattern by itself has a completely random appearance, but when viewed in a stereoscope, the parallax produced by the lateral displacement causes the central square region to appear either in front of or behind the surround, depending on the direction of displacement. Several interesting features emerge from this method of presentation in which monocular cues are eliminated. For example, several seconds or even minutes may elapse before the depth effect is perceived, presumably while the eye and brain are searching the pattern and assimilating the information being presented to the subject. When the viewing is repeated, the perception-time may be shortened as the process of learning facilitates recognition of the pattern. The effect of varying the contrast of the pattern, its sharpness, different perturbations of the pattern and the introduction of a monocularly recognizable pattern have all been studied to see how far the depth effect is enhanced, although just what is meant by depth enhancement is not immediately obvious.

The Night Sky in January

FULL moon occurs on Jan. 1d. 23h. 06m. U.T., new moon on Jan. 16d. 21h. 30m. and full moon on Jan. 31d. 18h. 47m. The following conjunctions with the Moon take place: Jan. 1d. 17h., Mars 8° N.; Jan. 20d. 05h., Venus 0·6° N.; Jan. 26d. 13h., Aldebaran 0·3° S.; Jan. 28d. 07h., Mars 8° N. Mercury will be visible as an evening star near the end of the month, setting about one and a half hours after the Sun. Venus is an evening star, and is favourably placed for observation. Venus sets at 20h. 00m., 20h. 35m. and 21h. 15m. on January 1, 15 and 31, respectively, about four hours after the Sun. During the month its distance from the Earth decreases from 83 to 63 million miles, the visible portion of the apparent disk from 0·639 to 0·499, and its stellar magnitude from −3·7 to −4·1. Mars is above the horizon all night on January 1, and sets at 7h. 10m. and 6h. 5m. on January 15 and 31, respectively. Mars is very conveniently situated for observation. It is at a distance of 61 million miles from the Earth on January 15, and its stellar magnitude is −1·0. Jupiter and Saturn are too close to the Sun for observation. Occultations of stars brighter than magnitude 6 are as follows, observations being made at Greenwich: Jan. 7d. 5h. 09·8m., 59 Leo. (*R*); Jan. 24d. 19h. 57·2m., +11° 445 (*D*); Jan. 26d. 23h. 59·6m., 318 B. Tau. (*D*). *D* and *R* refer to disappearance and reappearance, respectively. The Quadrantid meteors are active on January 3, but conditions are unfavourable for observation. The Earth is at perihelion on January 2, its distance from the Sun being 91·4 million miles.

Announcements

DR. DETLEV BRONK, president of the Rockefeller Institute, has been elected an honorary member of the Brazilian Academy of Science and has been awarded an honorary doctorate of the University of Brazil.

DR. AMYAND DAVID BUCKINGHAM has been awarded the Harrison Memorial Prize for 1959 in consideration of his work on solvent effects on molecular spectra and the theory of pressure-induced spectra. Dr. Buckingham is at present in the Department of Inorganic Chemistry, University of Oxford.

DR. H. HAROLD HUME, of Gainsville, Florida, has been awarded a gold Veitch Memorial Medal by the Council of the Royal Horticultural Society for his work on horticulture and in particular for his work in connexion with camellias.

THE Systematics Association are arranging a meeting on "Multivariate Methods in Taxonomy" to be held in the Department of Botany, the University of Southampton, during April 24–25, 1961. Further information can be obtained from Dr. J. M. Lambert, Department of Botany, University of Southampton.

"RADIO Techniques and Space Research" will be the theme of next year's British Institution of Radio Engineers' Convention which will take place during July 5–9, 1961, at the University of Oxford. The Convention will contain at least six sessions, provisionally entitled: "Review of the Role of Radio Techniques in Space Research"; "Satellite Engineering Problems"; "Extra-terrestrial Measurements"; "Telemetry"; "Techniques in Radio Astronomy"; "Satellites in Terrestrial Communications". The Convention Committee has invited offers for papers, and these should be addressed to the British Institution of Radio Engineers, 9 Bedford Square, London, W.C.1.

THE Chemical Society, Burlington House, London, W.1, has published "Periodicals in the Chemical Society Library", giving the complete periodical holdings in the Library (Pp. 48. London: The Chemical Society, 1960. 5*s*. post paid). This will be useful not only to members of the Society but also to librarians and users of chemical literature generally.

ORGANIZATION OF SCIENTIFIC RESEARCH IN LATIN AMERICA

A REGIONAL meeting to discuss the organization of scientific research in Latin America was held during October 3–7 in the Central University of Venezuela, Caracas. The meeting was arranged by the Unesco Science Co-operation Office for Latin America, under the patronage of the Ministry of Education and the University of Venezuela. Heads of national research councils, rectors of universities, deans of science faculties and senior scientists from Argentina, Bolivia, Brazil, Chile, Colombia, Cuba, Ecuador, Mexico, Peru, Uruguay and Venezuela had been invited to attend, and the World Health Organization and the National Academy of Sciences of the United States sent observers. The meeting was held at the Central University.

The president of the Republic, Sr. Rómulo Betancourt, spoke briefly at the opening ceremony, welcoming the delegates with the assurance that they would find in the Venezuela of to-day complete freedom for the development of scientific research. Among other speakers were Dr. Establier, head of the Unesco Science Co-operation Office for Latin America; Dr. Rafael Pizani, Minister for Education, and Dr. Francisco De Venanzi, rector of the Central University.

The meeting elected Dr. Venanzi as its chairman. The working sessions were opened by a review of the general tendencies of scientific research in Latin America by Prof. Bernardo Houssay, president of the Council for Scientific and Technical Research of Argentina. This paper provoked a valuable discussion which formed a background for the other papers presented at the meeting.

The paper by Dr. David Stitchkin, rector of the University of Concepción, Chile, on funds available for scientific research, with special reference to equipment, was the one which caused least discussion, since the meeting was unanimous in concluding that the amounts at present available were notably insufficient. It was recommended that Governments should accept as a target the allocation of 2 per cent of the national budget for scientific research.

During the discussion of the paper by Dr. Mario Gonzalez (Cuba) on the basic and applied sciences, it became clear that the meeting did not wish to emphasize the distinction between the two, and preferred to think of science as a whole, recommending that firms in industry and agriculture should strengthen their links with research and teaching institutions in view of the profound effect which science has on modern commercial life.

Prof. Houssay introduced the question of national research councils, which exist in only a very few Latin-American countries, including the Argentine, Brazil and Mexico. The other Governments of the region were recommended to give serious thought to the advantages of establishing research councils, and Unesco was asked to provide information to Governments about the functions and possible types of organization of research councils.

Dr. Marcel Roche, director of the Venezuelan Institute of Scientific Research, presented a paper on the career of the research worker. He analysed and compared the careers offered by the research councils of Argentina, France and Venezuela. It was thought that the arrangements adopted by the Argentine and Venezuelan Councils, whereby their staffs were able simultaneously to accept teaching posts, was valuable in the Latin-American scene, since it made maximum use of the small scientific man-power available, and kept the research worker in touch with universities and youth. This subject was very closely related to the next one discussed, the shortage of teaching and research personnel in Latin America, which was introduced by Dr. Rodolfo Talice, dean of the Faculty of Science in the University of Montevideo.

One of the topics of greatest interest at the meeting was the paper by Dr. Paulo Sawaya, dean of the Faculty of Philosophy of the University of São Paulo, on the results of the adoption in certain universities and institutions of the full-time system. Most universities and research organizations permit their staffs to hold one or more posts outside the organization, and the virtues and vices of this system form one of the most hotly debated subjects in scientific circles in Latin America. The meeting recommended that Governments and universities should establish the full-time system as the ideal in research and higher teaching posts, and that they should provide salaries and working conditions adequate for this purpose.

Unesco has encouraged and assisted the formation of regional research centres, such as that for mathematics in Buenos Aires, and of groupings of research centres, such as the Latin-American Council for Cosmic Radiation. Dr. Ismael Escobar, head of the Cosmic Ray Physics Laboratory at Chacaltaya, Bolivia, introduced this topic, the discussion of which led the meeting to call on Unesco to continue its efforts in this field, so that teams of research workers might be brought together, animated by the desire to achieve Latin-American unity in research.

Dr. De Venanzi analysed the attitudes of Governments and of public opinion towards scientific research problems in Latin America. Though much improvement has occurred in the past few years, a great deal remains to be done. The meeting felt that the Press, radio and television had a paramount part to play, and hoped that ways could be found to establish training in scientific journalism. In this connexion, delegates were happy to note the complete and accurate coverage of the meeting in the Caracas Press.

In Latin America, fellowships tenable in more scientifically developed areas will, for some time to come, provide the principal source of higher training for research workers in many fields. Dr. E. Beltran, Under-Secretary for Forestry and Game Resources in Mexico, discussed the subject in all its aspects. An increase in the number of fellowships granted by governments and other agencies was recommended, as well as greater emphasis on instruction in foreign

languages, since language deficiencies frequently prevented full benefit from fellowships. The paper by Dr. M. A. Garrido Malo, dean of the Science Faculty in San Marcos University, Lima, was on a closely allied subject—exchange of scientists between Latin-American countries. Unesco was asked to publish its *Boletin* with greater frequency, so that news of courses, special facilities, visits of foreign scientists, etc., might be more rapidly disseminated, and all laboratories were exhorted to use to the utmost the facilities offered.

The subject of scientific documentation in Latin America was introduced by Dr. Manuel Sadosky, vice-dean of the Science Faculty in the University of Buenos Aires. A lengthy discussion led to a series of recommendations: that Unesco should make a survey of scientific journals in Latin America, with the object of formulating a plan for rationalizing them; that the Mexican Scientific Documentation Centre should make its services more easily available to scientists in other countries; that more national scientific documentation centres should be established, that Governments should grant free postal services to scientific journals; and that financial help might be given to a select number of journals.

The final subject on the agenda was a review of Unesco's science programmes, particularly that of the Latin American Science Co-operation Office in Montevideo. Dr. Establier described proposals to be debated at the general conference of the Organization held in Paris in November, and also outlined a series of long-term projects which might be undertaken by the Montevideo office. Among these was one for an International Andean Year, during which teams of specialists in different fields would attack the problems of this vast mountain chain which so profoundly affects living conditions in those countries through whose territories it runs. Another proposal was for a full-scale operation towards rationalizing scientific journals. A third would deal with the problems of the unproductive areas of the seas, lakes and rivers of the continent. At the end of this discussion Dr. Establier received the warm congratulations of the meeting, both for the way he has directed Unesco's science activities in Latin America, and for the organization of the meeting.

B. A. HOUSSAY

INTERNATIONAL OPERATIONAL RESEARCH

FROM its War-time start in Britain, operational research has become an international movement. The first conference on this basis was held three years ago at Oxford. It led to the establishment of the International Federation of Operational Research Societies, of which the chief architect was Sir Charles Goodeve, who was elected its first general secretary. Under his guidance the Federation continues to expand. Great Britain has acted as the Federation's first 'foster' society, an office which shortly passes to America; and France was designated 'host' society for the second of the triennial conferences, called at Aix-en-Provence during September 5–9. The Société Française de Recherche Opérationnelle has discharged its duties with grace and efficiency, at a conference presided over by its own president, Prof. G. T. Guilbaud.

The Second International Conference on Operational Research had the object of surveying the whole scene, and its organizers limited the attendance to 350 delegates. Representation at the national level was strictly allocated according to the sizes of national societies, who themselves had the invidious task of selecting their delegations from long lists of applicants. The programme was determined in outline by a committee which appointed leading workers in this field as sponsors of more than twenty sessions; each sponsor was responsible for designing and presenting his own session, for inviting some papers, for selecting others from among those submitted freely, and for taking the chair at his session at Aix-en-Provence. These arrangements led to a more tightly controlled conference than is customary at this level, and were intended to produce a coherent pattern, high-quality material, and authoritative discussion.

Delegates arrived from no less than twenty-three countries; and although two-thirds of them were drawn from America, Britain and France, there was plenty of evidence that significant operational research efforts have been mounted in at least a dozen more countries. The extent of the applications of operational research to-day might have surprised those who first embarked on the attempt to apply the methods of science to the strategic problems of war. But there are strategic problems in all managerial situations, and eighty papers presented at Aix-en-Provence attest to the fact that operational research has by now penetrated into the intricacies of most of them.

The conference opened with a plenary session dealing with the methodological aspects of operational research. Whispers were heard complaining that once again the subject had succumbed to mere introspection, to a self-conscious preoccupation with its own anatomy. Most scientists in the field of operational research would agree, however, that a subject devoted to scientific investigation of the methods of management has something to gain from the examination of its own. Thus it proved. The session brought out clearly the fact that the goals of an organization are various and not necessarily consistent, that they are constantly changing, and that they reflect a process of learning to survive by adaptation. It follows that crude statements of aim, such as 'maximum profit', which have often been naïvely emulated by equally crude scientific models, are inadequate. There are always ways of estimating and comparing organizational efficiency, but they require experimentation on possible models and not merely experimentation within some plausible model. The sensitivity of a top-level decision to explicit assumptions about likely circumstances is itself an object of study; but its sensitivity to implicit assumptions about goals is still more important. For this reason the model of an adaptive organism adjusting itself to its environment is valuable, and much was said about attempts to use scientific descriptions of biological learning and

goal-seeking processes as models of business behaviour.

The first group of parallel sessions then set out to discuss two general problems and five areas of application. Six papers were presented dealing with new mathematical methods: they concerned especially the use of the theory of graphs in studying supply networks, and various treatments of the problems of sequential decision. Another group of papers dealt briefly with the question of controlling production, but without much originality. The areas of application were: transport, oil, power, steel and local government. Examples of transport operations by road, rail and air were given in which operational research had solved the strategic problems of scheduling fleets, and of choosing between alternative policies, for example, in overhaul, cargo carried and design. The oil industry put forward studies of the flow of traffic and the problems of stock-holding, and of the selection of investments. There were three papers in the session on power dealing with the operation of nuclear reactors, and studies were also presented of the central planning of an atomic energy industry and of an electricity distribution system. From the steel industry there were discussions of the control of spare parts and of the unloading of ore, and a study of track times. The local government session was devoted to city and land-use planning, and included a consideration of a city as a teleological mechanism generating its objectives intrinsically.

The formal sessions were broken up by a series of discussion groups. These were often extremely spirited conversations. They dealt, for example, with the organization of operational research, with its future needs, and with education—the latter subject leading to a considerable clash about the role of the universities and possible syllabuses. One group discussed economic decisions that could involve loss of life, and two more the allied techniques of operational gaming and of simulation. There was a meeting on operational research for under-developed countries. But perhaps the most remarkable session of all dealt with operational research at the top-decision-making level in industry. This involved some of the most forceful interchanges of the whole conference, and continued all day—although it was billed to last for the morning only. The discussion was too frank, too fast, and too heated ever to reach the printed proceedings: an added reason for the agreement of the main protagonists that this day alone had been worth the journey to France.

At this point, the second plenary session was held, to consider the relationship between operational research and computers. It was held that the existence of these machines, considered properly as logical engines rather than as calculators, had enabled operational research to forge new tools. Those discussed were a computer language for the automatic programming of simulations, which had quartered the time required to prepare an intricate programme, and a computer analysis of the field of heuristic decision processes. Secondly, however, computer applications themselves received benefit from operational research assistance. In this area, a mathematical model was presented for the optimal storage and retrieval of information, and an operational research survey was made of the factors involved in the introduction of on-line computers for controlling production.

The second series of parallel sessions included two general problem areas, those of inventory control theory and mathematical programming, and descriptions of operational research in three applied fields; mining, war and national government. Inventory theory is by now an extensively explored topic, but seven more contributions were made dealing with particular aspects of the problem. There were nine contributions also to the subject which began as linear programming, but which has long since been extended to such cases as the linear programme under uncertainty, various non-linear models, and quadratic programming—all discussed here. In the mining session, a general account of operational research at the National Coal Board in Britain was presented, as well as papers on the determination of optimal mining limits and the study of pit haulage. The presentation of military applications was necessarily restricted, but the relevance of the theory of games was discussed, as well as problems of communications and stock-holding policy. The growing effort in operational research at the national level was well expressed in various papers dealing with the whole economic system of a country, with national planning in India, with the co-ordination of investment in transport, and with social decision-making.

The third and last plenary session was concerned with human factors. Hospitals were considered as viable organisms, according to an adaptive model reminiscent of the methodological talk at the beginning of the week, and there were other papers on the human element in decision systems. A doleful note was sounded at the end of a strenuous conference by the report of some interesting research into the acceptance of solutions. Teams involved in business gaming were presented with the mathematically optimal strategy for their game after they had become implicated in the play; but in no case could any means be found by which they could be persuaded to use it.

The conference was closed with an address by Sir Charles Goodeve, who characteristically eschewed the usual valedictory platitudes. Instead, he issued a considerable challenge to the movement to play a bigger part in the social field, by bringing operational research to bear on the problem of evaluating alternative policies by developing a measure for human happiness. His address is reported *in extenso* elsewhere[1], and it will be interesting to see what fruit it has borne when the Third International Conference on Operational Research meets in Oslo in 1963, when the Norwegian society is expected to be host.

The proceedings reported here were set in the familiar context of receptions, tours, committee meetings, and arbitrarily arranged discussion groups—some of which lasted until dawn. Enthusiasm was a keynote of the assembly, as befits a young endeavour, and it was quite evident that much important operational research is being done that does not reach print. The first reason for this is an occupational hazard of the work: the advisors of management cannot readily air the secrets of institutional policy in public. But the second reason seems to be the convention that reports of operational research ought to include wads of respectable mathematics, whereas in real life the mathematics involved in operational research are often trivial.

Much was said at Aix-en-Provence publicly to acknowledge this fact, and to emphasize again the approaches for which operational research has always stood: scientific method, with its insistence on

measurement, experimentation and logical inquiry; interdisciplinary collaboration; above all, the seeking of usable insights rather than the production of abstract and possibly sterile formulæ. This reaffirmation should do something to increase the supply of good literature on operational research. It will certainly encourage those whose intentions are concentrated whole-heartedly on the essentially practical task of helping policy-makers reduce the influence of chance on the outcomes of their decisions.

STAFFORD BEER

[1] See *Nature*, **188**, 180 (1960).

BIOLOGICAL STRUCTURE AND FUNCTION

IN 1956, the International Union of Biological Sciences decided to set up a Biochemistry Section Committee which would be a co-ordinating committee between itself and the International Union of Biochemistry. One of the main functions of this Committee is to make recommendations to both Unions for international symposia, embracing subjects in which both biochemistry and the biological sciences are combining to produce a rapidly expanding sphere of knowledge; on this basis the subject "Biological Structure and Function" was chosen for the first joint symposium which was held at the Wenner-Grens Institute, Stockholm, during September 12–17. About 150 scientists attended the symposium, at which 72 members from 11 different countries presented invited papers to the seven sections of the symposium.

The first section was on macromolecular structure and function (chairman, A. Tiselius). Dr. J. C. Kendrew (Cambridge) described with great clarity the work which he has carried out on the elucidation of the structure of myoglobin, and Dr. P. A. Albertsson (Uppsala) discussed a new technique for separating macromolecules by partitioning them in aqueous two-phase systems containing polymers such as dextran and polyethylene glycol. This method has great possibilities in, for example, purifying viruses and separating different sized fragments of disintegrated mitochondria and chloroplasts. The second day, devoted to the subject of microsomes and protein synthesis, was memorable for a masterly discussion of the endoplasmic reticulum by the chairman, Dr. K. R. Porter (New York), which culminated in a series of electron micrographs which clearly demonstrated the existence of this structure in plant cells. In the more biochemical section the emphasis was on the role of ribonucleoprotein particles in protein synthesis.

Mitochondrial structure and function were discussed on the third day (chairman, O. Lindberg). At the moment, two subjects appear to polarize the interest of the various investigators studying the relationship between mitochondrial structure and function. One is the phenomenon of mitochondrial swelling. It seems, however, that different lines of approach are being followed by various laboratories. On one hand, swelling and shrinking are related to the transition of mitochondria from one to another well-defined functional state, for example, from a state of full respiration where the mitochondria are found to shrink, to a state in which the respiration is limited by the absence of phosphate acceptor and where the mitochondria are inclined to swell. On the other hand, mitochondrial swelling is considered to be the result of a more complete change of the normal structure with a loss of most of the mitochondrial functions; the inhibition of the swelling by different agents or the reverse of swelling by way of a 'contraction' of the swollen mitochondria are followed as means to define the physiological implications of the phenomenon. The other topic, to which numerous papers were devoted, was the mechanism of electron transport and phosphorylation in the diphosphopyridine nucleotide–flavin region of the respiratory chain. The interest in this point was raised both because of the finding that in the presence of flavo-substrates a reversal of electron transfer could take place by way of reactions requiring high-energy phosphate, and because of the suggestion that this phenomenon could be related to an adenosine triphosphate activation of succinate oxidation, which on the other hand is not inhibited by uncoupling agents. It seems that work on these two reactions may provide a good deal of information on the question of the synthesis and utilization of the high-energy compounds during the operation, both in the forward and backward directions, of the terminal part of the respiratory chain.

In the morning session on chloroplast and chromatophore structure and function (chairman, T. W. Goodwin), electron micrographs of chromatophores isolated from both purple and green photosynthetic bacteria were shown by Drs. A. W. Frenkel (Minneapolis) and J. A. Bergeron (Upton, N.Y.), and Dr. M. D. Kamen (Waltham) speculated ingeniously on the primary act of photosynthesis. Later in the day Dr. D. I. Arnon (Berkeley) described his latest investigations on photosynthesis in cell-free systems of *Chromatium* and Dr. Birgit Vennesland (Chicago) gave her views on photophosphorylation with particular reference to the possible role of a 'nascent formate' intermediate, recently postulated by Warburg. The developmental physiologists discussed intact cellular structure and function on the morning of the fifth day, under the chairmanship of Prof. J. Runnstrom. The topics discussed ranged from 'mitosis', when Dr. D. Mazia described it in terms of a multitude of individual reactions co-ordinated into a fixed time pattern, to electron microscopy studies on ciliary and flagellar movements (B. Afzelius).

In the afternoon an important session on polysaccharides (chairman, G. Blix) included lectures by Dr. S. Hestrin (Jerusalem) on "The Growth of Saccharide Macromolecules" and by Dr. A. Dorfman (Chicago) on "The Acid Mucopolysaccharides of Connective Tissues", and concluded with another important paper on technique from Prof. Tiselius's laboratory, when Dr. P. Flodin described the gel-filtration method for separation of oligosaccharides.

The final session on specific membrane transport and its adaptation (chairman, B. D. Davis) produced further lively discussion, and the closing half-hour

was a salutary reminder that, in spite of the mass of information imparted during the week, our knowledge of the relationship between structure and function is still fragmentary—apparently two currently irreconcilable views are held on the mechanism of amœboid movement.

The arrangements made by Prof. O. Lindberg and his colleagues in the Wenner-Grens Institute for this symposium were superb, and, thanks to their hard work and genius for organization, everything moved smoothly. Furthermore, the Wenner-Gren Foundation generously supported the symposium financially, and without its aid its existence would have been highly problematical. As could well be imagined, remembering the nationality of our hosts, the social side of the symposium was not neglected and highlights included a banquet in Skansen and a visit to a performance of Pergolesi's "The Music Master" at the famous seventeenth-century Drottlingholm Theatre. A specially delightful feature was that all foreign delegates spent at least one evening in a Swedish home.

The International Union of Biochemistry and the International Union of Biological Sciences are truly grateful to their Swedish hosts for arranging the first joint symposium, and hope that this Stockholm symposium will be the forerunner of similar international symposia based on fruitful co-operation between biochemists and biologists from all nations. It is hoped to publish the proceedings of the symposium in book form in the near future.

T. W. GOODWIN

POWDERS IN INDUSTRY

SIR ALEXANDER FLECK, the president of the Society of Chemical Industry, in opening the first symposium of the Surface Activity Group of the Society of Chemical Industry held during September 29–30, commented on the many imperfectly understood problems of physics and physical chemistry relating to industrial applications of powders, and referred to the largely empirical nature of many old-established manufacturing processes involving powders. "In recent years, however", he said, "application of the growing body of knowledge on the surface properties of powders has led to striking improvements in both processes and products and will undoubtedly lead to further developments, including the foundation of new industries".

In the words of Dr. M. G. Fleming, chairman of the organizing committee, the subject of powders was chosen for the symposium because so many industries make or use powders either as raw materials, intermediates or final products, many manufacturers being unaware of developments in otherwise unrelated industries which could assist them. The programme, he said, was planned to "sketch in the background and define the fundamental terms; next examine the particular requirements and problems of a diverse group of industries, and, finally, correlate these specialized applications, underlining their contiguity and exposing the shortcomings in our basic knowledge of the subject".

A laudable aim, but the event left the impression of unevenness and there were marked swings in the discussion from academic argument concerning, for example, the meaning of surface tension, to some severely practical details of powder processing. This was perhaps the inevitable result of covering so wide a field, theoretical and practical, in a relatively short time, but there was great value in bringing together so much material, the sequential grouping of which proved admirable.

Thirty-one authors contributed in the four sections, which covered "Principles of Production", "Properties of Powders", "Properties of Powders utilized in Industrial Fields", and "Principles of Application and Problems for the Future". There were seven sessions, each with its own chairman and an introducer, who presented the papers as a group on behalf of the authors

The papers of the first two sections concerned powder production by milling and by controlled precipitation, and the recovery and processing of natural powders; the surface energy of solids, adsorptive properties of powders, adhesion between particles, particle size, shape and surface area, and the electrical and flow-properties of powders. These together provided an excellent general background against which to study papers in the industrial section covering pigments and fillers in paints, printing inks, rubber and plastics (including a paper on whiting); powders as used in building cements, ceramics, bituminous road materials, cosmetics, detergents, pharmaceuticals, pesticides, paper, drilling fluids, and explosives; and problems of mineral dressing, soil mechanics, powder metallurgy, and coal and smokeless fuel production.

The papers revealed extensive basic research, much of it in relation to particular practical problems, and there was much evidence of considerable skill in process manipulation based on experience and technical appraisal of the products. In a brief report it is, however, impossible to give details of the numerous problems in powder production, manufacture and use, calling for further attention, or on which more fundamental knowledge would appear to be needed.

On the production side there were many references to the inefficiency of powder handling machines, particularly grinding mills (better understanding of energy relationships could lead to new methods of grinding), and to the unknowns in present methods of powder drying and powder size classification processes.

From the papers covering numerous industrial uses it was clear that while many of the outstanding problems are specific to particular industries, work in one field is not always being fully utilized in others. On the other hand, techniques of study successful in one industrial context can be unsuited to different materials and applications. For example, methods of particle-size determination adequate for size-ranges down to, say, one micron, giving useful information for particular applications, may be quite unsuitable for the much smaller particles sometimes involved in other types of product.

There is also the problem of how to measure effective or operative particle sizes, in particular

environments, for while knowledge of the geometry of individual primary particles is valuable, frequently the operative unit is an agglomerate, flocculate or cluster of particles. Often information about what is happening to the constituent particles in an industrial product has to be deduced from the rheological, mechanical or other properties of that product, there being an inadequacy of methods for directly observing the behaviour of particles within the mass.

In many industrial applications much more information is required about the interplay of particle and particle; about the behaviour of particles distributed in gas or liquid in various concentrations in relation to the behaviour of single particles in the same environments; also about the nature of the bond between such particles and the surrounding medium, not only in the static product, but also during the various processes involved in its application or use and subsequent life.

What is the present state of basic knowledge about powders? Here the conference was greatly assisted by the surveys made in the final section, with their collected information on well-established physicochemical principles, and on the forces known to operate in dry or wet powders. Careful consideration of such information in relation to particular systems could, it was suggested, indicate possible means of controlling the mechanical behaviour of powders or suspensions.

There were calls for more information on the fundamentals of powder formation, and of the flow properties, internal packing, etc., of powders; also on the molecular origin of electrostatic charges, adhesion between particles, and the cohesion of the mass. There were indications of the kinds of basic work needed to improve understanding of the factors affecting dispersion and flocculation of particles in solid/liquid systems, involving the inherent surface chemistry of solids, adsorption, chemisorption, etc., and the fine-structure of particles relative to methods (for example, adsorption methods) of measuring 'surface area'. Recent rapid advances in microscopy, and in electron microscopy in particular, were noted, with the suggestion that microscopists should seek still further to improve their techniques.

To summarize, the symposium brought together a mass of material, fundamental and practical. It revealed the 'zones of ignorance' and the kind of investigations required for further advance. Individual powder-using industries can be expected to continue the search for new basic knowledge pertinent to the solution of their own problems, but their task would be facilitated by more extensive fundamental studies at the universities and in central research organizations. The field having been so well surveyed, it would be well for the participants to meet again in two or three years time to examine progress.

S. H. BELL

COMPOSITION OF MILK IN THE UNITED KINGDOM

UNTIL quite recently the quality of milk has been judged mainly on its fat content, but in the past thirty years an increased understanding of the principles of nutrition has made it clear that the most important constituents of milk are not the fats but the proteins, minerals and water-soluble vitamins which are, of course, to be found in the non-fatty solids portion of the milk. Research in the past decade has indicated that since 1930 or so in England and Wales the content of solids-not-fat in milk, and therefore the nutritive value of the milk, has tended to decline slightly but significantly. For many herds the solids-not-fat content of the bulked milk has been maintained well above the presumptive legal limit of 8·5 per cent, but for an undesirably high proportion of herds it has frequently been below it.

These facts led in 1958 to the appointment by the Minister of Agriculture, Fisheries and Food, the Minister of Health and the Secretary of State for Scotland of an interdepartmental committee under the chairmanship of Dr. J. W. Cook to consider the composition of milk and to recommend any legislative or other changes that might seem desirable. The Committee's report has now been published*. Various members of the Committee formed three panels, which considered medical and animal husbandry aspects, and the freezing-point (Hortvet) test for detecting the presence of added water in milk. The reports of all three panels are published with the main report.

The Committee points out that great progress has been made in past years in improving the hygienic quality of milk; its members rightly believe that similar progress should now be made in improving its nutritive quality. To that end they have put forward some twenty-three main recommendations. They suggest, among other things, that the presumptive minimum legal standard of 8·5 per cent for the solids-not-fat content of milk should be abolished and that price penalties should ultimately be imposed when milk contains 8·4 per cent and less. They recommend also that milk-recording associations should provide means for testing the milk of individual cows for solids-not-fat as well as for fat.

There will certainly be many problems to solve before all the main recommendations made in the report can be implemented, and some breed societies and other bodies concerned will feel that the recommendations go much too far, while others will inevitably think that they do not go far enough. However that may be, it is clear that the Committee has done a very thorough job and that the adoption of its recommendations should have the desired effect of arresting and even reversing any tendency there may be for the nutritional quality of milk in the United Kingdom to decline. The report contains a wealth of information on the subject of the composition of milk and will long remain a most valuable and reliable work of reference on that subject.

* Milk Composition in the United Kingdom: Report of an Interdepartmental Committee. Pp. iii+92. (Cmnd. 1147.) (London: H.M. Stationery Office, 1960.) 5s. net

A THEORY OF THE MECHANISM OF ACTION OF CREATINE PHOSPHOKINASE

By Dr. B. R. RABIN and D. C. WATTS
Department of Biochemistry, University College, London

As part of a programme of investigations on the evolution of biological catalysts, extensive work has been carried out in this Department on the mechanism of action of creatine phosphokinase from rabbit muscle. This enzyme catalyses the reaction:

$$\underset{\text{adenosine triphosphate}}{ATP} + \underset{\text{creatine}}{Cr} \rightleftharpoons \underset{\text{adenosine diphosphate}}{ADP} + \underset{\text{creatine phosphate}}{Cr{-}P}$$

It has been shown that the rate of formation of creatine phosphate (forward reaction) is maximal at *p*H 8·8–9·0, whereas the *p*H optimum for the formation of adenosine triphosphate (reverse reaction) is 6·0–7·0, depending on the buffers used. The enzyme requires the presence of magnesium(II) or manganese(II) ions, and it has been suggested[1] that a metal adenosine tri- or di-phosphate complex is the active substrate for the enzyme. Dixon[2] has stated, without giving any evidence, that there is reason for believing that the enzyme-substrate combination involves the formation of a thiol-magnesium phosphate complex. The available evidence favours neither of these hypotheses[3].

Creatine phosphokinase has two reactive thiol groups per mole[4], and alkylation of these with iodoacetate or iodoacetamide, destroys the enzyme activity. The kinetics of this reaction have been studied by measuring both the loss of enzyme activity and the production of iodide ions (using a silver/silver iodide electrode). These investigations have shown that only one of the SH groups is associated with the enzyme activity.

The reaction of the enzyme with iodoacetate and iodoacetamide as a function of *p*H is shown in Fig. 1. It can be seen that, over the *p*H range studied, the reaction-rate is independent of *p*H. This surprising finding is explicable if both thiols are hydrogen-bonded to other groups. The effects of various components of the substrate system on the rate of alkylation of the thiol groups are shown in Table 1. The results were obtained by following the production of iodide ions, which measures the reaction of both thiol groups. Since only the thiol group at the active site is affected by modifiers, and the two thiol groups react at nearly the same rate (unpublished work from this Department), the kinetic effects on the active site are approximately twice those shown in Table 1. The significant effects have been confirmed by following the loss of activity. The simultaneous presence of all substrates and magnesium(II) causes considerable protection of the enzyme against reaction with both iodoacetate and iodoacetamide; in the absence of the metal, there is no significant protection.

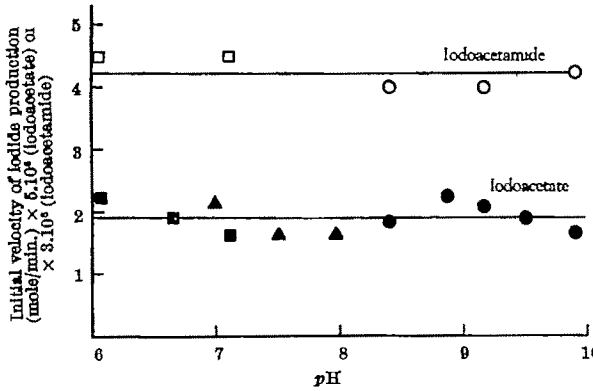

Fig. 1. Effect of *p*H on the rate of alkylation of creatine phosphokinase. The reagent and protein concentrations were, respectively: for iodoacetate, 0·0005 *M* and 0·42 mgm./ml.; for iodoacetamide, 0·0001 *M* and 0·4 mgm./ml.
Buffers: □, ■, diethylmalonic acid/sodium hydroxide; ▲, *tris*-(hydroxymethyl)aminomethane; ○, ●, boric acid/sodium hydroxide. Temperature, 25° C.; ionic strength, 0·12

Table 1. Effects of Substrates on the Initial Rate of Alkylation of Creatine Phosphokinase at 25° C. in Borate Buffer *p*H 9·0 at Ionic Strength 0·12

Substrate added	Relative initial rate of iodide production (rate in absence of added substrate = 1·0)	
	Iodoacetate	Iodoacetamide
Nil	1·00	1·00
Equilibrium mixture + Mg(II)*	0·65	0·66
Equilibrium mixture†	0·91	1·05
Mg(II) (0·001 *M*)	1·01	0·97
ATP (0·001 *M*)	0·96	1·00
ATP (0·001 *M*) + Mg(II) (0·001 *M*)	0·81	1·00
ATP (0·001 *M*) + Cr (0·01 *M*)	0·96	1·07
Cr (0·01 *M*)	1·03	1·07
Cr (0·01 *M*) + Mg(II) (0·001 *M*)	1·01	0·98
ADP (0·001 *M*)	1·00	1·00
ADP (0·001 *M*) + Mg(II) (0·001 *M*)	1·27	1·01

* Obtained by allowing 0·001 *M* adenosine triphosphate (ATP), 0·01 *M* creatine and 0·001 *M* magnesium(II) to proceed to equilibrium before adding the alkylating agent.

† Approximate only. Consisted of the following mixture: adenosine di- and tri-phosphate, 0·0005 *M*; creatine phosphate, 0·0007 *M* creatine, 0·005 *M*.

The effects of ionic strength on the reaction of the enzyme with iodoacetate and iodoacetamide are shown in Fig. 2. The decrease in reaction-rate with increasing ionic strength observed with iodoacetate could be due to an electrostatic interaction between the carboxyl group and a positive locus on the enzyme. Thus it is evident that the effects of the various substrate components on the reaction of the protein with iodoacetate will be difficult to interpret because of this complication.

The failure of the metal ion, alone or in the presence of some of the substrate components, to protect the thiol group at the active site against alkylation argues against the metal being bound to the thiol.

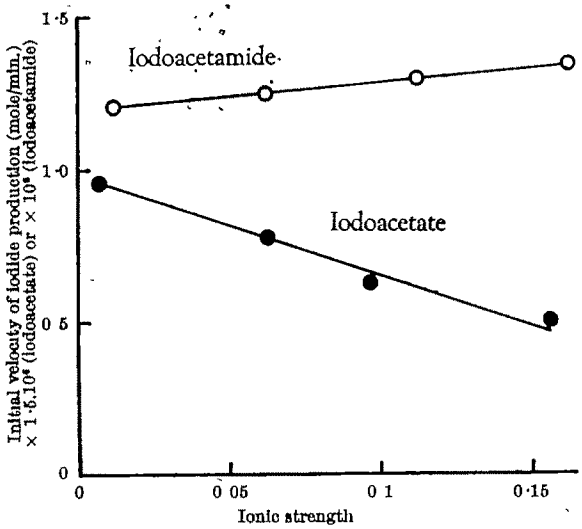

Fig. 2. Effect of ionic strength on the rate of alkylation of creatine phosphokinase. The reagent and protein concentrations were, respectively: for iodoacetate, 0·0005 *M* and 0·57 mgm./ml.; for iodoacetamide, 0·0001 *M* and 0·4 mgm./ml. Temperature, 25° C.; *p*H 9·0 (boric acid/sodium hydroxide)

The high degree of specificity possessed by the enzyme for both guanidine and purine components[1] indicates that these groups are bound at specific sites on the protein. If it is assumed that the thiol at the active site is hydrogen-bonded, perhaps to an imidazole residue, it is possible to visualize a mechanism for this enzyme which fits most of the data. The hydrogen-bonded thiol-imidazole system can be represented by Fig. 3. We suggest that interaction of the guanidine group with the thiol occurs only when both substrates and the metal are simultaneously present. The forward reaction can be represented by Fig. 4. In this the dashed lines are the bonds being formed or broken. The reaction proceeds by a synchronous set of bond re-arrangements, the rate-limiting step in which would be the simultaneous rupture and formation of the O—P and N—P bonds. The hydrogen-bond re-arrangements should occur with much greater facility than the nucleophilic displacement process at the phosphorus atom.

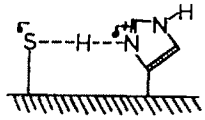

Fig. 3

The function of the metal in the forward process is to orientate the phosphate groups and assist the reaction by partial neutralization of the charges on the phosphate oxygen atoms. If the electronic tendencies shown in Fig. 4 are taken to completion, the species indicated in Fig. 5 are obtained. At high *p*H values a proton will ionize from adenosine diphosphate, probably while this is still attached to the enzyme surface, driving the reaction in the forward direction. Tautomeric re-arrangement, independent of *p*H, regenerating the thiol-imidazole hydrogen bond system shown in Fig. 3, would occur prior to dissociation of the substrates from the enzyme surface. The formation of adenosine triphosphate

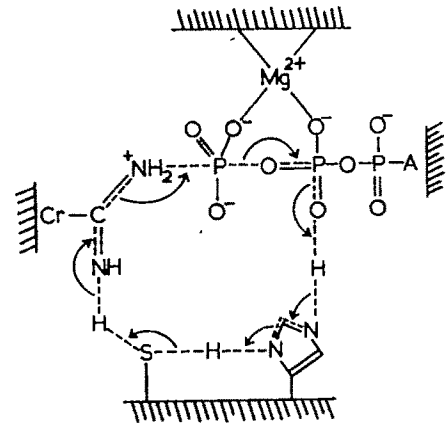

Fig. 4

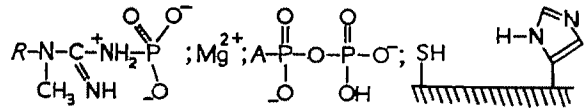

Fig. 5

would occur by complete reversal of the pathway of the forward reaction. Addition of a proton to enzyme-bound adenosine diphosphate is needed to trigger the reverse reaction, and this accounts for the lower *p*H optimum of the reverse process. The reverse reaction can be visualized as proceeding via the enzyme-substrate complex indicated in Fig. 6. Several tautomeric variants of this formulation are possible. A prototropic re-arrangement of thiol-imidazole would give the intermediate shown in Fig. 4 and the reaction would proceed by a counter-clockwise set of bond-shifts, the reversal of those in Fig. 4. The function of the metal in the formation of adenosine triphosphate is to hold the attacking phosphate of adenosine diphosphate near the phosphorus atom of creatine phosphate and assist the nucleophilic displacement at this atom by partial neutralization of the charges on the oxygen atoms.

It can be shown, by the use of models, that the proposed mechanism is stereochemically feasible. We have shown in the diagrams interaction of the sulphur with the guanidino group and interaction of

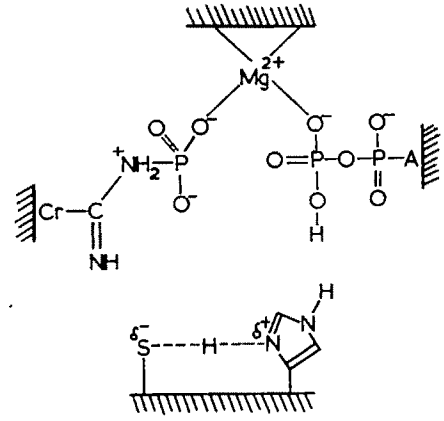

Fig. 6

the imidazole with a phosphate oxygen. It is, of course, possible that these sites of interaction are reversed without affecting the essential basis of the mechanism. This reaction is an interesting illustration of the principle of conjugate requirements[5]; in this instance the acid/base groups on the protein surface involved with attacking and departing groups are hydrogen-bonded together.

The mechanism we propose can easily be extended to other phosphokinases, and it is hoped that it will act as a guide and stimulus to further work on phosphate transfer systems.

We are indebted to the Central Research Fund, University of London, for a grant for the purchase of the automatic titration equipment used in these experiments. One of us (D. C. W.) thanks the Agricultural Research Council for a personal grant.

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A POSSIBLE SPECIFIC CHROMOSOME ABNORMALITY IN HUMAN CHRONIC MYELOID LEUKÆMIA

By A. G. BAIKIE, W. M. COURT-BROWN, KARIN E. BUCKTON, D. G. HARNDEN, PATRICIA A. JACOBS and ISHBEL M. TOUGH

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THREE reports have been published which indicate that in some cases of acute leukæmia in man there are abnormalities of both number and morphology of the chromosomes in the leukæmic cells[1-3]. However, no consistent abnormality has yet been found which can be linked to a specific cytological type of acute leukæmia. Baikie *et al.*[2] also reported that they were unable to detect any chromosome abnormality in bone marrow preparations from a number of cases of chronic myeloid and chronic lymphatic leukæmia. Nevertheless, it was said at the time that the standard of the preparations was such that the possibility of a small chromosomal lesion could not be excluded.

In recent months considerable developments have occurred as a result of the utilization of the technique of Hungerford *et al.*[4] for the culture of the leucocyte component of the peripheral blood. It is now recognized that chromosome preparations made from such cultures are of an appreciably better quality than those made from bone marrow. Using this blood culture technique, Nowell and Hungerford[5] noted the presence of a minute chromosome in dividing cells from the peripheral blood of two male patients with chronic myeloid leukæmia, and they regarded this as an unusually small *Y* chromosome. At about the same time as these observations were published, we noted the presence, in blood culture preparations, of a similar small chromosome in two female patients with chronic myeloid leukæmia. It was apparent, therefore, that if the same abnormal chromosome was being viewed by both groups of workers, then the abnormality must involve an autosome and not the *Y* chromosome. In the light of these findings we re-examined all our material from cases of chronic myeloid leukæmia, as well as studying two fresh cases of the disease. As a result of this we are satisfied that the presence of an unusually small autosome (Fig. 1) is a characteristic feature of many cases of chronic myeloid leukæmia.

Altogether we have studied the chromosomes in blood cultures from 12 patients (4 males and 8 females) suffering from chronic myeloid leukæmia. Among these were two patients who had had no previous treatment for their disease, either by X-irradiation or by chemotherapy. The remaining 10 patients had all been treated by radiotherapy some time prior to our work. The small chromosome was noted in preparations from eight patients, inclusive of both the untreated patients. Included among the 12 patients were three in a terminal acute transformation of the disease, and the relevant chromosome was noted in cultures from one of these. Marrow preparations have been studied from 10 patients, of whom four were males, and the small chromosome has been clearly seen in three patients, all three being fresh untreated cases. These three latter patients include two of those in whom the chromosome was also seen in blood culture. The remaining seven marrow preparations were of too poor a quality for us to be

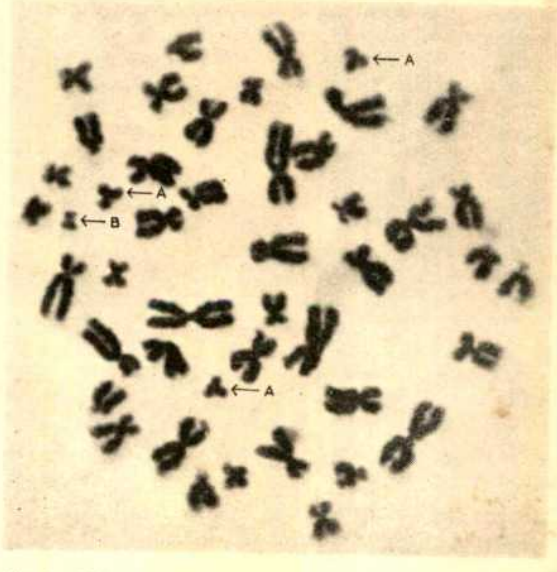

Fig. 1. Cell from the leucocyte component of blood cultured from a female with chronic myeloid leukæmia. The three normal-sized small acrocentric chromosomes are marked *A*. The unusually small acrocentric is marked *B*

certain as to whether the abnormality was present or not. In no case has the abnormally small chromosome been seen in every cell. The frequency of its occurrence has varied from 1/7 cells to 48/50 cells studied, and in all patients some normal euploid cells have been seen.

In addition to re-examining our material from cases of chronic myeloid leukæmia, we have also re-examined our preparations from the peripheral blood of individuals with apparently normal karyotypes, and our marrow and blood preparations from patients with acute leukæmia in which we had thought no chromosome abnormality to be present. Blood preparations were available from 90 individuals with apparently normal karyotypes and seven were selected at random, to which were added five preparations from cases of chronic myeloid leukæmia showing the small chromosome. These twelve preparations were then submitted to an independent observer who was ignorant of the patients involved. The five preparations with the small chromosome were readily identified, and in none of the seven control preparations was the chromosome thought to be present. We have also reviewed marrow preparations from eleven patients and blood preparations from six patients with acute leukæmia having an apparently normal karyotype, and we have no evidence in these of the unusually small chromosome. Finally, we have studied the blood cultures from five cases of mongolism associated with acute leukæmia and found no abnormality apart for the classical mongol karyotype which is presumed to be trisomy for autosome 21.

Before discussing the possible significance of these findings, the question of radiation exposure has to be considered, as chronic myeloid leukæmia is increased in frequency in heavily irradiated populations[6,7]. We have not been able to check with any certainty the histories of diagnostic X-ray exposure of our patients prior to the development of their leukæmic state. Two patients, however, have histories of radiotherapeutic exposure for conditions quite unrelated to leukæmia. One patient, a woman, was treated in December 1953, for a simple papilloma of the bladder by means of a radium implant. An area 3 × 3 cm. on the base of the bladder was given a dose of 6,000 rads over a period of 146 hr. This patient was diagnosed as having chronic myeloid leukæmia in May 1958, and the unusually small chromosome has been identified in cultured blood cells. The second patient, a male, was treated for ankylosing spondylitis between February and April 1955, a total dose of 1,500 rads being given to the skin over the whole length of the spine and the sacroiliac joints. A diagnosis of chronic myeloid leukæmia was made in March 1956. Only marrow cultures were available from this man and their quality was such that we could not be certain whether the small chromosome was present or not. On the basis of our knowledge of the distribution of the latent periods of radiation-induced leukæmias between radiation exposure and diagnosis, we cannot exclude the possibility that the first case was induced by radiation; it seems, however, unlikely that this was so in the second case, as the length of the latent period following a single heavy exposure usually lies between four and eight years, and the increased frequency of leukæmia is not noted until the second post-exposure year.

It now seems certain that the unusually small chromosome is one of the members of the two pairs of small acrocentric chromosomes numbered 21 and 22 in the Denver Classification. The most reasonable explanation for its small size is the occurrence of a deletion. The fact that we have in every preparation found some normal euploid cells suggests that the error does not occur in all the body cells and presumably is confined to cells from the bone marrow. We are at present undertaking the investigation of the chromosomes from skin culture preparations to help to clarify this point*. We have not noted the unusually small chromosome in any other person that we have studied. Carter *et al.*[8], however, have published ideograms of the chromosomes from blood cultures made from a mother and her mongol son, and in both these ideograms an unusually small chromosome appears to be present. The mother has a diploid number of 45, and is considered to have a translocation involving autosomes numbers 15 and 21, while the son has the full complement of small acrocentrics in addition to the same translocation, and is presumed to be effectively trisomic for number 21.

It has been established that mongols have a heightened probability of developing acute leukæmia[9-13], but not apparently of developing chronic myeloid leukæmia. From unpublished observations on death certificate data (Court-Brown and Doll) it does not appear that this increased liability relates to any specific cytological type of acute leukæmia, although the unreliability of such data must be borne in mind. It is also known that in most mongols there is a morphological abnormality of the polymorphonuclear leucocytes which takes the form of a deficiency in nuclear lobulation[14]. It is not unreasonable, therefore, to suggest that the autosome involved in mongolism may possess a locus or loci concerned with some aspect of the control of leucopoiesis. Our present findings in relation to chronic myeloid leukæmia indicate that in many cases of this disease there appears to be a deletion involving either autosome 21 or 22. In the meantime it would seem not unreasonable to adopt the working hypothesis that the same autosome is involved in many cases of chronic myeloid leukæmia and in mongolism.

**Note added in proof.* Since this communication was submitted for publication, it has been possible to examine the chromosomes in cells from skin cultures of three patients with chronic myeloid leukæmia. Blood culture studies of all three patients showed the presence of the unusually small chromosome, but this was not seen in any of the skin cells.

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BLUE WILDEBEEST AND THE ÆTIOLOGICAL AGENT OF BOVINE MALIGNANT CATARRHAL FEVER

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MALIGNANT catarrhal fever of cattle is a transmissible disease of world-wide distribution, sporadic occurrence and very high mortality[1-3]; it is not contagious[1,2,4] and fomites are not infectious on parenteral inoculation[1]. The ætiological agent is generally held to be a virus although, to our knowledge, there has been no reliable proof of its filterability.

In the majority of countries it is believed, largely on circumstantial evidence, that sheep are reservoirs of the virus without ever showing any clinical signs of its presence[3,5-8]. However, the mode of transmission from sheep to cattle has not been determined, and, in fact, the full clinical and pathological sydrome has never been reproduced in cattle by inoculation of materials from sheep. In Africa, infections among cattle often follow close association with apparently normal wildebeest[1,7,9,10], but the only experimental proof that the latter may harbour the agent of malignant catarrhal fever was provided by Mettam[1]. In one instance he inoculated the blood of a black wildebeest (*Connochaetes gnou*, Zimmerman) into an ox which showed a transitory pyrexia 14 days later. Blood collected at this time caused typical malignant catarrhal fever on sub-inoculation to another ox. Further attempts to demonstrate the virus in wildebeest consistently failed.

We have recently investigated the role of the blue wildebeest (*Gorgon taurinus taurinus*, Burchell) in the epizootiology of malignant catarrhal fever in Kenya. The causal agent has been isolated from them and successfully propagated in cattle, rabbits and monolayer tissue cultures; the latter, especially, have thrown new light on its salient characteristics, which are nere described in a preliminary manner.

During February 1959 and February–March 1960, 35 blue wildebeest of varying age and sex (Table 1) were shot in two game reserves of Kenya which are about 100 miles distant from each other. Heparinized blood and, occasionally, spleen and lymph-node tissue were collected immediately, stored on ice and within 48 hr. inoculated into cattle by the intravenous or subcutaneous routes. Monolayers were prepared from trypsinized cells derived from five near-term fœtuses and four calves 1–3 months old; all these cultures were observed for 28 days to detect cytopathic changes. Finally, leucocyte fractions from about 200 ml. of blood of 20 wildebeest were inoculated into monolayer cultures of normal bovine thyroid cells (*vide infra*) and suspensions of two fœtal spleens were used for cattle and culture inoculations.

Five isolates of malignant catarrhal fever virus were recovered from the 35 wildebeest, three from females in late pregnancy, one each from a yearling male and a yearling female (Table 1). Animal

Table 1. ISOLATION OF MALIGNANT CATARRHAL FEVER VIRUS FROM BLUE WILDEBEEST IN KENYA

Age	Sex	No. of animals	No. positive on cattle inoculation*	No. positive by all tissue culture tests	Remarks
Mature† Pregnant	F	8	3/8	0/8	One isolate recovered from fœtal spleen only
Mature	F	4	0/4	0/3	—
Yearling	F	6	0/6	1/6	First cytopathic changes, day 16
< 3 months	F	2	0/2	0/2	—
Mature†	M	7	0/7	0/5	First cytopathic changes, day 18
Yearling	M	6	0/6	1/3	
< 3 months	M	2	0/2	0/2	
Totals	—	—	3/35	2/29	5 isolates recovered from 35 wildebeest

* Blood was inoculated in a dose of 25 to 200 ml., tissue suspensions contained 3–10 gm. material.

† Mature means estimated to be two years or older.

inoculations yielded three isolates, bovine thyroid cultures two different strains, one of which was shown to produce typical malignant catarrhal fever in cattle. No infective virus was demonstrated in lightly centrifuged suspensions of pooled spleen and lymph node tissue from the two pregnant animals which were proved to have had a viræmia.

The disease developed in cattle after an initial incubation period of 34–38 days, being clinically identical in all respects to the virulent 'head-and-eye' form[11]. Pathological and hæmatological changes in infected cattle were similar to those described previously for cattle-derived strains of this virus[10-12]. In addition to the well-known perivascular accumulations of mononuclear cells, there was an angiitis of both arteries and veins characterized by necrosis and mononuclear cell infiltration of the media with swelling and proliferation of the endothelium[12].

One isolate was carried by two methods through more than 20 serial passages in cattle. The first line was maintained by the intravenous inoculation of heparinized blood, 5 ml. being an effective dose; for the second, crude 10 per cent suspensions were prepared in Ten Broeck grinders from prescapular lymph-node tissue and 5 ml. quantities of these were inoculated subcutaneously. Once established in cattle the incubation period decreased to a mean $18 \cdot 5 \pm 1 \cdot 1$ days, and the method of sub-inoculation did not

produce significant variations in this parameter. The mortality was 96 per cent with an average survival time of $8 \cdot 7 \pm 0 \cdot 8$ days.

Ten per cent lymph-node suspensions of the third to twenty-fourth passages produced the disease in cattle after 10^{-2}–10^{-3} dilution. Nevertheless, the supernatants remaining after centrifugation for 10 min. at 2,000 r.p.m. were devoid of infectivity in a dose of 20–25 ml. Similarly, 100 ml. of plasma was non-infective although whole blood had a titre of 10^{-1}–10^{-3} per 5 ml. These observations confirmed and extended previous findings[13,14].

The agent was established in rabbits[10] by the intracerebral or intraperitoneal inoculation of cattle lymph-node tissue and passaged by the intracerebral inoculation of brain or the intraperitoneal injection of spleen or lymph-node suspensions. The average incubation period in this species was $15 \cdot 2 \pm 0 \cdot 8$ days, death following invariably and usually suddenly after a further $4 \cdot 6 \pm 1 \cdot 3$ days. The post-mortem findings and histopathology were similar to those already described[10,12]. Plasma or low-speed supernatants from suspensions of infected tissues sometimes contained infective virus, thus differing from cattle materials treated similarly.

Initial attempts to propagate the virus in tissue culture were made by preparing monolayers from the kidneys, bone marrow and blood leucocytes of infected cattle. No cytopathogenic effect was observed at this time in living or stained cultures during an observation period of 28–30 days. Lymph-node suspensions produced no specific changes in established primary cultures of calf or sheep embryonic kidney and calf or sheep testis. Stimulated by the work of Pulvertaft[15], we then prepared monolayers from trypsin-dispersed cells of the thyroid of an infected ox, and these cultures showed a focal cytopathogenic effect first observed on the ninth day. The causal agent could not be passaged with cell-free fluids from the infected culture, but subcultivation to other thyroid monolayers was achieved by intact cells removed from the glass mechanically or with a mixture of versene and trypsin. These cell suspensions also reproduced malignant catarrhal fever in cattle following intravenous administration. Stained cover-slip preparations showed that the cytopathic changes observed were characterized by the formation of syncytia with intranuclear inclusions of type *A* (Fig. 1).

Similar cytopathogenic agents were regularly recovered by culture of the thyroid glands of other diseased cattle, infected with the same and other wildebeest isolates. The incubation period, when cell growth was satisfactory, was about 6–8 days. Furthermore, it was found that monolayers were readily prepared from adrenal gland tissue of infected cattle, and that these showed identical focal cytopathic changes, frequently detectable after 5–9 days. Virus of similar cytopathogenicity was also demonstrated in the blood of infected wildebeest (Table 1), cattle and rabbits and in lymph-node suspensions from the last two, by inoculation on to normal calf thyroid monolayers. Cytopathic changes were seen after as little as 3–4 days in the case of the last two species, blood titres reaching $10^{3 \cdot 2}$ TCD_{50} per ml. and gland titres $10^{4 \cdot 4}$ TCD_{50} per gm. in the ox. No cytopathogenic agent was ever recovered from uninoculated control cultures observed over prolonged periods.

Cell types which were found to be susceptible to the virus isolated in thyroid cultures included primary

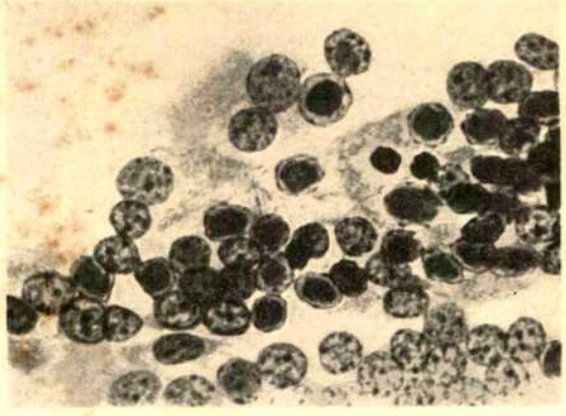

Fig. 1. Thyroid monolayer from an infected ox, eight days after seeding, showing a nuclear aggregation with intranuclear inclusions

sheep thyroid, calf testis and adrenal or rabbit and wildebeest kidney. In all these, however, as also in bovine thyroid, there was a tendency for the virus-induced changes to become progressively less extensive on passage or prolonged cultivation. Very satisfactory serial cultivation was eventually achieved by employing an 'established' line of calf kidney cells developed in this laboratory by one of us (R. D. F.). Suspensions were mixed, at the time of seeding into culture vessels, with infected trypsin-dispersed cells of the previous passage. Cytopathic foci then appeared after as little as 24 hr., often extending to involve a large proportion of the available cells in 5–7 days.

Five isolates were passed 14–38 times in this manner, the total period of time in culture varying from 3 to 10 months. Full cattle pathogenicity was retained at least up to the tenth to nineteenth passages for three isolates tested. Trypsin-dispersed cells from infected cultures were titrated by mixing 10-fold dilutions in growth medium with 'clean' suspensions of the cell line. The maximum number of infective centres was approximately 10 per cent of the total viable units as estimated by single cell counts after staining with neutral red. A suspension containing $10^{4 \cdot 9}$ TCD_{50} per ml. of fourteenth culture passage virus had a cattle infective titre of $10^{3 \cdot 2}$.

For a variable period no virus could be demonstrated in cell-free fluids from infected cultures, but after seven to thirty passages it was found that all four isolates produced free virus. This was not deposited at 5,000*g* for 30 min. and reached a titre of $10^{3 \cdot 3}$ TCD_{50} per ml. in one instance. Free virus was shown to be capable of passing graded collodion membranes of average pore diameter 430 mμ.

The cause of malignant catarrhal fever is therefore a virus which is present in the tissues of a proportion of apparently normal wildebeest in two widely separated areas of Kenya. The recovery of the virus from the spleen of a wildebeest fœtus *in utero* (Table 1) showed that trans-placental transmission occurs in this species. It can be propagated in suitable monolayer tissue cultures and produces a cytopathology which resembles that of herpes simplex[16], *B* virus[17], pseudorabies[18], varicella and herpes zoster[19]. It is remarkable that the histopathology of malignant catarrhal fever in cattle and rabbits has never been

reported to include either the formation of syncytia or the presence of intranuclear inclusions. A careful re-examination of material available to one of us (W. P.) has confirmed the absence of both these features.

Epizootiologically malignant catarrhal fever virus behaves like *B* virus, herpes simplex and pseudorabies in that these agents usually cause very mild infections in their customary reservoirs (monkey, man and pig, respectively) but highly fatal diseases when introduced into other experimental or natural hosts[20,21]. Herpes is a classic example of persistent infection, and some authorities[22,23] consider that herpes zoster may be a manifestation of recurrent pathogenic activity in individuals harbouring the virus of varicella. A viraemia extending over many months has been proved in this laboratory to be present in some of the few cattle which recover from malignant catarrhal fever. It is probable that the same virus persists for long periods, if not for life, in sheep and wildebeest.

The agent of malignant catarrhal fever resembles varicella and herpes zoster in its failure to produce free virus in early culture passages[10], but differs from them in that all tested isolates do so later and that cell-free virus cannot be demonstrated in the tissues of infected cattle. This last is a most important fact, which probably explains many failures to transmit the disease experimentally and also to filter and conserve the causal agent. In connexion with the last problem it may be noted that methods employed for the preservation of cell lines at low temperatures have been shown by us to be suitable for the long-term storage of the agent in cultured cells. The absence of free virus in cattle has an obvious bearing on the technique and interpretation of quantitative studies on the multiplication and distribution of the virus in tissues of infected animals. It is also fundamental to a study of its resistance to various physical and chemical agents, or neutralization by 'immune' sera.

The peculiar sensitivity of thyroid and, to a less extent, adrenal cells for the primary isolation of malignant catarrhal fever virus and the failure of other more widely employed types suggests that the former may possibly be used with advantage for other viruses which have so far failed to produce cytopathogenic effects *in vitro*.

More detailed results of these and other investigations will be published elsewhere.

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ROLE OF CEREAL FAT IN THE PRODUCTION OF NUTRITIONAL DISEASE IN PIGS

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IN Sweden nutritional diseases such as hepatosis diaetetica (dietetic liver necrosis) and muscular degeneration represent a serious hazard in pig raising. Through pathological and experimental work, Obel[1] demonstrated that two factors—vitamin E and the sulphur-containing amino-acids, methionine and cystine—are effective in preventing hepatosis diaetetica and suggested that Schwarz's factor 3 might also be involved. Since Schwarz and Foltz[2] detected the factor 3 effect of selenium compounds, and Eggert *et al.*[3] and Grant and Thafvelin[4] have shown the effectiveness of selenium salts for the prevention of experimental hepatosis in pigs, and since Schwarz *et al.*[5] have established that the protective effect of the sulphur-containing amino-acids almost certainly depends on contamination with selenium, attention is now mainly directed towards vitamin E and factor 3 (that is, biologically active selenium) in the ætiology of the lesions concerned. The absolute vitamin E content of feeds is *per se* of interest; but it is the relationship between the amounts of vitamin E and polyunsaturated fatty acids which seems to deserve emphasis. For this reason the unsaturated fatty acids of cereal grains have assumed a central place in current work on hepatosis diaetetica and muscular dystrophy in pigs.

In spite of conventional prophylaxis through dietary manipulation (cod liver oil is nowadays fed only sparingly to pigs), too many cases of hepatosis diaetetica and muscular degeneration occur among pigs in Sweden. There is reason to look into the ætiological importance of the grain fed since these diseases often occur among pigs fed nearly exclusively on grain.

Table 1. PROPERTIES OF THE VARIOUS FEEDS

Feed	Fat content (per cent)	Iodine No.	Free fatty acids ml. KOH/gm. fat	Peroxide value m.equiv./kgm. fat	Tocopherol content (α-tocopherol) mgm./100 gm.
Feed I, unheated	4·8	78	77	0	2 36
Feed I, heated	3 7	37	53	140*	0 48
Feed II, unheated	3 8	75	135	164	0·40
Feed II, heated	2 7	76	130	0	0 67
Maize oil, fresh	—	112	1·2	0	69 9
Maize oil, heated	—	109	1·4	250*	6 31

* Mean throughout experiment.

Theoretically, there are two aspects of the disease-producing properties of feed grains to be considered—the unsaturated fatty acids and the level of biologically active selenium. In a recent paper[6], we have published the results of work on cereal fats and have indicated their potentialities for becoming rancid in certain circumstances. This article gives a brief account of attempts to produce nutritional lesions in pigs by feeding grain containing rancid fats or fats with a tendency towards autoxidation. The results were checked by feeding pure vegetable oil of known oxidative status.

Apart from the experimental feeds to be described here, the pigs received daily supplements of 1–1·5 litres skimmed milk and minerals. Pigs of the Swedish Lantras breed, 10–12 weeks old, were used. Routine blood analyses and determinations of serum transaminase activities (glutamic-oxalacetic transaminase (GOT) according to Karmen-Ordell[7]) were performed. Our normal value for serum-GOT activity in pigs is $22 \cdot 5 \pm 7 \cdot 7$ ($n = 61$) Karmen–Ordell units. Through work on pigs of the same breed carried out by Reitman and Frankel's method, a normal value for serum-GOT activity of $28 \cdot 03 \pm 15 \cdot 39$ units was found by Wretlind, Orstadius and Lindberg[8].

'Peroxide'-levels in the cereal fat and vegetable oil were estimated by a method developed by K. Erne of this Institute.

The tocopherol contents were determined in the laboratories of AB Ewos, Sodertalje, by Dr. G. Ekstrom using the method of F. Bro-Rasmussen and W. Hjarde[9]. All pigs which died or were killed were autopsied (C. A. Grant[4]). The lesions of hepatosis diaetetica and muscular degeneration were evaluated by conventional standards[1]. The criteria applied for the diagnosis 'plotzlicher Herztod' have been briefly mentioned before[4] and will be presented more fully in another connexion.

Experiment 1. The effect of feeding grain containing fats of great susceptibility towards rancidity (feed I).

As shown in Table 1, autoxidation could be induced in this sample of grain by heating in an incubator (21 hr. at 100° C.). Five pigs received grain heated in this manner and five received unheated grain from the same sample. Significantly increased serum-GOT values were recorded for the first group from the twenty-first day (Fig. 1). Two died after 21 and 33 days, respectively, and the remaining three were killed after 56 days. The major autopsy findings are given in Table 2.

The five control pigs remained clinically healthy. All were killed on the thirty-sixth day. From the transaminase values given in Fig. 2 and from experience with previous experiments it appears most likely that tissue destruction did not occur during the experimental period. On several occasions during the last days of the experiment the pigs fought savagely; this experiment is to be repeated with precautions to eliminate fighting.

Experiment 2. The effect of feeding grain containing fat which had spontaneously oxidized during storage (feed II).

This sample of grain had produced nutritional lesions among pigs on a farm. Five pigs were given the feed as such. Five control animals received the grain heated in an incubator at 100° C. for 4 hr. at the beginning of the experiment and later for 6 hr. to accelerate the oxidative processes to stability (Table 1). Increased serum-GOT values were seen in the pigs of the first group by the sixth day (Fig. 3). One pig died on the thirteenth day, two on the fourteenth, and the remaining two were killed on the thirty-eighth and fortieth days, respectively.

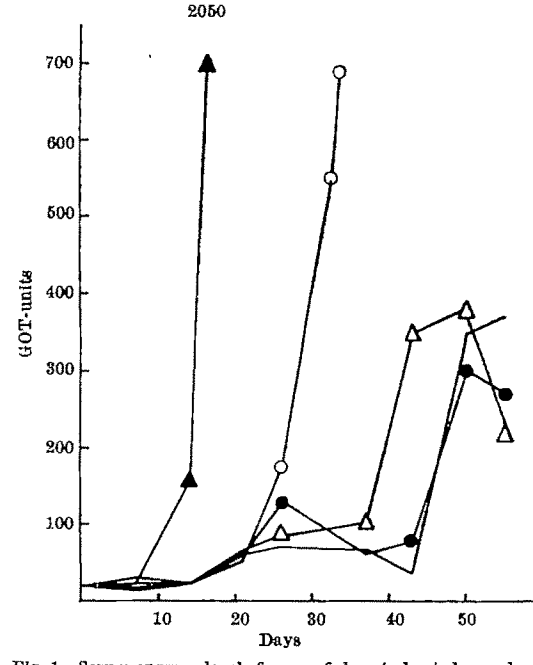

Fig. 1. Serum enzyme-levels for pigs fed grain heated in order to induce oxidation

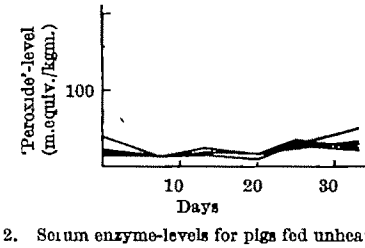

Fig. 2. Serum enzyme-levels for pigs fed unheated grain

Table 2. MAJOR AUTOPSY FINDINGS

Group	No. of animals	Lesions of 'plötzlicher Herztod'	Waxy degeneration of skeletal muscles	Hepatosis diaetetica
Feed I, unheated†	5			
Feed I, heated	5	4	5 + + +*	0
Feed II, unheated	5	5	5 + + +	1
Feed II, heated	5	0	5 + to + +	0
Maize oil, fresh	2	0	1 (+)	0
Maize oil, heated	2	2	2 + + +	1

Degree of degeneration:
* (+), only a few fibres involved; +, slight degeneration; + +, moderate degeneration; + + +, pronounced degeneration.
† See text under experiment 1.

No clinical signs were seen in the five control pigs although all showed slightly increased serum-GOT activities (Fig. 4).

The major autopsy findings are given in Table 2.

Experiment 3. The effects of feeding fresh and rancid vegetable oil.

As a pilot experiment four pigs were fed a normal diet to which was added a daily supplement of 250 ml maize oil per pig. Two pigs received fresh oil and two oil which had been oxidized by heating (Table 1).

The pigs fed rancid maize oil died after 16 and 37 days respectively. Serum-GOT values were elevated throughout the course of the experiment (Fig. 5).

No clinical signs and no increase in serum-GOT activities were evident for the two control animals (Fig. 6).

The major autopsy findings are listed in Table 2.

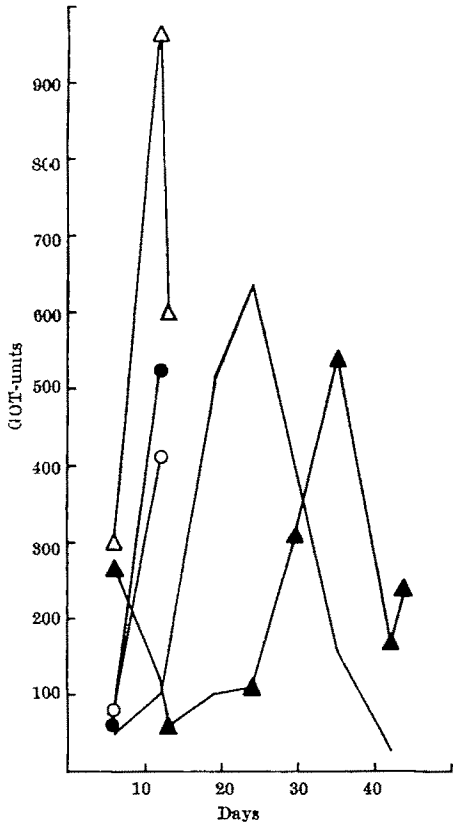

Fig. 3. Serum enzyme-levels for pigs fed grain containing fat which had spontaneously oxidized during storage

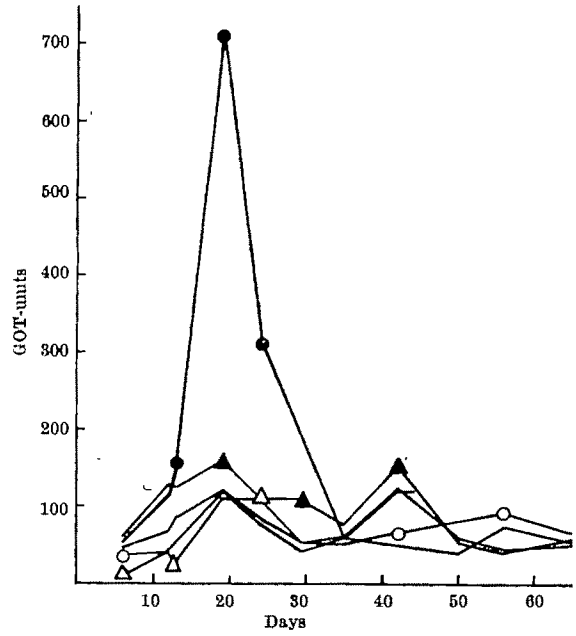

Fig. 4. Serum enzyme-levels for pigs fed grain heated in order to accelerate the oxidative processes to stability

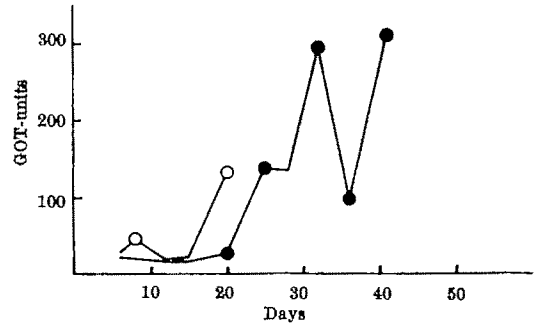

Fig. 5. Heated maize oil

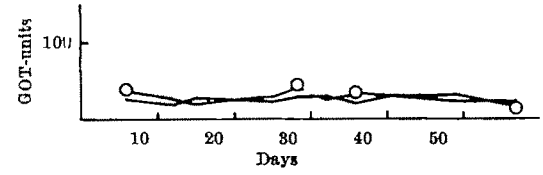

Fig. 6. Fresh maize oil

Discussion

It has long been known that hepatosis diaetetica, muscular dystrophy and allied lesions can be produced experimentally by feeds which contain unsaturated fatty acids of marine origin[1,10–14]. It is, however, an observed fact that the addition of marine fat to pig feed is by no means a prerequisite for the occurrence of these lesions in Swedish pigs. Grain, on the other hand, forms the greater part of conventional pig rations. With this in mind, the question could be posed whether or not the natural fat of the grain could in certain circumstances be the underlying cause of these disorders. Chemical studies of the properties of cereal fat during various phases of maturation and under various storage conditions have shown this hypothesis to be theoretically accept-

able[6,15-17]. The results of this initial work can be summarized as follows.

(1) 'New grain' contains fats characterized by little or no rancidity but also by great susceptibility to rancidity. This susceptibility steadily decreases during storage.

(2) If ground, grain will gradually lose the ability to protect its fat against oxidation and, depending on its original properties, sooner or later during storage in this state will become rancid.

Expressed in another way, grain can in certain circumstances contain unstable fats, that is, fats with a tendency to become rancid. This is especially apparent during rainy years with little sunshine. In experiment 1, grain of this type was ground and heated to give it roughly the same properties as ground grain stored under natural conditions. Treated in this way, the grain produced the lesions listed in Table 2.

The grain fed in experiment 2 was known to have produced spontaneous disease in a herd of pigs. The grain as such contained highly oxidized fats and produced the lesions described in Table 2. Through heating, it was possible to stabilize the fat and in that way greatly reduce its disease-producing propensity.

Finally, it could be shown in experiment 3 that pure vegetable oil, when oxidized, can produce lesions belonging to the same group as those encountered in the other two experiments and in pigs dying of the spontaneous diseases.

To sum up, then, there is ample evidence suggesting that when hepatosis diaetetica, muscular degeneration and allied disorders are seen in pigs fed mainly on grain, the occurrence of these lesions can be coupled with the properties of the cereal fat.

These investigations have been supported by grants from Jordbrukets forskningsråd. GOT reagents have kindly been supplied by AB Kabi, Stockholm.

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THE BIOSPECIES IN ENTOMOLOGY

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AT a recent joint discussion of the Linnean Society and the Systematics Association on the subject of the sub-species, it was quite evident that there is still no basic agreement between biologists on the nature of the species itself. Thus there can be little hope of defining the sub-species to the satisfaction of all workers.

It has been argued recently[1,2] that the term species should be restricted entirely to a morphological entity: that is, it would be the lowest taxonomic category (except the variety ?) above the individual and be defined entirely morphologically. In considering sexually reproducing forms, the justification for such a concept is that it represents the nearest approach to a true biological species which can be attained in the present state of knowledge for many animal and plant groups. Even to Linnæus the species was a biological entity characterized by a quality of breeding true[3]. Later workers stressed the importance of a sterility barrier between species. Poulton[4] developed the idea of the species as a freely interbreeding series of populations in Nature and coined the term 'syngamy' for such a free-interbreeding relationship. Even at the beginning of this century Poulton[4] was aware of the difficulty of determining the status of geographically isolated or allopatric forms, since it was not possible to determine whether or not such forms could interbreed in the field. This led to the modern polytypic species taking account of variation in space, that is, geographical variation. The concept has been fully developed by Mayr[5] and critically reviewed by Cain[6]. Unfortunately, the status of truly allopatric forms can never be determined with certainty. However, sympatric forms, that is those the breeding ranges of which either coincide or overlap in Nature, can be delimited objectively by the presence or absence of syngamy, of what Mayr[5] has termed "crossability", between them. There is no biological reason why morphological differences should always be associated with the breeding barrier and thus no *a priori* reason why there should always be morphological differences between species. Of course there usually will be such differences which can then be used as indicators of the true biospecific limits. This is the main justification for the use of the morphospecies in neontology when considering bisexually reproducing forms.

Dobzhansky[7,8] has developed the theory of speciation by spatial isolation of populations and subsequent selection for isolating mechanisms. It is supposed that the populations would diverge genetically when in spatial isolation due to the differential action of natural selection in the different environments. On meeting again, hybrids between the forms would be at a selective disadvantage to either of the parental types, and, providing that this disadvantage was large enough not to be swamped, there would be heavy selection for the establishment of isolating mechanisms and eventually separation as good species. Koopman[9] has been able to demonstrate the very

rapid evolution of isolating mechanisms in the laboratory between two very closely allied species of *Drosophila*, *D. pseudoobscura* Frolova and *D. persimilis* Dobzhansky and Epling, which can be made to interbreed at temperatures of about 16° C. These experiments strongly support Dobzhansky's theory, which also seems adequate to explain the existence of many groups of insects in which morphological specific differences are either very small or almost non-existent. In such groups the species often differ more obviously in biological features.

It is essential that there should be some ecological differences between closely allied sympatric species if they are to co-exist. Ecological differences such as separate breeding seasons may have arisen when the populations were spatially isolated and would then automatically be important as isolating mechanisms when the populations met again. However, some ecological differences may not be of importance in the actual process of speciation, but only in the avoidance of competition after specific differentiation. Thus differences between closely allied sympatric species may be of at least two kinds, associated either with the primary isolating mechanisms or with secondary ecological differences and usually with both. However, morphological characteristics need not always be associated with either. Thus in my view it is wrong to insist on distinct morphological characters for separating species when the only certain criterion is the presence of reproductive isolation. Perhaps the most satisfactory definition of the biological species or biospecies is that of Mayr[5], namely, "Species are groups of actually or potentially interbreeding natural populations, which are reproductively isolated from other such groups". The only weakness lies in the phrase "potentially interbreeding", which has to be introduced in order to include allopatric populations.

All grades of morphological differences between true biospecies have been recorded, including many in which the differences are very slight. Well-known examples of such sibling species are *Drosophila pseudoobscura* and *D. persimilis*[10] and the species of the *Anopheles maculipennis* group[11]. Undoubtedly many further examples exist and will be uncovered during the course of intensive biological investigations which are now being carried out in many insect groups. Recently, Claridge and Askew[12] have described a group of siblings in the genus *Eurytoma* (Hym., Chalcidoidea). *E. rosae* Nees and *E. brunniventris* Ratz. are inseparable on the adult characters which I have been able to study, but they differ in characters of the egg and in details of hosts and life-histories. Also in the family Eurytomidae, Neunzig and Gyrisco[13] have recently shown that *Bruchophagus platpyterus* (Walk.) (= *gibbus* Boh.) is an aggregate of at least three species with definite host plant preferences. There is also evidence of the widespread occurrence of sibling species in other groups of Chalcidoidea.

The desire to retain the species as a static morphological entity with little reference to biological reality must be overcome if taxonomy is to make further contributions to biological science. It may be, as suggested by Gilmour[2], that the problems in botanical taxonomy are so great that a completely new system of categories is required. However, this would be a very unfortunate change since it would obscure the similarities between the real biological entities of both zoological and botanical taxonomy.

I thank Dr. A. J. Cain for discussion on the subject-matter of this article.

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SOME OXIDATIVE AND HYDROXYLATIVE ACTIONS OF QUARTZ: THEIR POSSIBLE RELATIONSHIP TO THE DEVELOPMENT OF SILICOSIS

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THE existence of a special surface activity possessed by siliceous dusts and silicates has been frequently reported in the literature. Hauser[1] indicated that the formation of a free silica surface was accompanied by the liberation of protons and the formation of atomic oxygen, and found a correlation between particle size and amount of oxygen released. In essence, he postulated that the unusual oxidation potential of silica resulted from the decomposition of some superoxide ions to yield atomic oxygen. Weyl[2] considered a type of dynamic hydration–dehydration equilibrium which would account for the fact that siliceous materials were able to act as oxidation catalysts in the presence of air.

Our interest was given stimulus when we found that quartz dust could be employed successfully as an oxidant in a number of *in vitro* oxidation reactions, and we have since verified some of the postulates set out above.

Since the conversion of proline to hydroxyproline can be readily effected by hydrogen peroxide, we have been able to estimate quantitatively the oxidative activity of a number of dusts of known particle size as 'peroxide equivalents' per unit weight per

unit time for this conversion. The peroxide equivalent of a dust is obtained by comparing the amount of hydroxyproline (colorimetrically at 560 mμ) which can be produced by 1 gm. of dust shaken with 5 mgm. of proline for 30 min., with that amount produced by 2·5 mgm. of hydrogen peroxide under the same conditions. Table 1 shows a list of dusts in decreasing order of activity; in addition to the dusts listed, 'Aerosil' (250–500 Å. 'colloidal silica') has since been shown qualitatively to hydroxylate proline.

On the face value a correlation appears to exist between the 'oxidative activity' of the dusts and the known fibrogenetic potential of the materials examined. Crocidolite, however, is an exception; there are a number of suggestions for its apparently anomalous behaviour and these are being investigated together with the behaviour of other silicates. A further connexion between particle size and activity also seems apparent in the case of coarse quartz and the other quartz dusts of a much smaller size. Whether there is any relationship between oxidation and surface area is at present being examined.

It has been shown in the laboratory (Table 2) that quartz can bring about a number of oxidative and hydroxylative conversions, many of which have been previously demonstrated in biological systems.

In all cases the products were identified by paper chromatography with specific detection reagents and by the use of pure standards, and wherever possible the identity of the products was checked by colorimetric estimation, followed by examination of the absorption spectra obtained.

Particularly interesting conversions which have been listed above are the hydroxylations of proline and lysine to yield small amounts of hydroxyproline and hydroxylysine, respectively, amino-acids found almost specifically in collagenous protein. In addition, glycine, another important amino-acid of collagen, has been shown to be produced by quartz.

The maximum yield of hydroxyproline obtained with quartz under optimum conditions was 0·1 and 0·16 per cent in the presence of vitamin C. In most cases the yield was improved by dry shaking instead of wet, and in the case of hydroxyproline, it was enhanced by the addition of certain co-factors, the most important of which was ascorbic acid; this increased the yield up to 60 per cent. The additional observation was made that ascorbic acid can feebly hydroxylate proline *in vitro*, and this raises the question whether quartz does not actually synergize the ascorbic acid hydroxylation of proline.

Table 1. OXIDATIVE ACTIVITY OF VARIOUS DUST SAMPLES IN TERMS OF THEIR ABILITY TO CONVERT PROLINE TO HYDROXYPROLINE

Sample*	Per cent size distribution (μ)	Peroxide equivalent (mgm.)
Superfine quartz dust	87 < 1	3 25
Acid-washed quartz dust	92 < 1	3 00
Mine dust (Witwatersrand gold mine)	84 < 1	2 70
Coarse quartz dust	90 > 5	1 75
Coal dust	86 < 1	1 00
Crocidolite	86 < 1	nil
Kaolin	92 < 1	nil
Talc	76 < 1	nil

* The materials used have the following characteristics: superfine quartz dust (0 03 mgm. iron/gm.) (Dowson and Dobson); acid-washed quartz (trace of iron present after washing with hydrochloric acid), mine dust (54 per cent silica) (Witwatersrand gold mine); coarse quartz dust (0 05 mgm. iron/gm.), prepared by sedimentation; coal dust: anthracite (6·6 per cent silica); crocidolite: blue asbestos (50 per cent silica, 40 5 per cent ferrous oxide and ferric oxide); kaolin, washed and ignited, technical (J. T. Baker Chemical Co., Phillipsburg, N.J.); talc: hydrated magnesium silicate.

Table 2. OXIDATIVE AND HYDROXYLATIVE CONVERSIONS PRODUCED BY QUARTZ AFTER VIGOROUS SHAKING WITH STARTING MATERIALS

Material	Product	Other oxidants used for confirmation
dl-Proline	Hydroxyproline*†	H_2O_2
β-Alanine	Glycine†	H_2O_2 + Fe salts
Lysine	Hydroxylysine†	H_2O_2 + Fe salts
Phenylalanine	Tyrosine*	H_2O_2
Ascorbic acid	Dehydroascorbic acid*	Alumina
Thiamine	Thiochrome†	$K_3Fe(CN)_6$
Adrenaline	Adrenochrome†	H_2O_2; $K_3Fe(CN)_6$
N-N dimethyl *p*-phenylenediamine	Wurster's red†	H_2O_2
p-Phenylenediamine + α-naphthol	Indophenol purple†	H_2O_2
Calcium gluconate	Arabinose*†	Fenton's reagent (H_2O_2 + Fe salts)

* Dry shaking for 1 hr., then taken up in distilled water.
† Wet shaking throughout.

Hydrogen peroxide gave a greater yield of hydroxyproline compared with that given by quartz, and quartz added to a standard hydrogen peroxide–proline system gave the highest amount of hydroxyproline obtained. It is clear from Tables 1 and 2 that parallels exist between hydrogen peroxide and quartz-sponsored oxidations, and this suggests that quartz is functioning in a peroxidative capacity in most of the cases investigated. Kalyankar *et al.*[3] obtained similar conversions with peroxide in the presence of iron salts.

In general, it seems evident that the conversions sponsored by quartz are catalytic ones in the presence of air, and possibly of the type mentioned by Johnson *et al.*[4], where reactions involving free radicals *in vitro* were shown to simulate certain enzymatic processes.

It is not at the moment possible to relate these findings directly to the development of silicosis, and tentative suggestions only can be made. Quartz dust might give rise to peroxide in the tissues, or vitamin and hormonal activity might be interfered with at the site of deposition of dust. Furthermore, the possibility of the formation of toxic products from normal body constituents by the action of quartz should not be excluded: recent work (unpublished) in this laboratory by Marasas has shown that histamine and other imidazole derivatives are formed when histidine is allowed to react with quartz under simple laboratory conditions. In a different context, it has also been shown that measurable amounts of formaldehyde in some form or another can be readily detected in quartz and certain other dusts.

Finally, there is the possibility that quartz might in some way be involved in the direct synthesis of collagen from hydroxylated or oxidized precursor amino-acids or peptides, which might then be adsorbed on to the quartz surface in a manner similar to the template model proposed for such materials by Seifert[5].

We wish to thank the director of this Unit, Dr. H. S. Gear, for facilities extended to us during this work, the sub-director, Dr. Ian Webster, for helpful discussions, and Miss M. J. Matthews for undertaking particle sizing and counting.

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LETTERS TO THE EDITORS

ASTRONOMY

Bode's Law and the Solar System

In a recent communication[1] a model was proposed for the formation of the solar system. It was suggested that tides produced on the Sun by a passing star caused portions of the solar material to break away at regular intervals of time, the intervals being governed by the natural frequency of oscillation of the disturbed Sun.

The most outstanding feature of the solar system is Bode's law, which relates mathematically the radii of the orbits of all the planets other than Neptune. In fact, the form of the law

$$r \propto 4 + 3 \times 2^n \ (n = 0, 1 \ldots 7)$$

does not really include Mercury as a natural member. However, it is clear that the correct explanation of the origin of the solar system must include Bode's law as one of its consequences. It will be shown that a model of the type already proposed, with some modifications suggested by computational experience, explains the radii of the planetary orbits with reasonable accuracy.

The details of the process will be best understood by reference to Fig. 1. The Sun is considered to have been at rest (for illustrative purposes only—any mathematical analysis must take account of its motion about the centre of gravity of the system) and the star to have approached on an orbit which took it to within a distance, D, of the Sun. The solar tide grew as the star approached and rotated to face the oncoming star. Eventually, a point of instability was reached[2], and the tip of the tide broke away and moved henceforth under the combined gravitational influence of the Sun and star. It has been confirmed by computation that the embryonic planet would be very little affected in its subsequent motion by the star, and its orbit around the Sun may be calculated from the height, R, and the angular velocity, ω, of the tide at the time of its inception. This orbit, assumed elliptical, will have a major axis of length:

$$a = \frac{GMR}{2GM - R^3\omega^2} \text{ and eccentricity } e = \left| 1 - \frac{R^3\omega^2}{GM} \right|$$

where M is the mass of the Sun and G the gravitational constant.

After an interval, t, another planet was formed. The value of R would have been the same as before, but ω would have been greater due to the angular acceleration of the star. The point of release of the planet may be defined by the angle θ shown in Fig. 1; it is assumed that ω was the angular velocity of the star at the appropriate value of θ. In fact, ω would be somewhat less than this value due to an inertial lag of the tide which would be expected to build up gradually as the star accelerated towards the perihelion of the orbit. Once this lag was sufficiently great, the process of detaching material from the Sun would have ceased.

The eccentricity of the original orbits will have been reduced by the passage of the planet through the

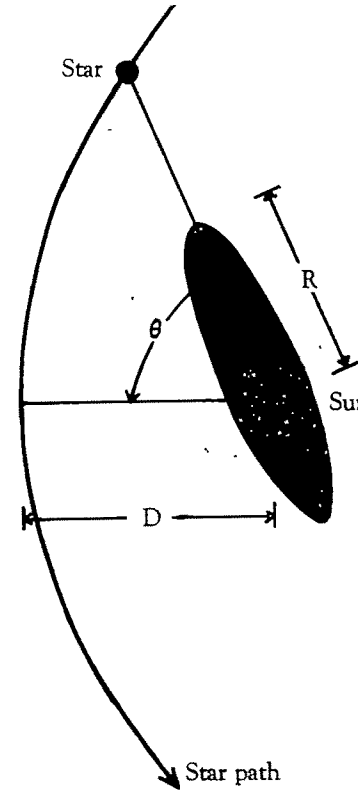

Fig. 1

material surrounding the Sun: tenuous though this may be, it has an appreciable effect over long periods of time. The planets for which $\omega < \sqrt{\frac{GM}{R^3}}$ have R as aphelion distance; with $\omega > \sqrt{\frac{GM}{R^3}}$, then R is the perihelion distance. As a general rule, the eccentricity should be smallest for the innermost planets. Mercury is a notable exception to this rule; another exception is Neptune, the orbit of which is almost circular. This provides the clue to the value of R, because the orbit of Pluto, which is rather eccentric, actually intersects that of Neptune. This suggests that the orbit of Neptune was originally almost circular and that R was approximately equal to the radius of that orbit.

Since the retarding medium has a density which falls off fairly sharply with increasing distance from the Sun, the characteristic of the orbit which should remain approximately constant is the perihelion distance, $a(1 - e)$, which depends on the value of ω. For the two outermost planets, which have been under no appreciable restraint, the function $a(1 + e)$ is that which corresponds to ω.

The values which are being considered at present are:

Perihelion distance of Sun–star orbit	$D = 5 \cdot 21 \times 10^{14}$ cm.
Tidal radius	$R = 4 \cdot 30 \times 10^{14}$ cm.
Mass of Sun	$R = 2 \cdot 20 \times 10^{33}$ gm. (about 10 per cent greater than at present)
Mass of star	$R = 3 \cdot 39 \times 10^{33}$ gm.
Period between planetary formation	$t = 2 \cdot 13 \times 10^{8}$ sec.

The star orbit is taken as parabolic.

The agreement between theory and observation is shown in Table 1.

Table 1

Planet	t ($\times 10^8$ sec.)	θ (°)	$a(1 \pm e)$ Theoretical ($\times 10^{13}$ cm.)	Observed ($\times 10^{13}$ cm.)
Mercury	?	?	?	0·46
Venus	0	96·4	1·09	1·08
Earth	2·13	92·3	1·53	1 48
Mars	4·26	87·5	2·12	2 05
X	6·39	81·8	3·17	—
Y	8·52	74·9	4·86	—
Jupiter	10·65	66·5	7·85	7·40
Saturn	12·78	56·1	13·42	13 43
Uranus	14·91	43·2	24·35	27·33
Neptune	17·04	27·5	45·00	45·30
Pluto	19·17	9·3	72·90	73·80

It will be seen that the agreement is generally good and that the following important features emerge: (i) Mercury does not fit into the system as, indeed, it does not fit properly into Bode's law. In view of the large eccentricity of its orbit, it is very unlikely to have started in its present course at the same time as the other planets. (ii) The model predicts two planets, *X* and *Y* in Table 1, between Mars and Jupiter. The asteroid belt may be explained as the debris of the collision of these planets. (iii) Neptune fits naturally into the planetary system and is not an odd member as Bode's law would suggest.

There have been substantial modifications of the model as originally put forward. In particular, the time-scale has been greatly increased (by a factor of about 10^6) and the origin of the asteroids is now explained as the results of a collision between two planets. However, the basic idea, that the planets were produced individually at regular intervals of time, has been preserved.

The full implications of the model are still being investigated, and, in particular, departures of the star-orbit from parabolic are being tried. Thus far, the model accounts satisfactorily for all those features of the solar system which have been examined.

The computations for this work were carried out on the University of Manchester *Mercury* computer, and I am indebted to the Electrical Engineering Department for the use of its facilities.

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Spheroidal Oscillations of the Moon

PERIODS of natural vibration of three spherical gravitating models of the Moon have been calculated on an IBM 7090 electronic computer. The values provide basic information for lunar space-research concerned with the design of experiments to investigate the structure of the Moon.

Three completely solid models of the Moon have been treated, each with radius, $R = 1{,}738$ km., and mean density, $\bar{\sigma} = 3 \cdot 33$ gm./c.c. Model I is a homogeneous sphere having throughout velocities for *P* and *S* waves of $\alpha = 8 \cdot 2$ km./sec., $\beta = 4 \cdot 7$ km./sec., respectively. Since only the differences between the principal moments of inertia of the Moon are known[1], there is no direct evidence, at present, that it does not possess a core or have a concentration of mass towards the centre. Thus the following Roche laws of density distribution which fit the total mass were used to define the other models:

Model II $\rho = 3\ 415 - 0 \cdot 185x^2$, $x = r/R$
Model III $\rho = 4 \cdot 430 - 1 \cdot 830x^2$

The density distribution in Model II is close to that calculated by Jeffreys[2], for the self-compression of a Moon composed of ultrabasic rock with a surface density near 3·28 gm./c.c. Model III has a rather extreme density distribution having a surface value of 2·60 gm./c.c., near that of granite. This model was constructed to indicate the effect on the free periods of an internal lunar structure which has an increase of heavy material with depth (or a heavy core). Variations of *P* and *S* velocities with depth have been calculated in both Models II and III from the following velocity–density relationships which were based mainly on the *P* and *S* velocity distributions of Jeffreys[2] for the Earth and the density values of Earth Model A, constructed by Bullen[4]:

$$\left.\begin{aligned} \alpha &= -2 \cdot 40 + 3\ 12\ \rho \\ \beta &= -0 \cdot 60 + 1\ 52\ \rho \end{aligned}\right\} 2 \cdot 5 < \rho < 4\ 5$$

(Linear velocity–density relations for longitudinal waves through considerable portions of the Earth's interior have been noticed by Francis Birch and J. E. Nafe (personal communication).)

The frequencies of the spheroidal oscillations were determined numerically from a sixth-order differential equation formulated by Hoskins[5] and Alterman *et al.*[6]. For this type of vibration the displacement has, in general, both transverse and radial components which are affected by the gravitational attraction. Integration was by a fourth order Runge–Kutta method, through homogeneous shells of thickness 100 km., using floating-point arithmetic and about eight decimal digits. Some solutions were also computed using a shell thickness of 50 km. and the agreement between corresponding frequencies was between 1 and 5 per cent. (For the present purpose it did not appear worth while to use additional machine time in order to improve the fit between calculations for a layered sphere and for a sphere with continuous properties by increasing the number of layers.) As a programme test, the period of oscillation of order 2 for a homogeneous Earth (called by Alterman *et al.* (*loc. cit.*) Model β) was computed, using shells 100 km. thick. The present programme yielded a period of 44·37 min. compared with 44·3 min. given by Alterman *et al.* The calculated lunar periods are shown in Table 1.

The case of the purely radial vibration ($n = 0$) of Model I allows a check on numerical accuracy. Pekeris and Jarosch[7] show that for a homogeneous sphere:

$$\varkappa R/\tan \varkappa R = (1 - \varkappa^2 R^2 \alpha^2/4\beta^2)$$

and

$$\varkappa^2 = (4\pi^2/T^2 + 4A)/\alpha^2$$

Table 1. PERIODS OF FREE VIBRATIONS (MIN.)

n		Models I	II	III
0	Fundamental	8·73	8·7	7·5
	First higher mode	6·8	—	—
2	Fundamental	14·6	15·1	12·5
	First higher mode	8·0	8·4	8·1
	Second higher mode	4·9	—	—
3	Fundamental	9·8	10·2	8·8
	First higher mode	6·0	6·3	6·8
4	Fundamental	7·7	8·0	7·2
	First higher mode	4·8	5·1	5·6
6	Fundamental	5·6	5·8	5·5
	First higher mode	3·6	—	—

where T is the vibration period, and surface gravity is AR. For Model I the highest solution of these equations is $T = 8{\cdot}75$ min., in close agreement with the corresponding value in Table 1.

Concentration of mass towards the centre causes a relatively large reduction in the fundamental periods for $n < 6$. It is probable that for $n > 6$ the free periods of Models II and III again become markedly different (in the opposite sense) because motion would be largely confined to the surface region. The above results indicate that a measure of the deviation of the Moon from homogeneity is possible using observations of the long-period spectrum of free vibrations. An investigation of Press *et al.*[8] has shown the capabilities of a single short-period seismometer in obtaining data on the deep interior of the Moon. This work suggests that, if the free vibrations are excited, an ultra-long period seismometer or tidal gravimeter designed to record periods up to 16 min. should provide more detailed information.

Acknowledgments for IBM 7090 computing time are due to the National Aeronautics and Space Administration, Theoretical Division, and International Business Machines Corporation, Watson Scientific Computing Laboratory at Columbia University.

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PHYSICS

Cæsium-137 Fall-out over Norway since September 1956

IN an earlier communication[1], we reported that concentrations of radioactivity in the lower stratosphere over south-east Norway had apparently increased for a month or two after high-yield test explosions, and then decreased with an effective half-life of about one month, corresponding to a residence half-life of about three months. Concentrations of radioactivity in the lower troposphere appeared to have increased for about six months, before decreasing at about the same rate as in the lower stratosphere. We suggested that deposition of fall-out materials from many explosions may have been fairly continuous, lasting months instead of years, and that during periods when explosions had

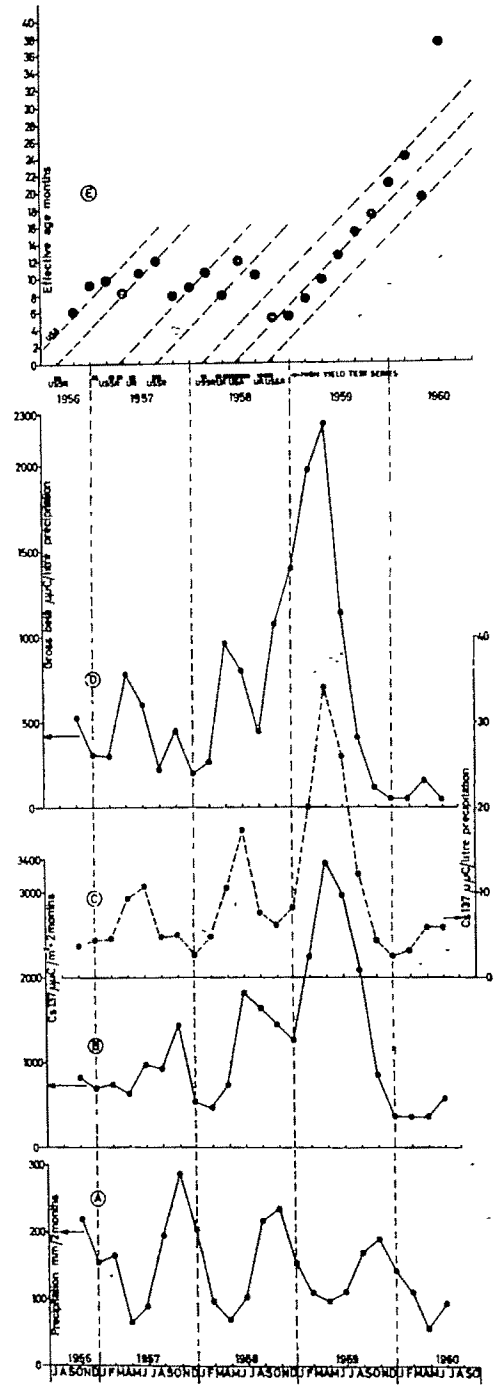

Fig. 1. Fall-out over Norway since September 1956. Curve A, precipitation, mm./2 months; curve B, cæsium-137/m.² 2 months; curve C, cæsium-137/l. precipitation, averaged over periods of 2 months; curve D, gross β/l. precipitation, averaged over periods of 2 months; curve E, effective age of fall-out materials, months. The points are plotted at the end of the 2-month periods. Each point represents an average value of measurements from ten stations

taken place rather frequently, there may have been considerable mixing of fall-out materials from different explosions.

These conclusions were based mainly upon measurements of gross β-activities. We have also investigated the problem by measuring concentrations of cæsium-137 in the same precipitation samples, using a γ-spectrograph. The results are shown in Fig. 1 as mean values for each period of two months between September 1956 and June 1960. Curve *A* shows the mean values of precipitation; curve *B* the mean values of cæsium-137 activity deposited per m.^{2}; curve *C* the mean values of cæsium-137 activity per litre of precipitation; curve *D* the mean values of gross β-activity per litre of precipitation.

Curves *C* and *D* are fairly alike with the main differences appearing shortly after large injections of fall-out materials.

Generally speaking, deposition of cæsium-137 activity over Norway appears to have followed the same sort of pattern as the overall deposition of β-emitting isotopes. The rather rapid decrease of deposition during the last eight months or so of 1959, following a pattern visible on previous occasions for shorter periods, has not continued into 1960. However, it is questionable whether the change is of great significance in the fall-out of materials injected into the lower stratosphere during the latter part of 1958.

From information communicated by Dr. E. A. Martell, materials from high-yield, high-altitude injections during 1958 may not have reached the lower stratosphere in significant concentrations before about the beginning of 1960. Another factor which must be borne in mind in considering the 1960 values shown in curves *C* and *D* is that although the values are shown as activities per litre of precipitation, deposition without precipitation is also included. In relatively dry periods the activity of surface air tends to increase, with a resulting increase in the rate of dry deposition and in activity per litre of precipitation. Certain variations in activity per litre of precipitation (curve *C*) may therefore be partly due to the seasonal variations in the amount of precipitation (curve *A*).

By comparing cæsium-137 activities with gross β-activities, it is possible to obtain some idea of the effective ages of deposited materials. The accuracy is limited because of the difficulties of calibrating β-counting equipment when measuring bomb debris of different ages and origins, and also because of uncertainties about the yields of cæsium-137 relative to other radionuclides, and uncertainties about possible fractionation effects. Nevertheless, as shown in curve *E*, there is reasonably good evidence from cæsium-137/gross β-activity ratios for the general conclusion that fall-out materials from many high-yield test series have reached the lower troposphere within a few months and been deposited rather rapidly.

The preponderance of materials from particular insertions during different periods is well illustrated. From about the end of 1959, however, there appears to have been considerable mixing.

In conclusion we would like to suggest again that a large part of the fall-out from many test explosions has been rather continuous over months instead of years.

There has been no outstanding seasonal variation in the rate of fall-out which cannot be related to the 'seasonal variation' in test explosions and seasonal variation in the amount of precipitation.

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New Delayed-Neutron Precursors

WITH the exception of a few cases (lithium-9, nitrogen-17 and thallium-210) all delayed neutron precursors so far identified[1] have been found among nuclides with two or more neutrons in excess of the major closed shells (50 and 82). The theory of delayed neutron emission probabilities given by Pappas[2] and the subsequent general systematics of delayed neutron precursors developed by Pappas and Rudstam[3] predict, however, that delayed neutron emission should be much more common among neutron-rich nuclides than had been anticipated earlier. Delayed neutron precursors are now expected to appear from the lightest to the heaviest nuclides on the neutron-rich side of the β-stability line. The distance from it in *Z* should be from about 3 to about 7 charge units, depending on the neutron number[3]. A search was therefore made experimentally for some of these precursors.

Because of the complex mixture of delayed neutron activities already found in fission[1], an approach via fission would not be easy. Chemical separations should also be avoided because of the short half-lives expected. A feasible way of studying the prospective delayed neutron precursors would, however, be by the way of spallation reactions. These give products in highest yields near the target nuclide, whereas yields of distant products depend mainly on the irradiation energy. Therefore, by choosing suitable target elements and bombarding energies, it should be possible to detect and probably also to localize eventual delayed neutron precursors.

The short half-lives and the low neutron yield (the latter caused by the rather small branching ratio to the neutron-emitting state of the delayed neutron emitter) necessitate that the measurements start immediately after irradiation. This requirement was fulfilled by placing the neutron detector at a small radial distance from the irradiated target in the vacuum chamber of the synchro-cyclotron.

The neutrons emitted were thermalized by a layer of paraffin between the target and the neutron-sensitive scintillator properly shielded from stray radiation. The light pulses were fed through a light-guide to a photo-multiplier outside the fringing field of the magnet. The pulses were amplified and fed to a fast scaler provided with a printer. The counting started immediately after the end of irradiation.

A possible source of error in such measurements could be introduced by counting γ-rays from spallation products. The sensitivity of the detector for γ-rays is many orders of magnitude lower than for neutrons, but the intensity of the γ-rays involved is much larger than the intensity due to the neutrons.

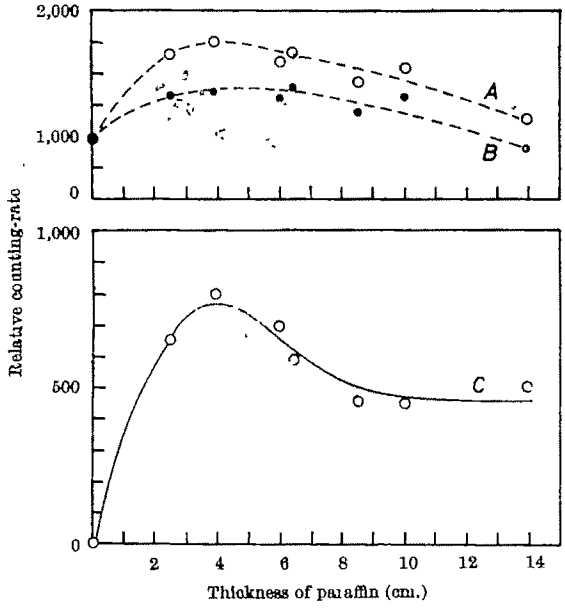

Fig. 1. Influence of paraffin and cadmium shielding on the detecting efficiency of the neutron scintillator. Curves *A* and *B* were taken without, and with, cadmium, respectively. Curve *C* gives the difference between *A* and *B*

Therefore, to make certain that only neutrons were counted, experiments were carried out using various amounts of paraffin under otherwise identical irradiation conditions. A typical curve obtained for a copper target (15 mm. 'radial thickness') is shown in Fig. 1 (curve *A*) In this figure the corresponding curve obtained with 2 mm. of cadmium between the paraffin and the scintillator (curve *B*) is also shown.

Even if Fig. 1 shows that the majority of the counts obtained with cadmium shielding are due to neutrons (the detector is also sensitive to fast neutrons, although the sensitivity for thermal neutrons is about 20 times larger), it was found appropriate to take decay curves with and without cadmium under otherwise identical experimental conditions, and then analyse the difference curve. Thus any possible contribution from γ-rays is completely eliminated. The optimum condition regarding the amount of paraffin was found by taking differences between curves *A* and *B* in Fig. 1. These are given in curve *C* as a function of the thickness of paraffin.

In Fig. 2 analyses of decay curves obtained from irradiations of radially thick copper and neodymium targets are given. Apparently the copper difference curve 3 can be resolved into several components A peeling-off analysis discloses two components with half-lives about 18 sec. and 8 sec., and in addition a third short-lived one.

The curve obtained by irradiation of uranium was too complex to be analysed, but the total neutron activity was about five times larger than for copper under the conditions used.

Preliminary runs with neodymium (Fig. 2) disclosed activities with half-lives of about 20 sec. and 6 sec. These should presumably be due to the known[1] delayed-neutron precursors, 24·3-sec. iodine-137 and 6·3-sec. iodine-138.

It might be argued that the neutrons observed in these experiments are due to (γ,*n*) reactions induced in the targets or surrounding material by γ-rays from spallation products. The thresholds, however, for possible photo reactions are greater than 10 MeV.[1]. Such energies are unlikely to be present in radioactive decay of spallation products, except for those having extremely low yield (far from stability). Moreover, the (γ,*n*) cross-sections involved are very small at these energies. Using very conservative estimates, about 1 of every 10^4 neutrons observed might be due to a photo neutron. Thus the activities found in copper are due to hitherto unknown delayed-neutron precursors.

Since the target itself moderates and to some extent absorbs the emitted neutrons, depending on its thickness in the radial direction toward the detector, it was found that the 18-sec. activity was suppressed, and only the 8-sec. activity appeared, when using a thin copper target. The opposite occurred when placing a cadmium sheet between a thick copper target and the paraffin. This filtering is caused by difference in kinetic energy of the delayed neutrons involved.

The new delayed-neutron precursors have not yet been identified by mass and charge, and the analysis of the decay curves might be more complex than assumed. Nevertheless, these findings give strong support to the validity of the delayed-neutron precursor systematics in the earlier papers[2,3] and

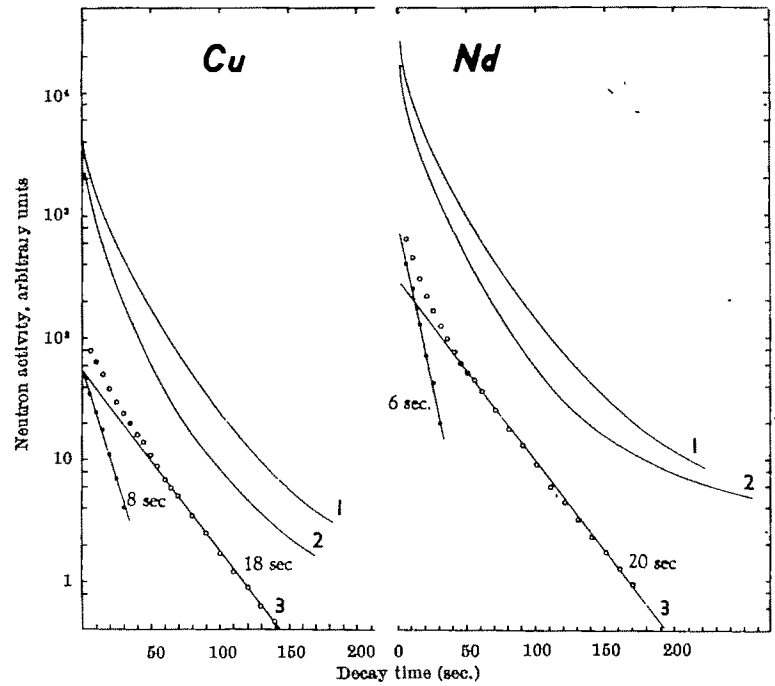

Fig 2. Delayed-neutron decay curves. Curves 1 and 2 were obtained without, and with, cadmium, respectively. Curve 3 is the difference curve. Curves are shown for a thick copper target + 3·9 cm. paraffin and for a thick neodymium target + 3·9 cm paraffin. (The difference curves are lower by a factor of 10 on the scale of the graph)

to the hypothesis of the existence of many delayed-neutron precursors[2]. These experiments are therefore being extended to other elements of the Periodic System.

A detailed description of the apparatus used will be published elsewhere, as well as additional results, including attempts to identify the delayed-neutron precursors by different approaches.

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Natural Occurrence of Samarium-146

SAMARIUM-146 was discovered in 1953 by Seaborg and Dunlavey, who produced the nuclide by an intense bombardment of neodymium with α-particles[1]. They reported that it emitted α-particles of 2·55-MeV. energy and decayed with an α-half-life of approximately 5×10^7 years.

Macfarlane and Kohman made a search for samarium-146 α-activity in natural samarium employing a large internal-sample cylindrical ionization chamber[2,3]. They obtained a negative result and set an upper limit of 0·01 disintegration/gm./sec. for the specific activity in natural samarium.

A report has recently been made by Vorob'ev, Komar, Korolev and Solgakin of an indication for the existence of samarium-146 α-particles in the natural samarium α-spectrum although the level observed was not considered by them to be statistically significant[4]. They established an upper limit of 0·03 disintegration/gm./sec. for the specific activity.

The purpose of this work was to increase the sensitivity over previous measurements for the detection of a natural samarium-146 α-activity by counting a sample 'enriched in samarium-146'. This sample was obtained from the mass 146 position of a calutron collection plate which had been used in the separation of macro amounts of samarium isotopes from natural samarium.

The samarium oxide was deposited on a stainless-steel sheet and placed in an internal-sample cylindrical ionization chamber similar in design to that used previously by me[3]. It measured 50 cm. in length and 14 cm. in inside diameter, providing an active sample area of 2,000 cm.^{2}. The collecting electrode was a 0·13-mm. stainless steel wire strung axially along the full length of the counter and operated near ground potential. A negative potential of 1,400 V. was applied to the sample backing. The counter was operated as a flow-counter at 1 atm. pressure with a gas mixture of 93 per cent argon and 7 per cent methane.

Electronic amplification was provided by a 'ball and chain' preamplifier and a 'Miemar' main amplifier

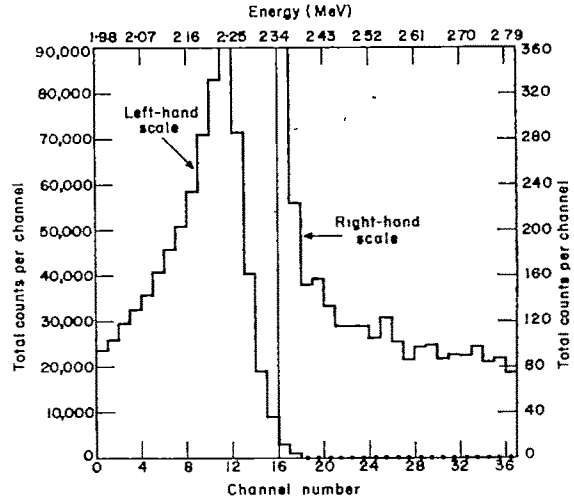

Fig. 1. α-Particle spectrum of 'enriched samarium-146' sample

(designed and fabricated at the Lawrence Radiation Laboratory, Berkeley, California). The spectrum was recorded on a 100-channel pulse-height analyser (manufactured by Pacific Electro-Nuclear Corporation, Culver City, California).

An 89-mgm. sample (approximately 45 μgm./cm.^{2}) of the samarium oxide 'enriched in samarium-146' was counted for a period of 64 hr. The α-particle spectrum obtained is shown in Fig. 1. Only the samarium-147 peak was prominent; there was no significant indication of the presence of second peak in the vicinity of 2·5 MeV.

It was estimated that a peak in the region between 2·4 and 2·7 MeV. would have been recognized had one channel been 20 counts higher than the neighbouring channels for the 64-hr. period. From the spectra of natural samarium samples of similar thickness, it was found that the channel in which the main portion of the α-peak was contained accounted for 3 per cent of the total disintegration rate. From these data, a limit of 0·03 disintegration/gm./sec. was established for the specific activity of samarium-146 in this sample.

On comparison of the samarium-147 specific activity in the 'enriched samarium-146' sample with that for naturally occurring samarium, it appeared that an enrichment of 1·7 was realized for samarium-147. Based on the mass analyses of other samples which had been mass-separated under the same conditions, an enrichment of 1·7 in an adjacent mass (samarium-147) would correspond to at least a factor-of-10 enrichment in the isotope of interest (samarium-146), provided it had been present initially in low isotopic abundance.

In terms of the specific activity for an equivalent natural samarium sample, then, the limit would be smaller by a factor of 10 than for the 'enriched samarium-146' sample, or 0·003 disintegration/gm./sec.

Using the value of the half-life of 5×10^7 years obtained by Seaborg and Dunlavey[1], an upper limit

Table 1. SUMMARY OF RESULTS ON THE SPECIFIC ACTIVITY OF SAMARIUM-146 IN NATURE

Investigator	Specific activity (disintegration/gm./sec.)
Vorob'ev *et al.* (ref. 4)	< 0·03
Macfarlane and Kohman (refs. 2 and 3)	< 0·01
This work	< 0·003

for the isotopic abundance of samarium-146 can be calculated from the results obtained here. An upper limit of 2×10^{-7} per cent for the isotopic abundance of samarium-146 in natural samarium was calculated. The best mass-spectrometric limit, obtained by Collins, Rourke and White, is 8×10^{-5} per cent (ref. 5).

Recently, the α-particle energy of samarium-146 (produced by bombardment of neodymium with α-particles) was rechecked and found to agree exactly with the value Seaborg and Dunlavey originally reported (2·55 MeV.) (M. C. Michel and R. D. Macfarlane, Lawrence Radiation Laboratory, unpublished results). From theoretical considerations based on this energy, an α-half-life in the neighbourhood of 6×10^{7} years is favoured. If this is the correct half-life, all primordial samarium-146 should now be neodymium-142.

The co-operation of the Oak Ridge National Laboratory in specially preparing the samarium sample is gratefully acknowledged. This research was supported by the U.S. Atomic Energy Commission.

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Radiation-induced Defects in Lead Silicate Glass

IN attempts to explain the process of coloration of glass by γ-radiation, it was suggested in a previous communication[1] that electrons are trapped in defects to form colour centres. Not only do these defects already exist in glass but they can also be created by exposure to radiation. If defects could not be so created, it would be expected that the concentration of colour centres, as measured by the optical density, would increase exponentially to a saturation value at a certain dose. In practice, it is found that the optical density increases exponentially with dose up to about $10^{5.5}$ rads, but thereafter the increase is linear. This effect is shown in Fig. 1, which is divided into two sections having different scales for dose, the first section illustrating the exponential portion and the second the linear portion of the curve.

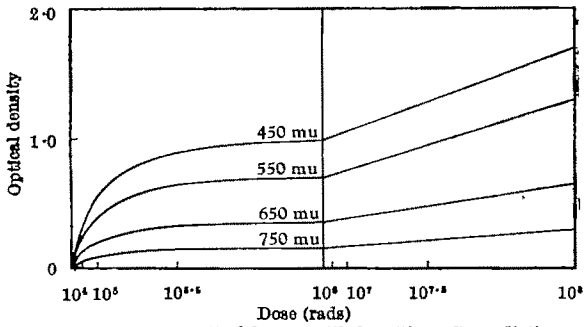

Fig. 1. Variation in optical density with dose (time after radiation, 1,000 min.)

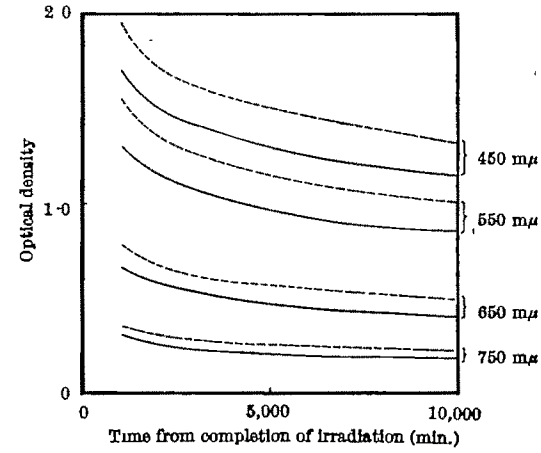

Fig. 2. Increase in optical density on second irradiation. ——, first irradiation; – – –, second irradiation after bleaching

The linear portion is attributed to the creation of defects by the radiation. Thus the extrapolation of the straight line to zero dose gives an indication of the defects already present in the glass. The difference between the extrapolated value at zero dose and the measured optical density is proportional to the concentration of defects produced by the radiation.

Exposure of irradiated glass to light at room temperature produces bleaching of the colour centres by excitation of the trapped electrons to such energy-levels as to enable them to escape from the defects and recombine with the positive holes. It might be expected that such treatment should release the trapped electrons but have little effect on the total number of defects. Hence such a bleached sample of glass should contain a greater concentration of defects or trapping centres than an unirradiated sample and, on further irradiation, should contain more colour centres than an originally unirradiated sample which is subjected to a first irradiation.

To test this theory a sample of the lead silicate glass used in the experiments described previously was given a dose of 10^8 rads of γ-radiation and its optical density was measured over the wave-length range 360–1,000 mμ at intervals of time during the week following the irradiation. The induced coloration was then bleached by exposure to light from a mercury lamp until the optical density of the glass was not significantly different from that measured before the irradiation. The sample was then given a further dose of 10^8 rads, and the optical absorption was again measured.

Fig. 2 shows the variation in optical density with time for four wave-lengths after the first and second irradiations. It can be seen that the optical density of the sample after bleaching and re-irradiation is at all times greater than that obtained after the first irradiation. This result is in accord with the proposed theory.

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ENGINEERING

Beneficial Effects of Reagents in Solution on Wet Crushing of Rock

EARLIER workers in this Department[1,2] have reported that substantial increases in the crushing efficiency of a drop-weight mill (stamp mill) may be achieved by pretreatment of the ore in aqueous solutions of certain reagents.

This work appears to have aroused interest, but, in the cases known to us, workers elsewhere have not been able to obtain significantly beneficial results[3,4]. In these latter investigations a ball mill was used, and it is of interest that the first exploratory work at Leeds was carried out with a ball mill; the results were not encouraging[2]. Possible reasons for this, and for the final choice of a drop-weight mill, have been discussed by Frangiskos[2]; arguments are based on the work of Rehbinder[5].

In view of these later findings it has been considered necessary to repeat some of the experiments reported by Frangiskos and Smith[1] with the drop-weight mill. The results are given in Table 1. Except for the actual rock samples (limestone) used, the experimental conditions are the same as those employed by Frangiskos and Smith. The amount of crushing achieved is measured in terms of the surface area of the product, determined by a gas-permeability method. The percentage increase shown in Table 1 is the extra amount of crushing achieved when the ore is pretreated in a solution instead of in distilled water. The beneficial effect with the particular samples of limestone used is even more pronounced than that observed by Frangiskos and Smith; their best results represented approximately a 50 per cent increase.

Table 1. EFFECT OF REAGENTS IN SOLUTION ON THE SURFACE AREA OF CRUSHED ORE

Reagent (mgm./L.)	Sodium hydroxide		Sodium carbonate	
	Surface area of product (cm.²/gm.)	Percentage increase (pure water basis)	Surface area of product (cm.²/gm.)	Percentage increase (pure water basis)
0	247*	—	156	—
100	305	23·5	185	18 6
150	367	48·6	—	—
200	346	40·1	273	75 0
300	278	12·5	296	89·8
400	261	5·7	320	105 0
500	279	13·0	293	89 0
600	301	21 9	244	56 4
700	354	43 3	217	38 2
800	282	14 2	187	19 9

Charge to mill: 15 gm. limestone (−2 05 mm. + 1 40 mm.). Conditioning time in solution, 10 min. Weight of crushing head, 2,026 4 gm. Height of fall, 13 6 mm. Blows per min., 120 Total number of blows, 600.

* Initial surface area approximately 1 5 cm.²/gm.

It is suggested that the reason for the success of the drop-weight method of crushing in contrast to the ball mill is basically as proposed by Frangiskos and Rehbinder. The essential feature of the hypothesis is that embryo microcracks produced by stress on the solid are made permanent points of weakness by adsorption in them of ions or molecules from solution; it is assumed that the relative adsorption of water molecules is so small as to permit resealing of the microcracks. A drop-weight mill is likely to be more effective than a ball mill in producing microcracks.

Furthermore, the choice of method for assessing the amount of crushing (fineness of product) is important. Most of the new surface area produced is contained in the extremely fine sizes[6], and the conventional sieve analysis gives no measure of this. Results which have been assessed in terms of a sieve analysis might therefore indicate no beneficial effect of reagents in solution. The work in this Department was terminated in 1956 after three years work due to lack of financial support. Finance has now been made available for the project for one more year, but it seems to us a pity that further development work on the process may have to be carried out elsewhere.

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Hydrogen Diffusion in Water-accelerated Rolling Surface Fatigue

THE pitting failure of rolling bearings is now generally regarded as a surface fatigue phenomenon, and recent work[1] has shown that the presence of water in mineral oil lubricants can accelerate the failure of ball-bearings manufactured from conventional *E.N.*31 steel. A possible mechanism for this phenomenon has been suggested by Grunberg and Scott[2]. The hypothesis is that vacancy-induced diffusion of hydrogen into the highly stressed surface material produces 'hydrogen embrittlement'. To test this theory, four-ball rolling tests[1,2] were carried out with a lubricating oil containing 6 per cent tritiated water of high activity (5 c./ml.). The rolling four-ball test produces a track on the driving ball in which pits are normally formed. The three driven balls are stressed to a lesser extent and usually do not show evidence of surface fatigue. Balls from tests using tritiated water were washed with acetone and partially immersed in a liquid scintillator (0·3 per cent 2,5-diphenyloxazole + 0·01 per cent 1,4[2-(5-phenyloxazolyl)]-benzene in toluene) and the activity counted using a (refrigerated) ECKO *N*612 unit. When the part of driving balls carrying the fatigued track was immersed in the liquid scintillator, counting-rates of between 1,000 and 2,000 counts/sec. were recorded. The unfatigued part of driving balls gave only counts of about 40 counts/sec. against the background count of 30 counts/sec. The activity in the fatigued tracks decreased with time and tended towards the background-level after about five days.

The preliminary experiments described provide support for the hypothesis that, in the presence of water, hydrogen penetrates into the material subject to surface fatigue. The decrease in activity with time can be ascribed to escape of tritium from the material.

The phenomenon is now being investigated in greater detail.

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METALLURGY

Fatty Acids and Adhesion of Electrodeposited Metals

THE deleterious effect of grease on the substrate on the adhesion of electrodeposited metals is well known, but quantitative data are sparse. A systematic study of the influence of monolayers of adsorbed surface-active agents on the adhesion of electrodeposits is in progress in this laboratory, and this communication reports the initial results obtained from the fatty acid series.

The adhesion was measured in the manner described by Williams and Hammond[1], with the test-pieces made of copper. The ends of the specimens to be plated were polished to 1μ diamond powder, electropolished in 50 per cent phosphoric acid and treated to have a monolayer of the fatty acid under test[2]. The acids used were the even-numbered acids of the series $CH_3(CH_2)_nCOOH$, where $n = 4$–16. The specimens with the monolayer were plated with nickel from a conventional Watts type solution at a *p*H of 4, temperature of 40° C., and a current density of 20 amp./sq. ft. until a deposit of at least 0·1 in. had been produced. After plating, the specimens were tested in a Denison tensile testing machine. To provide a reference point, a series of specimens was tested using the exact procedure outlined except that no fatty acid was used.

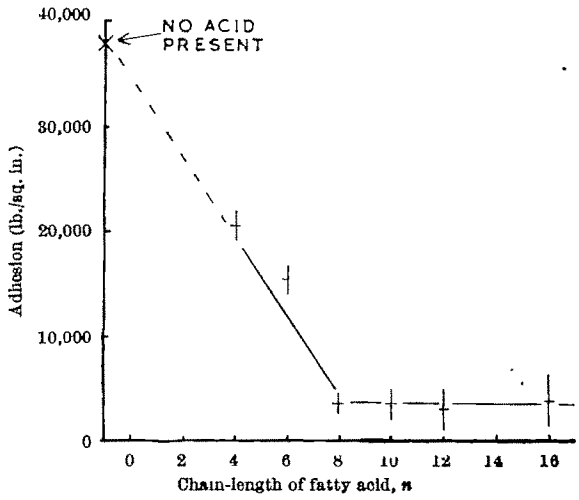

Fig. 1. Adhesion of electrodeposited nickel as a function of fatty acid chain-length

The results are shown in Fig. 1. They were reproducible for each acid, and when the experiment was repeated with caprylic acid ($n = 6$) the adhesion values were within a few hundred pounds per sq. in. of each other. The adhesion appears to be independent of the chain-length of the fatty acid when n is greater than 8 or 10; as n decreases below this value the adhesion progressively increases. This increase can be explained either by the increased desorption of the shorter-chain acids resulting in the nickel being discharged directly on the copper lattice, or by a decrease in the long-range forces between copper and nickel as the distance increases. It is impossible to distinguish between these alternatives at this stage, but it may be pertinent that there is no evidence of epitaxis.

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Fatigue Straining of Copper Whisker

BRENNER[1] has shown that copper whiskers can be strained elastically to as much as 2·8 per cent in tension. I have found that similar whiskers remain elastic in cantilever bending at static strains up to 4 per cent corresponding to a stress of 470 kgm./mm.$^{-2}$ in a whisker of $< 110 >$ orientation.

When plastic deformation occurs it is by 'kinking', as has been described by previous workers[2] with other materials. The 'kink' formed is a bend of radius of curvature of the order of the thickness of the whisker; it is produced suddenly, with release of the elastic strain in the rest of the whisker. It can be shown that this behaviour is to be expected from a cantilever bent by a 'hard' device, if it is of a material that has clearly defined upper and lower yield points and yield extension. These phenomena are very pronounced in copper whiskers[2].

I have performed experiments to see whether the behaviour of copper whiskers under repeated straining differs from that under static conditions. The experiments were performed in cantilever bending with the whisker encased in diphenyl carbazide glass[4] and deflected by a 'hard' probe. The whiskers were grown by hydrogen reduction of cuprous iodide[5].

Since the static strain at which kinking occurs varies very much from one whisker to the next, it was not possible to test whiskers in cyclic loading at a known fraction of the static kinking strain. Instead, whiskers that were less than about 3μ thick, straight and optically smooth, were selected and were then tested as follows.

A whisker was bent to a strain, S ($\simeq$ 1 per cent), which it was thought very likely to be able to sustain elastically. The bending-probe was then removed, and the whisker examined for permanent bending. If there were none, the probe was then made to vibrate so that the maximum strain in the whisker fluctuated between 0 and S at 900 c./s., the test being observed stroboscopically. After 10^6 cycles of vibration the probe was stopped and removed. If no permanent deformation had taken place, a static strain of ($S + \Delta S$) ($\Delta S \simeq 0{\cdot}3$ per cent) was applied, and the whole procedure repeated, the vibrations being this

time with maximum strain fluctuating between 0 and $(S + \Delta S)$. This procedure was repeated with successive increments of strain. Thus the whisker was subjected, at each value of strain amplitude, to one slow (quasistatic) cycle of strain, followed, if nothing had happened, by 10^6 fast cycles.

I found that whiskers were generally capable of surviving such tests apparently unaffected to strains of the order of 3 per cent, with 10^6 strain cycles at each value of strain amplitude. Then, during the next period of oscillatory straining, at a slightly higher strain, the whisker would suddenly kink, after it had already been subjected to a large number of cycles at this high strain. The kinking would be instantaneous, so far as could be judged by eye; that is, it must have happened in less than 100 cycles. The vibrator would reach maximum amplitude in at most a few hundred cycles, and kinking was observed less than a few thousand cycles after the increment of strain was made. Several times the kinking occurred after more than 10^5 cycles.

The strains at which whiskers kinked dynamically were not very reproducible, just as the static kinking strains show a large scatter[1]. It sometimes proved possible to re-embed a whisker that had kinked dynamically in such a way that the undeformed part of the whisker could be re-tested. The strain at which dynamic kinking occurred was then of the same order as in the first experiment. For example, a whisker that had kinked after being strained from 0 to 1·9 per cent for 10^5 cycles was re-embedded; it afterwards withstood 10^5 cycles at 0–1·1 per cent and 10^5 cycles at 0–1·7 per cent strain and it kinked after 10^6 cycles at 0–2·3 per cent strain.

If the vibrator was stopped immediately after the whisker kinked, then the whisker looked just as if it had kinked statically. The kink was a plastic hinge, but its appreciable strength often made it possible to continue elastic vibrations with much-reduced amplitude (perhaps 0·3 per cent elastic strain). When this was done, the whisker usually fractured in the kink after a few thousand cycles. As a corollary, if the vibrator were not stopped when the whisker kinked, fracture occurred a few thousand cycles after kinking. Fracture was never observed in oscillatory loading of this type unless kinking had occurred first.

If the whisker was fixed both at the root and to the vibrator (instead of merely being pushed by the latter) and vibrated so that the strain oscillated symmetrically about zero, then fracture did occur. But in this case kinking was not easily detectable, and, if it had taken place, the plastic kink would have been subjected to large cyclic strains, so that it would have failed very quickly, perhaps too quickly to see the kinking. Therefore this test does not provide adequate evidence of the existence of fatigue fracture in elastic whiskers.

Whiskers were also statically strained for periods long compared with the times of the oscillatory experiments. Kinking was never observed unless it happened immediately the strain was applied. This shows that the delayed kinking is due to the oscillatory loading and not to the passage of time.

Both statically and dynamically kinking occurs near the root of the whisker, where it is embedded in diphenyl carbazide glass and where the bending moment, and hence the elastic strain before kinking, are greatest. But the kink very often starts, not at the point of entry of the whisker into the glass, but at distances up to ten times the thickness of the whisker away from that point, towards the free end. Therefore, the failure of the whisker is not determined by stress concentration or corrosion at the point of entry into the glass: the concentration is probably small, owing to the low elastic modulus of the glass compared with that of the copper, and to the wetting-fillet, the radius of which is of order $\frac{1}{4}$–$\frac{1}{2}$ the whisker thickness. The failure is more probably precipitated by stress concentration at defects in the whisker[6].

There is much evidence[6] that in copper whiskers subject to large, static, elastic strain, no slip occurs below the yield point. We have shown that if they are subjected to large, repeated, elastic strain, fatigue fracture is not observed, even at strains of the order of 3 per cent. The sudden onset of plastic flow does occur; the reason for this is not understood, and is being investigated. As soon as the whisker has flowed plastically, it can fracture in fatigue, in the yielded region, at quite small, mainly elastic strains. This serves to confirm the belief, hitherto assumed without direct evidence, that slip is an essential process in fatigue failure.

I wish to thank Mr. H. B. Holland, who has carried out these very delicate experiments. This communication is published by permission of the Ministry of Power.

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RADIOCHEMISTRY

Effect of γ-Radiation on Nisin

THE antibiotic nisin is known to reduce the heat-resistance of spore-forming organisms, and consideration has been given to its use as an additive to lower the heat-process requirements of canned foods[1]. The radiation resistance of spore-formers might also be influenced by nisin, and the dose required for the sterilization of food lowered to a level where radiation-induced flavour and odour changes are not detectable.

Experiments were first conducted to determine the effect of radiation on the antibiotic activity of nisin when it was suspended in a variety of media and at different *p*H values. Samples were made up in McCartney bottles in triplicate and irradiated with γ-rays at a dose-rate of 1×10^5 rads/hr. using a 10,000 c. cobalt-60 source. The temperature of the samples was maintained at 4° C. during irradiation and until assay, 30 hr. after their preparation. Nisin was assayed using both the resazurin[2] and plate methods[3], the latter being modified to handle liquid samples.

The result of irradiation with a dose of 2·7 megarads is shown in Table 1. At this dose-level nisin activity is completely destroyed irrespective of the nature of the suspending medium or of the *p*H in the short

Table 1

Media	Nisin concentration (U./ml.) mean of triplicates			
	Theoretical	Before irradiation	After 30 hr. storage (controls)	Irradiated 2 7 megarads
Sterile skim milk	200	220	190	< 4
Sterile skim milk	2,000	1,900	1,750	< 4
Unprocessed soup pH 6·08	200	—	238	< 4
Processed soup pH 5·85	200	—	180	< 4
pH 3 5 phthalate buffer	200	175	170	< 4
pH 5 0 phthalate buffer	200	235	200	< 4
pH 6 0 phthalate buffer	200	200	205	< 4
Pure nisin in sterile distilled water	2,000	2,250	2,250	< 4

range studied. No activity could be detected even when the initial concentration of nisin was increased from 200 to 2,000 U./ml. as shown in skim milk and distilled water. No significant loss of unirradiated nisin occurred during the 30-hr. period of the experiments. The soup medium used was a meat and vegetable broth chosen to demonstrate any possible protective effect which might be exerted by food constituents.

Sterile skim milk with an initial concentration of 200 U./ml. of nisin was chosen as suspending medium to study a range of radiation dose-levels. The experiment was run in triplicate and results are shown in Table 2. At the lower levels about 17 per cent of activity is lost, there is a marked drop at 0·5 megarad when 80 per cent is lost and a complete loss occurs at 1·5 megarads and above.

Table 2

Dose (megarad)	Nisin concentration (U./ml.) mean of triplicates	
	Resazurin method	Plate method
Nil (control)	183	182
0·13	153	152
0·25	150	153
0·5	37	24
0·75	< 20	22
1·0	< 60	14
1 5	< 60	< 5
2 0	< 60	< 5
2·5	< 20	< 5

The evidence presented indicates that nisin added to foodstuffs prior to radiation processing will be rendered ineffective against bacterial spores which survive the radiation treatment, especially in the sterilization dose-range of 1–3 megarads. There is a possibility, however, that nisin might be protected from radiation damage to some extent in the presence of spores, particularly if it acts by absorption on the spore coat.

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CHEMISTRY

Electron Paramagnetic Resonance Studies of Stable Free Radicals in Lignins and Humic Acids

ELECTRON paramagnetic resonance studies[1] of wood ; lignins ; tannins, and humic acids, such as are found in soils and coals, show an electron paramagnetic resonance line of 6 ± 2 gauss width at $g = 2{\cdot}003 \pm 0{\cdot}002$, indicating the presence of a free radical. I find that this free radical is stable over a period of years in air and is not present in protolignin in plant materials nor is it necessarily the result of simple ageing or rotting of wood. However, it is formed when protolignin in plants is polymerized into lignin by either acid or fungal attack. I also find that the 6 ± 2 gauss electron paramagnetic resonance line is restricted to the fraction of humic material which is extractable with aqueous bases.

Freudenberg[2] indicates that lignin polymerization results from dehydrogenation or oxidative removal of a phenolic hydrogen on coniferyl or sinapinic alcohol or by hydrolysis of a phenolic glycoside linkage. According to Freudenberg the polymerization is a free-radical process involving a semi-quinone radical intermediate. My electron paramagnetic resonance results indicate that free radicals are indeed present and that some free radicals persist in the lignin polymer where they are protected from their macro-environment. They survive within the lignin micelles through the process of coal formation and persist apparently for geological time ($\sim 10^8$ years).

Air-dried fresh wood samples (fine shavings) of oak, pine, eucalyptus, redwood, and spruce showed a very low free radical concentration of $< 10^{14}$ spins per gram (s./gm.). The carbon disulphide-soluble, absolute ethanol-soluble, and dioxane-soluble Soxhlet fractions (extracted in this order) and the corresponding residual wood fractions showed no electron paramagnetic resonance ($< 10^{14}$ s./gm.). Dioxane (catalysed by hydrochloric acid) lignin extracts showed strong electron paramagnetic resonance $\sim 10^{18}$ s./gm. at $g = 2{\cdot}00$ even though the lignin precursors in the wood did not. A similar high free-radical content was observed with a 'Soxhlet' water extraction that turned acid by formation of organic acids from the wood. Electron paramagnetic resonance was not evident in the unfractionated cellulose and pentosan fractions of wood. Freshly cut redwood ranging from sapwood to rotted heartwood (40 years old) showed no difference in a very weak electron paramagnetic resonance signal. Scots pine buried for 600 years in damp soil, and spruce buried for more than 450 years[3] likewise showed no, or barely detectable, electron paramagnetic resonance. These same woods showed depletion of cellulose and pentosans, but no change of lignin concentration. On the other hand, fresh pine needles about to drop from a tree but already attacked by fungi, and plant debris which had collected in soil as peat showed strong electron paramagnetic resonance with both a line of 8 gauss and a broad line of 1,000–1,200 gauss both centred on $g = 2{\cdot}00$ (Fig. 1*a*). The material showing the sharper electron paramagnetic resonance line is extractable with an aqueous base (Fig. 1*b*) and behaves as the polyelectrolyte humic acid while the broad line (Fig. 1*c*) characterizes the non-extractable residue. Tannin extract (quebracho) showed the same 6-gauss

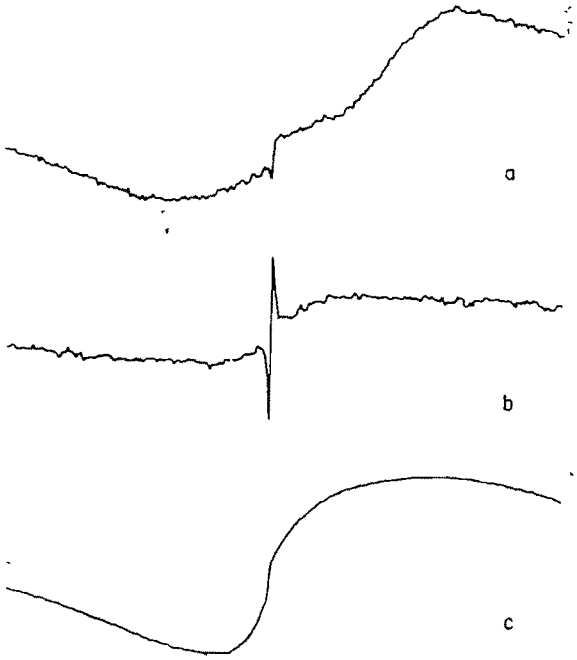

Fig. 1. Electron paramagnetic resonance of free radicals in post-Pleistocene peat from Point Barrow, Alaska (grass–sedge–moss flora). *a*, Fresh peat; *b*, *N* sodium hydroxide extract, precipitated with hydrochloric acid, washed and air dried, *c*, peat residue after extraction

electron paramagnetic resonance line shown by humic acids.

These results suggest that lignin does not normally occur in living plants. Rather it is the polymerization product of those compounds capable of forming or reacting with semiquinone free-radicals formed during dehydrogenative or hydrolytic degradation of plant tissue. These polymers with their trapped free radicals in turn survive the geochemical processes of humification and coalification without loss of their free radicals. This suggests that post-depositional chemical modifications do not destroy the aromatic semiquinoid properties of these compounds.

It should be remembered that not only aromatic —OH groups but also aromatic —NH_2[4] and aromatic —SH[5] groups can be dehydrogenated to yield semiquinone-type radicals. For this reason a wide range of compounds can be expected to contribute to the formation of natural semiquinone polymers such as lignins, humic acids and tannins.

The comments and assistance of my colleagues and the research assistants at this Laboratory have been both helpful and stimulating. Especial appreciation is due to Dr. R. R. Unterberger for providing the facilities of his electron paramagnetic resonance spectrometer.

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Surface Renewal and Molecular Diffusion in Interphase Mass Transfer

IN 1953 Lewis and Pratt[1] described violent spontaneous movements of the liquid–liquid interface which they observed during measurements of interfacial tension in the presence of mass transfer by the drop-weight method. These phenomena have since been investigated more fully[2–5]. It is now generally accepted that they are due to the formation of local gradients of interfacial tension caused by local variations of solute concentration at the interface as the result of mass transfer.

It can be argued that such spontaneous 'interfacial eruptions' would cause considerable portions of the interface to be replaced by fresh liquid from the interior and thus result in an increase of the rate of surface renewal. This could mean that for solutes of different interfacial properties the rates of mass transfer may be different even under conditions of equal flow parameters of the bulk phases and equal molecular diffusivities. No conclusions can thus be drawn from such experiments about the effects of molecular diffusivity on the transfer process. If, however, the transfer of two solutes takes place simultaneously, that is, under identical interfacial as well as hydrodynamic conditions, some conclusions could be arrived at. In order to test this possibility, experiments were conducted on the separate and simultaneous transfer of propionic acid and phenol between carbon tetrachloride and water, using vertical and horizontal laminar co-current liquid–liquid contactors with moving interface.

From the theory of mass transfer with surface renewal[6] it can be shown that for the transfer of a solute A between two immiscible solvents 1 and 2 the overall resistance to mass transfer, R_A, can be expressed as:

$$R_A = (1/\sqrt{D_1} + m/\sqrt{D_2})/s_A = 1/\sqrt{(d_A s_A)} \quad (1)$$

where s is the fractional rate of surface renewal; D_1, D_2 the solute diffusivities in the two phases; m the distribution coefficient; and d an effective overall diffusivity. Thus, for the separate transfer of the two solutes A and B:

$$R_A/R_B = \left(\frac{d_B s_B}{d_A s_A}\right)^{1/2} \quad (2)$$

and for simultaneous transfer, since $s_A = s_B$:

$$R_A/R_B = (d_B/d_A)^{1/2} \quad (3)$$

The results obtained for separate transfer of phenol and propionic acid at equal Reynolds numbers could not be correlated by equation (3), thus indicating that for the two cases the rates of surface renewal were different. Observations on simultaneous transfer, involving transfer of phenol in either direction but of propionic acid from carbon tetrachloride to water only, covering a thirty-fold range of R and a four-fold range of m_A/m_B, confirm that equation (3) holds within 95 per cent confidence limits of ± 5 per cent. In all the runs the existence of interfacial turbulence was confirmed by visual or schlieren observation. Thus it is highly probable that, under conditions of spontaneous interfacial turbulence, the rate of mass transfer depends to a large extent on the induced rate of interface renewal and is directly proportional to the square root of molecular diffusivity. Values

of fractional surface renewal up to 100 per sec. were found.

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Growth and Adhesion of Oxide in Furnace Deposits

DURING the oxidation of steel there are formed on the surface a variety of needle or plate-like growths of oxide which, for convenience, have been called 'oxicles'. The present investigation, supported by and in collaboration with the Thornton Research Centre of Shell Research, Ltd., began with the idea that these oxicles might entrap particles in burnt gases and thus act as the nucleation for the build-up of ash deposits. Accordingly a series of experiments have been undertaken in which specimens of 5 per cent chromium, 0·5 per cent molybdenum steel sheet have been oxidized in an oil-burning rig and examined by reflexion electron microscopy.

The results show, first, that whether or not oxicles are formed by pre-oxidation in air before the specimens are put into the oil-burning rig, the subsequent growth is similar. Secondly, there is a very large difference between the oxicle growth which occurs when the specimen is exposed to clean oil products and that obtained with oil containing a soluble metallic salt expected to give greater build-up of deposits. In the first case the growths are small, as shown in Fig. 1, whereas in the second case when oil containing a soluble metallic salt is used, large spiky oxicles occur of composition as yet unknown and these in turn do seem to collect very small particles of ash among their branches in accord with the original hypothesis (Fig. 2). Thus, although the oxicles trap some fine ash particles, this mechanism is not necessarily the dominant factor in the build-up of deposits.

The mode of attachment of the fluffy material at the tops of some of the oxicles suggested an electrical effect. The oil-burning apparatus was therefore modified so that the specimen holder was insulated from the rest of the rig and could be raised to $\pm 3{,}000$ V. with respect to it. Depending on the sign of the applied voltage, there was a marked difference in oxidation behaviour. In the tests with positive or zero potential, the scale was adherent, and the specimen developed a dull surface finish; but in the tests where the charge was negative, the scale was non-adherent and the metal surface retained a bright appearance. The pick-up of fine ash material did not seem to be appreciably affected. Fig. 3 shows the flaking away of the oxicle growth after oxidation with $-3{,}000$ V. applied to the specimen.

Work is proceeding to investigate these effects more fully.

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New Data for the Calcium Silicate, 'Phase Z'

THIS compound was first described by Roy[1,2], who considered it to be $9CaO.6SiO_2.H_2O$. Further work now shows that, while specimens prepared at relatively low temperatures and pressures may be hydrated, those prepared at sufficiently high temperatures and pressures are anhydrous, with the composition $Ca_3Si_2O_7$. They also establish the approximate unit cell parameters.

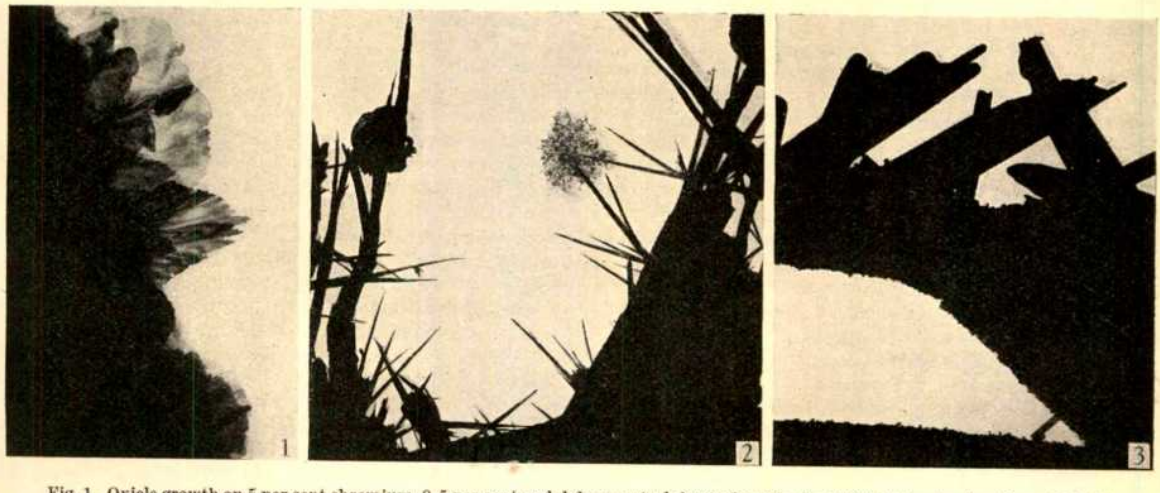

Fig. 1. Oxicle growth on 5 per cent chromium, 0·5 per cent molybdenum steel sheet after 15 min. at 600° C. in air plus 6 hr. at 600° C. in an oil-rig burning pure kerosene. (× 2,960)

Fig. 2. Oxicle growth on 5 per cent chromium, 0·5 per cent molybdenum steel sheet after 15 min. at 600° C. in air plus 6 hr. at 600° C. in an oil-rig burning kerosene containing 1 per cent of a soluble metallic salt. (× 1,480)

Fig. 3. Oxicle growth on 5 per cent chromium, 0·5 per cent molybdenum steel sheet after 30 min. at 600° C. in air followed by 6 hr. at 600° C. in an oil-rig burning kerosene containing 1 per cent of a soluble metallic salt. A potential of $-3{,}000$ V. was applied to the specimen. (× 960)

A specimen prepared hydrothermally at 715° C. and 1,100 bars showed negligible loss of weight over the range 100–1,400° C. There was no change in X-ray powder pattern up to 954° C., but by 1,090° C. transformation to rankinite had occurred. Specimens prepared under these or similar conditions are therefore anhydrous. 'Phase *Z*' can, however, also be obtained at temperatures at least as low as 200° C., and it seems unlikely that a product so obtained would be anhydrous. Preliminary results suggest that, as the temperature of preparation decreases, the phase becomes hydrated and that its calcium : silicon ratio rises. This can possibly be attributed to a hydrogarnet-like replacement of Si by 4H, which would cause the composition to trend towards $6CaO.3SiO_2.2H_2O$. So-called 'dicalcium silicate hydrate (C)'[3], and similar preparations, appear to be mixtures consisting principally of lime-rich 'phase *Z*' with smaller amounts of calcio-chondrodite ($Ca_5(SiO_4)_2(OH)_2$).

The equilibrium *P*—*T* curve for the transformation of 'phase *Z*' into rankinite has been reported previously[2]. Further work suggests that this curve represents a metastable equilibrium, as sufficiently long runs under conditions lying in the 'phase *Z*' field yield 'phase *Y*' ($6CaO.3SiO_2.H_2O$) and wollastonite or foshagite, with or without 'phase *Z*'. The latter is therefore probably always metastable, at least at the higher temperatures at which it is formed. This, together with the supposedly variable composition, may explain the difficulty of preparing large crystals: the compound disproportionates before these are able to grow. From a combination of selected area electron diffraction and X-ray powder photographs for several specimens, the unit cell was found to be orthorhombic or pseudo-orthorhombic, body-centred, with *a* 5·07, *b* 11·3, *c* 23 Å. approx.; the crystals are flaky with (001) cleavage. These parameters were confirmed by X-ray study of single crystals of afwillite ($3CaO.2SiO_2.3H_2O$) which had been first heated in air at 500° C. and afterwards treated hydrothermally at 200° C. under saturated steam pressure; these crystals contained both 'phase *Z*' and tobermorite, both in strongly preferred orientation. The calculated density, assuming cell contents $8(Ca_3Si_2O_7)$, is about 2·9 gm./c.c. This agrees with the value of 2·99 gm./c.c. calculated from the mean refractive index of 1·652[2] by the method of Howison and Taylor[4].

The unit cell of 'phase *Z*' is closely related to those of γ-Ca_2SiO_4 and calcio-chondrodite, the face with approximate parameters *a* 5·07, *b* 11·3 Å., γ 90° being common to all three compounds. We have found that 'phase *Z*' forms particularly readily on hydrothermal treatment of γ-Ca_2SiO_4; this can perhaps be attributed to a structural resemblance. It is often difficult to distinguish 'phase *Z*' from calcio-chondrodite by selected area electron diffraction, as in both cases the crystals normally lie on the face mentioned above. Distinction can be made by the fact that the lattice of 'phase *Z*' is body-centred, while that of calcio-chondrodite is primitive, and also by the differing values of *c*. These differences are only detectable, however, if the Laue zones corresponding to different *l*-indices are well resolved; for this purpose a tilting stage technique can be used[5]. If they are not well resolved, *c* cannot be determined, and 'phase *Z*' shows an apparently primitive lattice indistinguishable from that of calcio-chondrodite.

Further work is in progress, and a fuller account will be published later.

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BIOCHEMISTRY

Different Action of 2 : 4-Dinitrophenol on the Oxidation of Exogenous and Endogenous Substrates by Baker's Yeast

IT is recognized[1] that 2 : 4-dinitrophenol (DNP) stimulates the total oxidation of glucose by baker's yeast, which takes place mostly through the combined action of the Embden–Meyerhof and the citric acid cycles[2]. Nevertheless, the oxidation of pyruvate, a compulsory intermediate of glucose degradation in yeast, is strongly inhibited by DNP in the same experimental conditions that stimulate glucose oxidation[3]. In order to elucidate this apparent contradiction our previous experiments have been extended using substrates labelled with carbon-14.

Table 1 shows that with [3-^{14}C]pyruvate, DNP prevents incorporation of carbon-14 into the cells, the evolution of radioactive carbon dioxide and the oxygen uptake. On the other hand, with [6-^{14}C]-glucose (or [1-^{14}C]glucose), which yields [3-^{14}C]-pyruvate inside the cell, DNP stimulates the oxygen consumption and evolution of labelled carbon dioxide, and, accordingly, diminishes incorporation of carbon-14 into the cell constituents. It is noteworthy that in the presence of DNP, the total carbon-14 counted in carbon dioxide from [6-^{14}C]glucose is about that obtained from exogenous [3-^{14}C]pyruvate (without DNP).

Enhancement by DNP of glucose oxidation through the pentose pathway[2], which does not involve pyruvate as an intermediate, can be ruled out because in experiments carried out separately the ratio of the specific activities of carbon dioxide formed after simultaneous oxidation of glucoses marked in the C-1 and C-6 respectively is not increased by DNP. Furthermore, paper chromatograms and radioautograms of the methanol–water extracts from the yeast cells after oxidation of [3-^{14}C]pyruvate or [6-^{14}C]glucose show, qualitatively, the same distribution of carbon-14 in the citric acid-cycle and related substances. From this evidence, it may be concluded that the action of DNP on exogenous pyruvate consumption is not due to inhibition of the mechanism of pyruvate oxidation (the citric acid-cycle) but rather to diminished accessibility of pyruvate to the cell compartment where the oxidation takes place. Similar results are found with [1,4-^{14}C]succinate and [^{14}C]glutamate (Table 1) and also with [1,4-^{14}C]-fumarate.

Table 1. EFFECT OF DNP ON THE OXIDATION OF CARBON-14-LABELLED GLUCOSE, PYRUVATE, SUCCINATE AND GLUTAMATE BY BAKER'S YEAST

Exp.	Substrate	DNP (m*M*)	Q_{O_2}	^{14}C in the yeast cells (counts/min. / mgm.)	^{14}C in $BaCO_3$ (counts/min.) (× 10^3)	^{14}C in $BaCO_3$ (counts/min. / mgm.) (× 10^3)
A	[3-^{14}C]Pyruvate, 10 m*M*	0	53·5	18,270	60·9	11·40
A	[3-^{14}C]Pyruvate, 10 m*M*	0·05	8·4	740	0·3	0·30
A	[6-^{14}C]Glucose, 5 m*M*	0	52·5	24,870	32·9	9·10
A	[6-^{14}C]Glucose, 5 m*M*	0·05	80·2	10,960	59·2	9·30
A	[3-^{14}C]Pyruvate, 10 m*M* + glucose, 5 m*M*	0	67·2	5,520	12·8	2·20
A	[3-^{14}C] Pyruvate, 10 m*M* + glucose, 5 m*M*	0·05	32·5	1,520	1·3	0·20
A	None	0	3·1	—	—	—
A	None	0·05	15·7	—	—	—
B	[1,4-^{14}C]Succinate, 20 m*M*	0	6·1	278	5·4	1·94
B	[1,4-^{14}C]Succinate, 20 m*M*	0·05	10·4	45	3·0	0·73
B	[1,4-^{14}C]Succinate, 20 m*M* + glucose, 5 m*M*	0	38·2	326	10·6	1·23
B	[1,4-^{14}C]Succinate, 20 m*M* + glucose, 5 m*M*	0·05	38·2	91	5·7	0·45
B	[^{14}C]Glutamate, 20 m*M*	0	4·0	160	0·5	0·18
B	[^{14}C]Glutamate, 20 m*M*	0·05	4·5	16	0·1	0·03
B	[^{14}C]Glutamate, 20 m*M* + glucose, 5 m*M*	0	36·1	1,500	30·3	2·10
B	[^{14}C]Glutamate, 20 m*M* + glucose, 5 m*M*	0·05	40·8	250	6·8	0·50
B	Glucose, 5 m*M*	0	34·7	—	—	—
B	Glucose, 5 m*M*	0·05	42·9	—	—	—
B	None	0	4·7	—	—	—
B	None	0·05	10·0	—	—	—

Starved baker's yeast (8·1 mgm., exp. *A* and 23 mgm., exp. *B*) suspended in 2·0 ml. 25 m*M* phthalate buffer with additions as shown. 5 μc. [3-^{14}C]pyruvate and [6-^{14}C]glucose: 2·5 μc. [1,4-^{14}C]succinate and 2 μc. [^{14}C]glutamate (1 μc. ^{14}C = 1·19 10^8 counts/min.); final *p*H, 4·5; 0·15 ml. 5 *N* sodium hydroxide (carbonate free) in the central well of the Warburg flask; air in the gas space; temperature, 30°. After incubation (2 hr. exp. *A* and 3 hr., exp. *B*) the carbon dioxide absorbed in the alkali was precipitated as barium carbonate, washed, filtered, weighed and the radioactivity counted. The yeast suspension was diluted with 5 ml. cold phthalate buffer and centrifuged at 1°. The dilution and centrifugation were repeated and the yeast cells finally suspended in 5–10 ml. methanol for carbon-14 counting. Experimental details as before (ref. 8).

If non-radioactive glucose is added to the yeast cells in the presence of the substrates referred to and DNP, the later inhibitory action diminishes as shown by the comparatively higher incorporation of carbon-14 into the yeast cells and the total amount of carbon-14 in the carbon dioxide evolved (Table 1). Glucose effect is particularly noteworthy if it is taken into account that the carbon-14 from pyruvate becomes diluted with glucose carbon, which dilution is reflected by the relative diminution of specific activity of carbon-14 in the respiratory carbon dioxide. With the dicarboxylic acids and glutamate, the action of glucose is more striking because glucose increases absolute incorporation of carbon-14 into the yeast cells or in carbon dioxide, irrespective of the presence of DNP.

Yeast cells are divided by membrane barriers into an outer region identical with the cell wall, and a central region where organic acids like pyruvic, succinic, fumaric, glutamic, glycine, etc., do not enter or enter at a slow rate[4]. The central region includes the cytoplasm and mitochondria[5] that catalyse the citric acid cycle oxidations[6]. On these grounds, the results quoted support the hypothesis that, as in other instances[7], the transfer of substrates across the yeast membranes is an active, metabolically controlled process.

With ^{14}C-acetate as substrate, which oxidation is also inhibited by DNP[9], similar results can be observed, namely, inhibition of the oxygen uptake, the incorporation of carbon-14 into the cell constituents and the evolution of labelled carbon dioxide; the addition of glucose strongly decreases the effect of DNP. At variance with the other substrates studied, acetate diffuses freely into the yeast cell inner compartment[4], and its oxidation through the citric acid cycle in yeast requires as initial step activation with adenosine triphosphate[10], or in other words, is dependent on energy. The already established uncoupling action[6] of DNP on oxidative phosphorylation in yeast seems to be, therefore, the ultimate mechanism of the inhibition of substrate oxidation at the citric acid cycle-level. The effect of glucose can be easily understood because DNP does not inhibit phosphate esterification during glycolysis[11].

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Mechanism of Activation and Reduction of α-Aminoadipic Acid by Yeast Enzyme

PREVIOUSLY[1] we reported the reduction reaction of α-aminoadipic acid by a yeast enzyme(s) which will now be referred to tentatively as α-aminoadipic acid reductase. The reaction by which α-aminoadipic acid is converted to the corresponding δ-semialdehyde requires the participation of adenosine triphosphate, reduced triphosphopyridine nucleotide and Mg^{++}, and the enzyme is activated by glutathione. The present communication reports the formation of δ-adenyl-α-aminoadipic acid by the α-aminoadipic

Table 1. REQUIREMENTS FOR THE PYROPHOSPHATE (PP)–ADENOSINE TRIPHOSPHATE (ATP) EXCHANGE REACTION

Complete system plus or minus	c.p.s./γp of PP in ATP	Exchange (per cent)
Complete	103	76·7
Minus α-aminoadipic acid	19	14·3
,, glutathione	115	84·9
,, Mg^{++}	46	33·7
,, Mn^{++}	106	78·3
,, Mg^{++}, Mn^{++}	45	33·1
,, α-aminoadipic acid reductase	0	0
Plus *iso*citric acid dehydrogenase*	102	76·6
Minus inorganic labelled pyrophosphate, plus labelled orthophosphate	0	0

* Purified *iso*citric acid dehydrogenase (0·5 mgm.).

Complete system consisted of (in μmoles) 2 adenosine triphosphate, 2 inorganic labelled pyrophosphate (2×10^6 c.p.m.) or ^{32}Pi (10^6 c.p.m.), 6 DL-α-aminoadipic acid, 2 magnesium chloride, 0·5 glutathione, 0·18 manganous chloride, 10 potassium fluoride, 10 barbital buffer *p*H 7·4 and 0·4 mgm. of α-aminoadipic acid reductase, in a total volume of 1·0 ml. Incubation was for 10 min. at 37°.

acid reductase, together with a possible mechanism of α-aminoadipic acid reduction reaction.

The isolation of the enzyme and steps of the purification were identical with those of the previous communication[1] except that the enzyme was dialysed for 2½ hr. against demineralized water and then for 34 hr. at 0° against 0·1 *M* potassium chloride solution containing 0·01 *M* potassium bicarbonate. After dialysis the enzyme solution was centrifuged at $10^4 g$ for 10 min. and the supernatant was saved. *Iso*citric acid dehydrogenase was purified by the method of Kornberg and Pricer[2].

The α-aminoadipic acid-dependent exchange between labelled inorganic pyrophosphate and adenosine triphosphate catalysed by the enzyme was studied by Hoagland's method[3]. The reaction was stopped with 6 per cent perchloric acid. Adenosine triphosphate was separated from the labelled pyrophosphate and determined according to the method of Craine and Lipmann[4].

Typical results are presented in Table 1. α-Aminoadipic acid reductase catalysed a rapid exchange of labelled inorganic pyrophosphate with the pyrophosphate moiety of adenosine triphosphate. The exchange reaction was dependent on the presence of α-aminoadipic acid and Mg^{++}. In contrast to the overall reduction reaction, no requirement for glutathione was observed, and monoiodoacetate also did not give any appreciable effect on the rate of the exchange reaction. This indicates that the reduction reaction of α-aminoadipic acid is separable into two coupled reactions. The exchange reaction occurred only with the intact pyrophosphate molecule without prior hydrolysis to orthophosphate. The exchange reaction was completely inhibited by versene and recovered by addition of Mg^{++}. The reaction occurred over a broad *p*H range of about 6–8 and was optimal at about *p*H 7·4. Of twelve amino-acids tested including homoglutamine, lysine, glutamic acid and aspartic acid, α-aminoadipic acid only was active in this system. It should be emphasized that homoglutamine, the δ-carboxyl group of which is blocked in the form of acid amide, was lacking in activity.

In the previous communication, we reported the formation and accumulation of a derivative of α-aminoadipic acid-δ-semialdehyde in the α-aminoadipic acid reduction system. In the subsequent experiments, it was found that under ultra-violet light the paper chromatogram of the α-aminoadipic acid-δ-semialdehyde derivative fraction showed one main spot (concomitant with other spots), the R_F (0·08–0·12, with *n*-butanol–acetic acid–water; 4·5 : 1 : 2 v/v) of which corresponds to that of the area occupied by the colour reaction with *p*-dimethylaminobenzaldehyde[1], and both are superimposable. The other spots appearing on the chromatogram may be attributed to the deteriorated products of the primary reduction product of α-aminoadipic acid, since highly labile and deterioration properties of the reduction product might be expected. When the reduction reaction was carried out in the presence of potassium fluoride (10^{-2} *M*), pyrophosphate was accumulated in the system. The reduction reaction was inhibited about 50 per cent of control by 5×10^{-4} *M* of adenosine-5′-phosphate, while pyrophosphate at higher concentrations than adenosine-5′-phosphate was only slightly inhibitory to the system, and the latter, on the other hand, had little effect on the exchange reaction.

These findings permit a tentative formulation of the process by which α-aminoadipic acid is reduced to its semialdehyde. First, α-aminoadipic acid reacts with adenosine triphosphate through the δ-carboxyl group splitting off pyrophosphate and forming possibly δ-adenyl-α-aminoadipic acid as an activated α-aminoadipic acid. δ-Adenyl-α-aminoadipic acid is then an obligatory participant in the reduction reaction, and the reactions can be written as follows:

(1) α-AAA + ATP ⟶ δ-adenyl-α-AAA + PP

(2) α-AAA-AMP + TPNH.H⁺ ⟶ α-AAA-H_2-AMP + TPN⁺

(3) α-AAA-H_2-AMP + H_2O ⟶ α-AAA-δ-semialdehyde + AMP

These reactions would account for the strong inhibition of adenosine monophosphate to the reduction reaction of α-aminoadipic acid, as the result of adenosine monophosphate and δ-adenyl-α-aminoadipic acid competition for the enzyme at the reduction step (reaction 2). The above reactions would also account both for the α-aminoadipic acid-dependent exchange between pyrophosphate and adenosine triphosphate, and for the accumulation of a derivative of α-aminoadipic acid-δ-semialdehyde and pyrophosphate in the reduction system of α-aminoadipic acid. The primary reduction product of α-aminoadipic acid appearing in the 6 *N* hydrochloric acid eluate might be an adenosine-5′-phosphate derivative of α-aminoadipic acid-δ-semialdehyde (tentatively to be referred to as δ-adenyl-α-aminoadipic acid-δ-semialdehyde), which might equilibrate with the dehydrated form.

By assuming these structures, it is possible to account for the labile property of the primary reduction product toward heat treatment, resulting in the formation of Δ^1-piperidine-6-carboxylic acid[1].

Details of this work will be published elsewhere.

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Paper Chromatography and Paper Electrorheophoresis of Tuberculoproteins

PAPER electrophoresis of proteins has on the whole proved to be a more satisfying means of separation than paper chromatography, owing to the physico-chemical properties of the proteins that make them rather unfit for the latter method[1,2]. Nevertheless there do exist methods of paper chromatographic separation of, for example, enzymes, blood and serum proteins, mainly based on a kind of adsorption analysis, in addition to the more usual procedures of partition-, ion exchange- and adsorption-chromatography on columns.

Franklin *et al.*[3] claimed to have made separations of sera into a great number of fractions by means of two-dimensional paper chromatography. Conditions and results of these procedures provoked severe criticism. Though inclined to be sceptical I, too, agreed with E. and M. Lederer[1] in their opinion on the possible value of these investigations and so undertook similar experiments. The method of two-dimensional chromatography with respectively 0·1 *M* sucrose and 0·1 *M* potassium sodium tartrate[3], applied to my bovine tuberculin purified protein derivative, and some of its fractions[4], produced strange irregular patterns of no practical value, though a certain reproducibility was observed. For practical purposes I then proceeded in the following way: 0·1 *M* sucrose in the first direction and 0·041 *M* acetic acid + 0·009 *M* sodium acetate in the second. The *p*H of this last-named buffer, being 4, is the isoelectric precipitation point of the *C* fraction under certain defined conditions[5].

Fig. 1 shows that with my chromatography these conditions were rather well fulfilled.

The corresponding preparations from non-heated culture filtrates[5] gave the same pictures; only the ratio $A+B/C$ was higher[6] as expected and demonstrated by quantitative colorimetric measurement of the eluates. The patterns are in their entirety reproducible, but not in detail. So, for example, the $A+B$ spots vary in shape and show a division into two or more parts. I doubt if there can be attributed any meaning to this partition from the viewpoint of protein separation. How far we are dealing with artefacts remains to be investigated. My method, based on a previously known chemical separation and therefore somewhat dissatisfying like others of this kind[7], can be used in comparing different tuberculin samples.

Among many other experiments only chromatography with pyridine/sucrose solutions, combined with electrophoresis in borate buffers, showed patterns of some reproducibility, though as yet not good enough for practical use.

The difficulties encountered in paper electrophoresis of heated tuberculoproteins, the properties of which are apparently unfavourable for this kind of separation, have been mentioned before[4]. In this case the molecular weight of the *C* protein is twice the normal, while the *A* and *B* fractions consist probably of molecules smaller than when they do not originate from heat-sterilized culture media[8], facts that may account for the greater separation troubles[9]. In trying to cancel unfavourable effects in paper

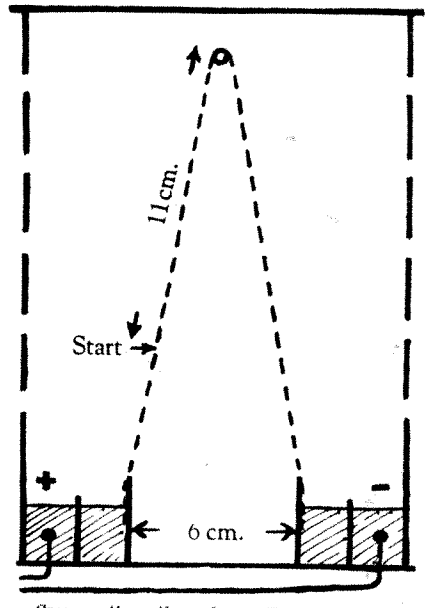

Fig. 2. Cross-section through a 'Perspex' electrophoresis apparatus of the Macheboeuf type

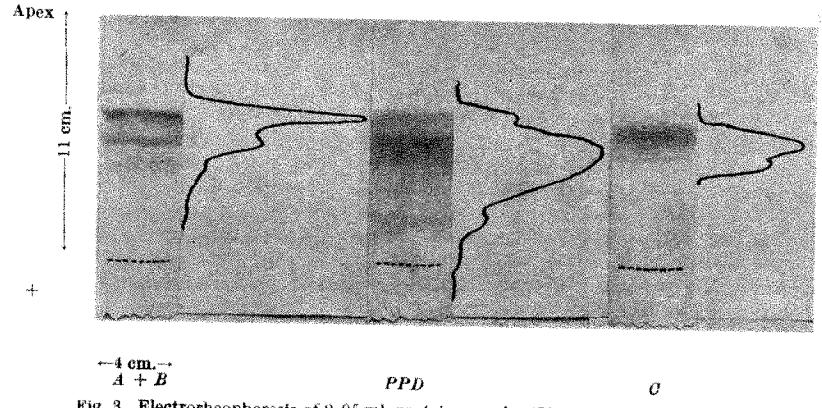

Fig. 3. Electrorheophoresis of 0·05 ml. protein samples (50 mgm./ml.). The curves were obtained with a Zeiss scanner

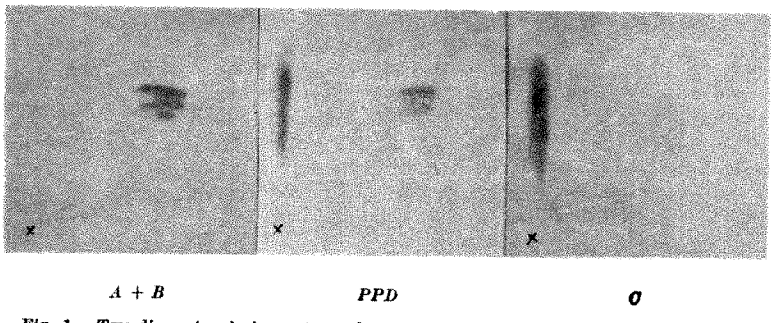

Fig. 1. Two-dimensional chromatography at 4° C. for about 3 hr. in each direction. Circular spots of 0·02 ml. protein solution of about 50 mgm./ml. In between, drying in the cold, for example, with a fan. Staining of the heat-dried Whatman No. 1 sheets with 'Amidoschwarz 10*B*' (Bayer). Dimensions of the sheets, 11 in. × 11 in.

electrophoresis due to the above-mentioned protein properties, I found a method, based on the electrorheophoresis principle of Macheboeuf[10], in which a rather vigorous evaporation-flow counteracts the electrophoretic movement of the proteins. The apparatus and results are shown in Figs. 2 and 3. A *p*H 8 buffer was used, consisting of 10 gm./l. boric acid, 0·5 gm./l. disodium salt of ethylene di-amino-tetraacetic acid, 0·05 ml./l. of 'Tween 80' and *tris* hydroxy methyl amino-methane so as to make the *p*H of the solution 8. Separations took place on Schleicher and Schüll paper No. 4032*b Mgl* at 7–9 V./cm. during 4–6 hr. at 24° C. For standardizing electrophoresis conditions and identification of the fractions obtained further investigations remain to be carried out.

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Evidence for the Existence of Two Corticotrophin-releasing Factors, α and β

WE wish to report here the presence of two distinct peptides with corticotrophin-releasing factor activity in hog posterior pituitary extracts. All the separation methods as well as the bioassays for corticotrophin-releasing factor, adrenocorticotrophic hormone, vasopressin and melanocyte stimulating hormone have been described previously[1–6].

A single peak of basic peptides obtained by preparative chromatography on carboxymethylcellulose had as its main components lysine-vasopressin and α-melanocyte stimulating hormone[3]. This peak, which also contained all the corticotrophin-releasing factor activity, was distributed for 100 transfers in a system of *n*-butanol/0·03 *M* *p*-toluene sulphonic acid. Lysine-vasopressin ($K = 0{\cdot}32$, 300 pressor U./mgm.) was well separated from the α-melanocyte stimulating hormone area ($K = 6$, $1{\cdot}3 \times 10^7$ melanocyte stimulating hormone U./mgm., 0·2 pressor U./mgm.). The α-melanocyte stimulating hormone area contained corticotrophin-releasing factor activity, which could be separated from the α-melanocyte stimulating hormone on analytical scale carboxymethylcellulose columns. This corticotrophin-releasing factor activity was found to be due to a peptide or a group of peptides containing the amino-acids of α-melanocyte stimulating hormone[7] plus threonine, alanine and leucine. The peptide with corticotrophin-releasing factor activity apparently related to α-melanocyte stimulating hormone, containing methionine as the sulphur amino-acid, has been designated α-corticotrophin-releasing factor.

Some inherent adrenocorticotrophic hormone activity of α-corticotrophin-releasing factor ($\leqslant 0{\cdot}2$ U./mgm.) and the presence of alanine and leucine support the concept that this molecule may serve as a biosynthetic precursor of adrenocorticotrophic hormone. The peptide obtained by Gros and Privat de Garilhe[8] appears to be similar or identical to α-corticotrophin-releasing factor. Since the latter was active in releasing adrenocorticotrophic hormone only at relatively high levels of 2–3 μgm. *in vivo* or 0·5γ *in vitro*, this discrepancy in corticotrophin-releasing factor activities as compared with our previous results[2–4,6] had to be explained. Similarly the amino-acid composition of α-corticotrophin-releasing factor closely resembling that of α-melanocyte stimulating hormone led us to believe that we were dealing, in α-corticotrophin-releasing factor, with a substance quite different from the one we had purified earlier[1–4], which appeared to be related to vasopressin.

The peak of pressor activity in the countercurrent distribution system was then carefully explored. It was possible to detect corticotrophin-releasing factor activity on the descending edge of the vasopressin peak after countercurrent distribution. A separation from vasopressin was achieved by paper partition chromatography[3]. Corticotrophin-releasing factor activity was found to be due to a small peptide, apparently related to vasopressin, on the basis of preliminary amino-acid composition and chromatographic behaviour. This peptide, active at 0·05γ *in vitro* or 0·1γ *in vivo*, was designated β-corticotrophin-releasing factor. Additional support for the concept of two distinct corticotrophin-releasing factor molecules was provided by the detection of two corticotrophin-releasing factor active areas with different specific activities on an analytical scale column of carboxymethylcellulose. This was achieved under conditions in which the order of elution of vasopressin and α-melanocyte stimulating hormone is reversed[5], the starting material being posterior pituitary concentrates[3].

Since both α- and β-corticotrophin-releasing factor are very basic peptides, our results are not in agreement with the data of Royce and Sayers[9]. One of the two corticotrophin-releasing factor active areas obtained by these authors after chromatography of median eminence extracts on carboxymethylcellulose must be explained by the presence of an acidic component or more probably, according to our own results, by overloading of the column. In our work, results from preparative chromatography of median eminence extracts on carboxymethylcellulose have revealed the presence of only one corticotrophin-releasing factor active area, in the position occupied by basic peptides emerging just before vasopressin. Under the conditions used here it is likely that this corticotrophin-releasing factor activity in hypothalamic extracts was due to β-corticotrophin-releasing factor, although on a preparative scale carboxymethylcellulose column the presence of some α-corticotrophin-releasing factor cannot be eliminated with certainty.

In view of the discrepancy in the specific activities and preliminary amino-acid composition of the two substances, one might propose that β-corticotrophin-releasing factor is the true chemical mediator for release of adrenocorticotrophic hormone, whereas α-corticotrophin-releasing factor is an α-melanocyte stimulating hormone analogue, possibly a pre-

cursor in the biosynthesis of adrenocorticotrophic hormone.

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Spontaneous Plasma Kinin Formation in Human Plasma collected during Labour

DEFICIENCY of substrate for induced plasma kinin production in the stored plasmas collected from women at the time of delivery has been shown[1]. This substrate deficiency was not observed in normal plasma (that is, from non-parturient individuals) stored for long periods at −20° C., or in plasma collected at time of delivery from women undergoing Cæsarean section at term before the onset of labour.

In the present series of experiments the plasmas were collected as previously described[1]; but, as soon as possible after their collection (5–25 min.), plasma aliquots were placed in polythene containers at 0° C. and tested forthwith, in doses of 0·1–0·01 ml., on the isolated rat uterus in a 10 ml. bath. It was then found that plasmas collected from women in labour showed marked oxytocic activity, which increased further for ½–1½ hr. This unusual activity was observed a short time before the onset of labour. The rapidity of its development increased throughout the first and second stages reaching, at its maximum, an activity equivalent to several units of oxytocin ('Syntocinon', Sandoz) per ml. plasma. It then declined, but was demonstrable for a variable period (usually 1–4 hr.) after completion of the third stage. These findings are in contradistinction to the negligible oxytocic activity which develops in normal plasma kept in polythene containers at 0° C. for 1 hr.[2].

The spontaneously produced oxytocic activity in parturition plasmas kept at 0° C. resembled that due to plasma kinin[3]. It rapidly disappeared when the temperature of the plasma was raised to 20° C. Conversely, the rate of disappearance of kinin added to plasma was markedly reduced when the plasma temperature was lowered from 20° C. to 0° C. This can be explained by the influence of temperature on plasma kininase. Since we have found the same kininase activity in normal and parturition plasmas, we consider that the rapidly developing oxytocic power of the latter, at 0° C., was almost certainly due to abnormally rapid formation.

The amount of spontaneous kinin formation in plasma samples collected at different stages of parturition was directly correlated with the degree of substrate depletion measured at these different stages[1].

We think it unlikely that plasmin was the enzyme responsible for the spontaneous production of oxytocic activity since the peak period for development of the latter in the plasma, and the subsequent depletion of kininogen, corresponds with the nadir of fibrinolytic activity reported in pregnancy plasma[4]. Moreover, normal plasma with high fibrinolytic activity (for example, after severe exercise or surgical operations) failed to develop a similar marked oxytocic activity. In addition, agents such as heparin (25 I.U./ml.) and ε-amino caproic acid (0·12 *M*), which inhibit plasmin, promoted the spontaneous kinin formation. These substances also potentiate kinin formation in normal plasma when it is exposed to glass, and this is known to be independent of the plasminogen–plasmin system[5,6].

The active oxytocic principle did not develop in parturition plasma to which the soya bean trypsin inhibitor (2 mgm./ml.) had been added. Like plasma kinin, it was extractable in boiling ethanol from active (that is, oxytocic) plasma kept at 0° C., but not from control samples of the same plasma kept at room temperature, and the activity of the extracts was rapidly destroyed by a crude amino-peptidase (*E. coli*) preparation. It is our opinion that it is probably a polypeptide.

The oxytocic activity in plasma or extract, unlike oxytocin, was not rapidly destroyed by sodium thioglycollate, though the build-up of kinin in parturition plasma kept at 0° C. was inhibited by this agent. In these respects the spontaneous kinin production resembled that of kinin formed by exposure of human plasma to glass, and, to a certain extent, the formation of bradykinin by trypsin added to human pre-active plasma. Differences in dose–response relationships between the spontaneously arising kinin of parturition plasma and oxytocin, and the marked lack of tachyphylactic response of the uterus towards the former, also suggest that we were not dealing with oxytocin itself.

The increasing rapidity of development of the parturition kinin throughout labour, reaching its maximum at the end of the second stage, suggests that the oxytocic activity may be related to the increasingly powerful contractions observed in the human uterus up to this time. The source of the active enzyme producing this oxytocic activity is not at present known.

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Isolation of Hyaluronate from Human Synovial Fluid by Zone Electrophoresis

LITTLE is known about the condition of hyaluronate in normal human synovial fluid because it is difficult to isolate the former in good yield by mild methods from small quantities of highly viscous fluid. Although hyaluronate can be completely precipitated from small amounts of synovial fluid by adding acetic acid or a complex cobalt salt, some degradation of hyaluronate may occur, and 50–60 per cent of the proteins of the fluid are co-precipitated in the mucin clot[1]. Isolation of hyaluronate from synovial fluid by moving-boundary electrophoresis is feasible, for at *p*H 8·6 hyaluronate migrates toward the anode slightly ahead of albumin. In normal synovial fluid, one or two components that migrated ahead of albumin were found[2] but were not isolated for further study. Electrodeposition of pooled synovial fluids was carried out three times at *p*H 7·0 by Roseman *et al.*[3], and hyaluronate was isolated in yields of 70 per cent or less, with a ratio mgm. protein/mgm. hyaluronate of 0·13, or about 11·5 per cent protein in the hyaluronate.

In the present work the use of zone electrophoresis permitted hyaluronate to be isolated from small quantities of viscous fluid and recovered for analysis. A weighed amount (about 1 gm.) of synovial fluid from apparently normal knee joints of deceased or living subjects was diluted to 5 gm. with a phosphate buffer (0·047 *M*, *p*H 6·5) and then dialysed for about 18 hr. at 2° C. against 500 ml. of an acetate buffer (0·087 *M*, $\Gamma/2 = 0{\cdot}075$, *p*H 5·4) changed twice (10·2 gm. crystalline sodium acetate and 0·7 ml. glacial acetic acid diluted to 1 litre with distilled water that was also de-ionized). An aliquot (about 0·1 gm.) of the diluted and dialysed synovial fluid was analysed for hexuronic acid[4]. The protein content of diluted and dialysed normal synovial fluid is too low to interfere with this analysis. All the hexuronic acid measured is a component of hyaluronate, since testicular hyaluronidase hydrolyses and renders dialysable 95 per cent of the hexuronic acid of the fluid.

The remainder of the diluted and dialysed synovial fluid was applied to a 2½-in. long slit in a solid block (18 in. × 5 in. × ½ in.) of polyvinyl chloride ('Geon' resin No. 427 from B. F. Goodrich Chemical Co., Cleveland, Ohio). Electrophoresis was carried out in the acetate buffer at 2° C. either for 14 hr. at a voltage gradient of 8·7 V./cm., or for 21¼ hr. at a gradient of 5·5 V./cm. The equipment and technique were modified from that used for zone electrophoresis of serum[5].

After electrophoresis, strips of Whatman No. 1 filter paper were pressed on the wet block and were dried at 90° C. for 20 min. The paper strips were stained with bromphenol blue or toluidine blue to locate approximately the positions on the block of proteins and hyaluronate respectively. The block was cut into segments (½ in. wide × 3½ in. long) starting near the anodal end. Each segment was placed in a sintered glass (coarse) funnel and eluted with a total of 10 ml. of a buffer (0·01 *M* sodium bicarbonate, 0·05 *M* sodium chloride, *p*H 8·1) by applying air pressure to the funnel. The eluates were evaporated to dryness *in vacuo* and then dissolved in 2 ml. of de-ionized distilled water. Insoluble resin was removed by centrifugation. All the eluates were examined for protein by a modified Folin method. Each eluate containing hyaluronate was analysed for hexuronic acid. (Hexuronic acid × 2·5 = hyaluronate.)

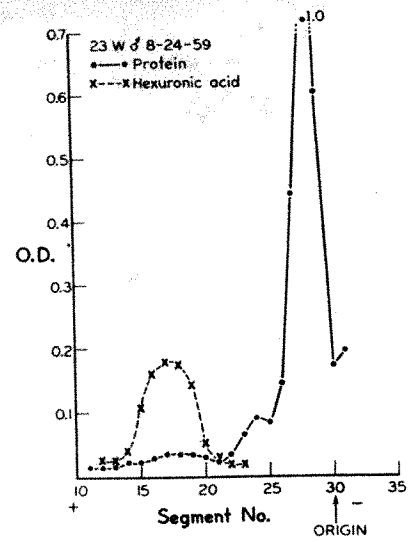

Fig. 1. Electrophoresis of normal human synovial fluid in acetate buffer (*p*H 5·4) on a block of polyvinyl chloride for 20¼ hr. at a gradient of 5·5 V./cm. Hyaluronate zone, segments 14–20; orosomucoid, segments 22–25; albumin forms the main component of segments 26–28

At *p*H 5·4 hyaluronate migrated faster than most of the proteins of synovial fluid, but a small amount of protein was present in the hyaluronate zone (Fig. 1). Hyaluronate was recovered in a yield of 80–90 per cent (Table 1). Further results shown in Table 1 were obtained by pooling all the eluates containing hyaluronate and measuring hexuronic acid and protein (Red Cross Fraction 2 was used as the protein standard). These experiments were done only when the zone of hyaluronate and protein was completely separated from the rest of the proteins of synovial fluid, as shown in Fig. 1. The ratio mgm.

Table 1. ANALYSES OF THE HYALURONATE ZONE AFTER ELECTROPHORESIS ON BLOCKS OF POLYVINYL CHLORIDE OF NORMAL HUMAN SYNOVIAL FLUIDS IN ACETATE BUFFER *p*H 5·4

Synovial fluid*	Voltage gradient (V./cm.)	Hyaluronate: Applied (mgm.)	Hyaluronate: Recovered (mgm.)	Hyaluronate: Recovered (per cent)	Pooled eluates, hyaluronate zone: Protein (mgm./gm.)	Pooled eluates, hyaluronate zone: Hyaluronate (mgm./gm.)	Pooled eluates, hyaluronate zone: Ratio (mgm. protein/mgm. hyaluronate)
23†	5·5	3·45	2·83	82	0·192	1·90	0·10
33	8·7	5·15	4·90	95	0·096	1·54	0·06
38	8·7	5·18	3·78	73	0·052	1·62	0·03
41	8·7	4·39	3·70	84	0·031	0·97	0·03
59	8·7	3·73	3·18	86	0·022	0·91	0·02
62	8·7	2·75	2·57	94	0·152	1·29	0·12
70	5·5	3·10	2·78	90	0·107	1·31	0·08

* Age of subjects from whom fluid was obtained.
† Part of this synovial fluid was also incubated with testicular hyaluronidase and zone electrophoresis was then carried out. Hyaluronate fragments were recovered in a yield of 80 per cent and the ratio mgm. protein/mgm. hyaluronate fragments was 0·018.

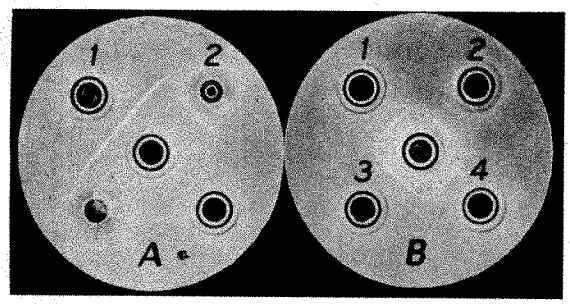

Fig. 2. Double gel diffusion in agar of pooled, concentrated eluates from normal synovial fluid after zone electrophoresis. *A*, Centre cup, anti-γ-globulin (absorbed with fraction V and a β-globulin fraction). 1, Fraction II, 0·2 per cent. 2, Hyaluronate zone (segments 14–20) from normal synovial fluid shown in Fig. 1. A faint, broad precipitin line formed near slowly diffusing antigen. Concentration of antibody was in excess. *B*, Centre cup, anti-fraction VI. Orosomucoid standard 0·025 per cent. 2, Fastest migrating protein component of normal serum isolated by zone electrophoresis at *p*H 5·4. 3, Protein (segments 22–25) from normal synovial fluid shown in Fig. 1. 4, Protein that migrated just behind hyaluronate zone isolated by zone electrophoresis of another normal synovial fluid. Precipitin lines formed by all antigens coalesced (reaction of identity). These experiments were carried out by Dr. L. Korngold

protein/mgm. hyaluronate of the isolated hyaluronate was 0·02–0·12. Double-diffusion studies in agar showed that the protein in two samples (Table 1, 23 and 62) of isolated hyaluronate formed a precipitin line against anti-γ-globulin (Fig. 2). Neither orosomucoid nor albumin, which migrated just behind the hyaluronate zone, could be detected in these samples of hyaluronate by this immunological method.

Eluates containing the isolated hyaluronate from four synovial fluids (Table 1, 33, 38, 41, 59) were pooled, concentrated to a small volume and dialysed in distilled water to remove salts. After adding potassium acetate (1 per cent w/v) and 1 vol. of cold ethanol, part of the hyaluronate formed a ropy clot. Addition of two more volumes of ethanol resulted in a flocculent precipitate of more hyaluronate. Each precipitate was separately washed with ethanol and ether, and dried over phosphorus pentoxide in a vacuum. Analytical results are shown in Table 2. The hyaluronate obtained contained the lowest quantity of protein (4 per cent) yet reported when mild methods have been used for isolation. The calculated protein content of the hyaluronate obtained by three electrodepositions[3] was 11·5 per cent; the isolation of protein-free hyaluronate was reported in a later abstract[6], but analyses were not given. Ogston and Stanier, after 16 or more ultrafiltrations of bovine synovial fluid, isolated hyaluronate in the ultra-filter residue in what was called a firm complex with about 25 per cent protein, composed largely of α-globulins, with smaller amounts of β- and γ-globulins[7]. Ogston and Sherman recently found[8] that 65 per cent of the protein in the complex could be removed by proteolytic enzymes without altering the physical properties of the hyaluronate in solution. In the present work the finding of γ-globulin in the hyaluronate zone is unexpected and worth further study.

Table 2. ANALYSES OF HYALURONATE OBTAINED BY ZONE ELECTROPHORESIS OF NORMAL HUMAN SYNOVIAL FLUIDS

Eluates containing the isolated hyaluronate from four synovial fluids were pooled. On addition of 1 vol. of ethanol part of the hyaluronate was precipitated as a ropy clot; addition of two more volumes of ethanol caused a flocculent precipitate of hyaluronate. Each precipitate was separately dried and analysed

	Ethanol added 1 vol.	Ethanol added 3 vol.
Yield (mgm.)	2·8	1·3
Hexosamine (per cent)	28·6	
Hexuronic acid (per cent)	31·6	34·2
Molar ratio $\frac{\text{hexosamine}}{\text{hexuronic acid}}$	0·98	
Nitrogen (per cent)	2·88	3·36
Molar ratio $\frac{\text{nitrogen}}{\text{hexosamine}}$	1·26	1·36
Protein (per cent)	2·47	4·53

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Note added in proof. Further to identify protein in the isolated hyaluronate, rabbits were injected with this material in Freund's adjuvant. Antibodies to α_2-globulin as well as to γ-globulin were detected by the tanned cell hæmagglutination technique.

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Inhibitor of the Cytochrome Oxidase of Unfertilized Sea Urchin Eggs

IN a previous communication[1] the presence of an inhibitor of cytochrome oxidase in the unfertilized sea urchin egg was described. It was shown that its activity decreases considerably following fertilization, that it is a low-molecular compound, that it is heat- and alkali-labile and that its action is of a competitive type.

We wish to report here some further experiments aimed mainly at obtaining the inhibitor in a purified form and at finding out about its chemical nature and its mode of action.

Fig. 1 illustrates a typical experiment showing that the inhibitor (prepared as described by Maggio and Monroy[1]) interferes with the oxidation of reduced cytochrome *c* by cytochrome oxidase (a preparation of mitochondrial membranes[2]). On the other hand, we have found that the reduction of cytochrome *c* is not inhibited. These results, taken together with the previous ones on the competitive type of the inhibition, suggest that the mechanism of the inhibition may be interference with the oxidation of cytochrome oxidase.

Most of our efforts have been directed towards the purification of the inhibitory substance. After several unsuccessful attempts, encouraging results have been obtained using columns of 'Ecteola' cellulose. Homogenates of jelly-free unfertilized eggs of *Paracentrotus lividus* in 0·05 *M* phosphate buffer at *p*H 7·2 were centrifuged at 12,000*g* for 15 min. in the cold and the supernatant centrifuged again at 105,000*g* for 1 hr. The final supernatant was dialysed overnight against distilled water and the dialysate

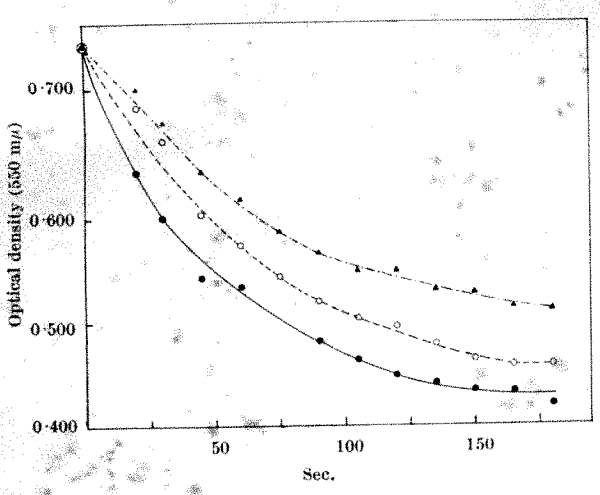

Fig. 1. Inhibition of the re-oxidation of cytochrome *c* by a crude preparation of the inhibitor (effluent from a 'Dowex-50' column, see ref. 1). The system contained in the final volume of 3·3 ml. of 0·1 *M* phosphate buffer *p*H 7·4, $2·78 \times 10^{-6}$ *M* cytochrome *c*, $8·1 \times 10^{-5}$ *M* sodium ascorbate, mitochondrial membranes from rat liver (0·1 ml. containing 0·1 mgm. protein). ●, control; ○, + 0·3 ml. of inhibitor; ▲, + 0·6 ml. of inhibitor. The re-oxidation of cytochrome *c* is indicated by the decrease of the absorbance at 550 mμ

containing the inhibitor was lyophilized. The dry material was dissolved in cold glass-distilled water to a final concentration of 0·04 *M* phosphate and the *p*H adjusted to 7·2. This solution was passed through an 'Ecteola' column prepared in phosphate buffer 0·04 *M*, *p*H 7·2. The unadsorbed material was collected, together with the first washing (carried out with 20 ml. of phosphate 0·04 *M*, *p*H 7·2), which was followed by a stepwise elution with 10 ml. portions of 0·04 *M* phosphate at *p*H 6·5, 6·0 and 5·0. The washing and the eluates were lyophilized, redissolved in distilled water to a final concentration of 0·08 *M*, and, after adjusting the *p*H to 7·2, assayed for the cytochrome oxidase inhibiting activity by the manometric technique, as already described[1]. The results of two such experiments are given in Table 1. While in most cases the activity was present only in the *p*H 5·0 fraction, in others, as in Exp. 2, some activity was eluted also with the other fractions. We take this as an indication that our method of fractionation is not yet entirely satisfactory. No ninhydrin-positive spots appeared in the chromatograms of the *p*H 5·0 fraction and nitrogen determinations were also negative. Hence it may be concluded that the inhibitor is not a nitrogen-containing substance.

It has happened sometimes, especially during purification, either that an originally active preparation lost its activity in the course of purification,

Table 1. CYTOCHROME OXIDASE INHIBITING ACTIVITY OF THE FRACTIONS OBTAINED FROM AN 'ECTEOLA' COLUMN

	Exp. 1		Exp. 2	
	Q_{O_2}	Δ (per cent)	Q_{O_2}	Δ (per cent)
Control	441		404	
Washing			380	−5·95
Eluate *p*H 6·5			371	−8·20
Eluate *p*H 6·0	479	+ 8·6	320	−20·8
Eluate *p*H 5·0	284	−35·6	274	−32·2

Each Warburg vessel contained, in the final volume of 3·0 ml., 0·2 ml. of rat liver mitochondria, 0·2 ml. of cytochrome *c* $2·46 \times 10^{-4}$ *M*, sodium ascorbate 30 μ*M*, phosphate buffer 0·048 *M*, *p*H 7·4, sample of the inhibitor 0·6 ml. Values are expressed as μl. oxygen/hr./mgm. of mitochondrial proteins (Q_{O_2}).

or that the preparations were inactive from the beginning. We have then tried to re-activate such inactive inhibitors and positive results have been obtained with reduced glutathione and cysteine. The former compound has given more constant results, evidently due to its greater stability at the neutral or slightly alkaline *p*H used in the manometric tests. When the re-activation was tried on the fractions obtained from the column, this was obtained only with the *p*H 5·0 fraction. The results of a typical experiment are illustrated in Table 2.

Table 2. RE-ACTIVATION BY REDUCED GLUTATHIONE 10^{-3} *M* FINAL CONCENTRATION. OTHER CONDITIONS AS IN TABLE 1

	Q_O	Δ (per cent)
Control mitochondria	548	
Mitochondria + glutathione	576	+ 5·1
Mitochondria + *p*H 5·0 eluate	590	+ 7·2
Mitochondria + *p*H 5·0 eluate + glutathione	474	−13·5

These results seem to suggest that thiol groups may be responsible for the inhibitory activity.

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PHYSIOLOGY

Thyroid Function and Oxidative Phosphorylation in Cold-exposed Rats

THE presence of the thyroid gland appears to be necessary for prolonged survival of the cold-acclimatized rat[1,2]. Rats in the cold also appear to turn over iodine-131 more rapidly than normal[3–6], indicating a more rapid than normal accumulation of iodide and release of thyroid hormone. Since oxidative phosphorylation, a process thought by some[7–10] to be regulated by the thyroid, has been noted to be partially uncoupled[11–13], as well as physically and biochemically more labile in the cold-acclimatized rat[12,14], we have investigated the alteration of mitochondrial function following thyroidectomy of cold-exposed and normal rats.

Rats used in these experiments were exposed to 0–2° C. for 4–5 weeks. Thyroids were removed surgically at this time, and three weeks were allowed for recovery. The completeness of thyroidectomy was ascertained by relative concentrations of labelled potassium iodide in the neck region versus leg musculature 5–7 days after isotope injection. Ratios between 1 and 2 were accepted as indicating complete thyroidectomy. Controls were maintained at 25° C. Twice-washed liver mitochondria were prepared essentially according to Schneider and Hogeboom[15] in 0·25 *M* sucrose. Oxidation was measured by Warburg manometry and phosphate esterification according to the isotope distribution method of Lindberg and Ernster[16]. The lability of the mitochondrial oxida-

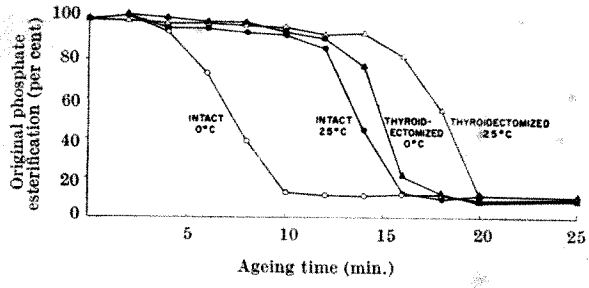

Fig. 1. Loss of phosphorylative ability of mitochondria during ageing

tive phosphorylation system was measured according to Ernster and Löw[17]. Lability of phosphorylative ability is expressed as the 'Ageing Index^P', which is equal to the time of ageing, in minutes, required to depress the phosphorylative capacity to a value half-way between maximal and minimal phosphorylation. Values of the statistical quantity t were obtained by a small sample, paired comparison method[18], and P derived from standard probability tables.

No difference was observed in the efficiency of oxidative phosphorylation (P/O) between preparations from control and thyroidectomized rats maintained at 25° C. (Table 1). On the other hand, the same mitochondrial suspensions showed a greater resistance to ageing on the part of the thyroidectomized preparation, this phenomenon being reflected in the difference in 'Ageing Index^P'. A comparison of the P/O ratios of mitochondria from intact animals, one group maintained for 4–5 weeks at 0–2° C., the other at 25° C., confirms previously published data on the lowering of the phosphorylative efficiency[11] and the 'Ageing Index[12]' of the cold-exposed group. Thyroidectomy of the cold-exposed rat results in mitochondrial preparations with normal phosphorylative efficiency as well as a normal 'Ageing Index^P'. When preparations from rats maintained at 25° C. and 0–2° C., and which have been thyroidectomized are compared, the P/O ratios are normal while the 'Ageing Index^P' of the 25° C. thyroidectomized preparation is greatly increased. Ageing curves from a representative experiment involving the four preparations discussed above are presented in Fig. 1. The 'Ageing Indices^P' were calculated from such data.

These data indicate that: (1) The stability of the oxidative phosphorylation system may be in part regulated by thyroid hormone. (2) Under conditions where the P/O ratio does not reflect thyroid regulation (hypothyroidism) an indication of regulation may be observed by the determination of the 'Ageing Index^P'. (3) The rat is not wholly dependent on an intact thyroid to regulate uncoupling of oxidative phosphorylation and 'Ageing Index^P' since the P/O ratio and 'Ageing Index^P' of thyroidectomized preparations are returned to normal in the cold-exposed animal by thyroidectomy, but not to the cold-exposed level, indicating a control in addition to the thyroid state. This type of control may reside in the tissue itself and may consist of an autoregulatory device on the tissue-level of organization.

Table 1. THE EFFECT OF THYROIDECTOMY ON THE P/O RATIO AND THE RESPONSE TO AGEING OF LIVER MITOCHONDRIA FROM CONTROL AND 4–5-WEEK COLD-EXPOSED RATS

No. of exp.	Environmental temperature	P/O		P	'Ageing index^P'		P
		Intact	Athyroid		Intact	Athyroid	
7	25° C.	1·84	1·82	>0·57	14·2	>21·4	0·02
8	25° C.	1·83		0·03	14·0		<0·01
	0–2° C.	1·48			8·3		
8	25° C.	1·83		0·54	14·0	13·0	<0·57
	0–2° C.		1·80				
7	25° C.		1·84	0·51		>21·4	0·01
	0–2° C.		1·80			13·6	

Each Warburg or Erlenmeyer flask contained: Mitochondria from 1/20th rat liver, 50 μmoles dipotassium hydrogen phosphate; 150 μmoles potassium chloride; 4·3 μmoles adenylic acid; 60 μmoles glucose; 125 μmoles sucrose; 30 μmoles succinate; 7·5 μmoles magnesium sulphate; and 330 KM units hexokinase; final pH, 7·4. 20 ml. reaction volume, 20 min. incubation, air gas phase. Oxygen consumption extrapolated for initial 5 min. (ref. 17).

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Abolition by 2:4-Dinitrophenol of the Protective Effect of Succinate and Adenine Nucleotides on the Onset of the Thyroxine-induced Swelling of Liver Mitochondria

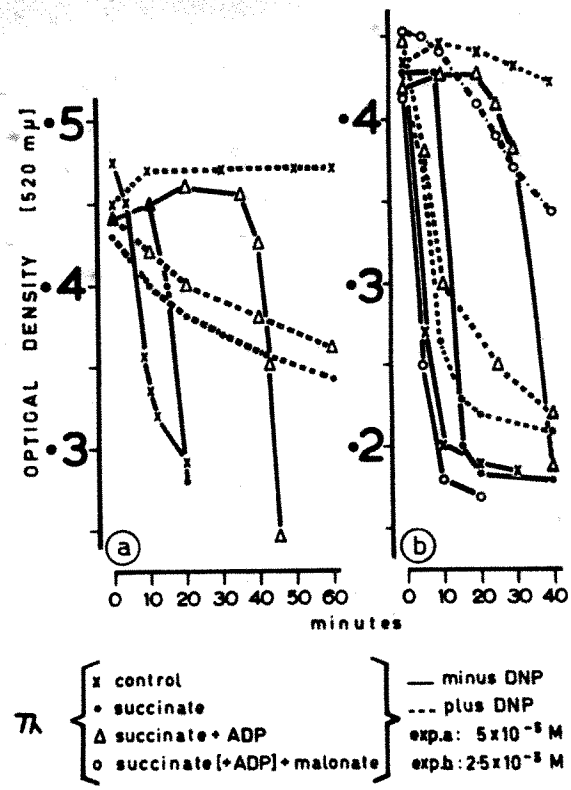
THYROXINE is known[1,2] to induce a rapid and extensive swelling of freshly isolated rat and mouse liver mitochondria suspended in a deficient medium. It has been reported recently[3] that succinate (5×10^{-4} M) and adenine nucleotides (10^{-5} M) protect against the onset of this swelling for a certain time, but not against the extent of swelling ultimately reached. The former effect was very pronounced with liver mitochondria from rats maintained on a polished-rice diet for 3–12 months. These experiments were carried out with inbred albino rats of the strain R-Amsterdam and F_2($C57$ Black × CBA) hybrid mice. It has now been found that the protective effect is weaker when liver mitochondria from several inbred strains of mice (CBA, $C57$ Black and O_{20}-Amsterdam) or from a partly inbred strain

(*LE*) of piebald rats are used than with the particles isolated from the livers of the former animals, all animals being maintained on the standard laboratory diet. The order of activity of the nucleotides appeared to be: adenosine di- $\geqslant$ -tri- $\gg$ or $>$ -monophosphate, the latter being in many cases scarcely effective, if at all. Evidence has been obtained[3] that the adenine nucleotides, added in a sufficiently low concentration as to make any chelating effect unlikely, were especially active when added in conjunction with succinate. The conclusion was, therefore, drawn that the protective effect of the latter compounds on the onset of the thyroxine-induced swelling (that is, the retardation thereof) was mediated by promoting the process of oxidative phosphorylation under the adverse conditions of the deficient medium. This view has now been substantiated by the following results, which may also shed some further light on the anomalous effects of 2 : 4-dinitrophenol (DNP) on the swelling of isolated liver mitochondria.

DNP has been shown[1,2] to abolish completely the spontaneous or thyroxine-induced swelling of liver mitochondria suspended in deficient medium, but to induce swelling when oxidizable substrate is also present[4-6]. When taking into account that electron transport in the respiratory chain is required for swelling[6-8] and that DNP may inhibit respiration[9], the conclusion can be drawn (compare ref. 6) that DNP abolishes the spontaneous or thyroxine-induced swelling by inhibiting the electron transport from intramitochondrial substrates, and thus prevents swelling. Since there is also evidence[9] that added oxidizable substrates may counteract the inhibitory effect of DNP on respiration, the above anomaly may be more apparent than real. In this connexion it should be noted, when comparing the concentrations of DNP used in manometric and swelling experiments, that the mitochondria in the latter case are much more diluted than in the fomer.

Figs. 1*a* and *b* represent two experiments in which effects of DNP ($5 \times$ and $2 \cdot 5 \times 10^{-5}$ *M*, respectively) on the pattern of swelling of *R*-rat liver mitochondria in the presence of thyroxine, succinate and adenosine diphosphate (ADP) were studied, using the same technique as described previously[3]. In both cases DNP not only inhibited the thyroxine-induced swelling of the particles observed in the absence of added substrate, but also abolished the protective effects of succinate and succinate plus ADP on the onset of the thyroxine-induced swelling. In the first experiment with 5×10^{-5}, but not in the second with $2 \cdot 5 \times 10^{-5}$ *M* DNP, the rate of swelling in the presence of thyroxine (3×10^{-5} *M*), DNP and succinate (and ADP) was much less pronounced than that observed in the absence of DNP once the protective effect of succinate (and ADP) was overcome. This difference may be accounted for by assuming that 5×10^{-5} *M*, in contrast to $2 \cdot 5 \times 10^{-5}$ *M* DNP, still inhibited the electron transport from succinate to a certain extent. If so, it might be expected that, when the oxidation of the latter is prevented by malonate (5×10^{-3} *M*), the inhibitory effect of DNP on the electron transport, now stemming mainly from the endogenous substrates, may predominate again and thus abolish the swelling effect of thyroxine. Fig. 1*b* shows the latter prediction to be true for the low concentration of DNP.

The finding that the protective effect of succinate and adenine nucleotide on the onset of the thyroxine-induced swelling is abolished by either malonate or



Figs. 1, *a* and *b*. **Effect of 2 : 4-dinitrophenol and/or malonate on the thyroxine-induced swelling of fresh rat liver mitochondria incubated in the presence of succinate (and adenosine diphosphate).** 2 : 4-Dinitrophenol, 5×10^{-5} *M* in exp. *a* and $2 \cdot 5 \times 10^{-5}$ *M* in exp. *b*; DL-thyroxine, 3×10^{-5} *M*, present in each flask; succinate, 5×10^{-3} *M*; adenosine diphosphate, $1 \cdot 5 \times 10^{-5}$ *M*; malonate, 5×10^{-3} *M*. Note that the curves indicated by small circles in Fig. 1*b* represent the situation as found in the absence and presence of adenosine diphosphate

DNP indicates that the former effect is dependent on both the oxidation of succinate and the accompanying phosphorylation.

The *in vitro* swelling action of thyroxine on liver mitochondria has been shown[10] to represent an acceleration of a process which the mitochondria are already inherently capable of undergoing spontaneously; a similar conclusion has been drawn previously[11] in regard to the loss of diphosphopyridine nucleotide from isolated mitochondria, the action of thyroxine being then described as representing an acceleration of the structural and biochemical labilization of the particles such as is manifested after their ageing. The correspondence between spontaneous and thyroxine-induced swelling was further substantiated by the finding[3] that both processes responded in a similar manner to succinate and the adenine nucleotides, the response being determined by the type of mitochondrial preparation (fresh; intact or damaged by washing[12] at 0° C.; aged at 0° and 37° C.). Since for swelling to occur electron transport along the respiratory chain is required, and since intact mitochondria capable of phosphorylating do not swell, a labilizing change in the biochemical structure of isolated liver mitochondria suspended in deficient medium, leading to uncoupling, has been postulated as necessarily preceding mitochondrial swelling. Thyroxine appears to accelerate the latter change, which has been identified[3,12,13], albeit tenta-

tively, as caused by or to involve a loss of adenine nucleotides from the particles in the deficient medium lacking magnesium.

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Accelerated Recovery from Reserpine Depression by Monoamine Oxidase Inhibitors

IT is generally accepted that pretreatment with a strong monoamine oxidase inhibitor, for example iproniazid, antagonizes the behavioural depression induced by reserpine[1]. The converse experiment in which the inhibitor is given after reserpine in an attempt to terminate the depression apparently has not been as well explored; at least two papers, however, have reported failures to obtain such a reversal[2]. In the present experiments, chronically reserpinized animals were under observation for extended periods (weeks) before and after treatment with iproniazid or β-phenyl*iso*propylhydrazine (*JB* 516). The conditioning techniques used provided an objective assay of behaviour changes. Under these conditions, the behavioural depression produced by reserpine was clearly alleviated by a single injection of a monoamine oxidase inhibitor, although the onset of the arousal lagged about a day after the dosing.

Five hungry male rats, maintained at 80 per cent of their weight when feeding *ad libitum*, were trained to obtain a drop of sweetened condensed milk by pressing a lever in the wall of a small chamber. Not every press was rewarded; eligibility for reinforcement was programmed randomly and occurred, on the average, once a minute. This variable-interval reinforcement schedule produced a steady, high response-rate throughout the 1-hr. experimental sessions, and thus furnished a dependable behavioural base-line for the measurement of drug effects.

Administration of reserpine phosphate (0·2 mgm./kgm. base intraperitoneally) was begun after the lever-pressing rates had become stabilized. Injections were made immediately after every experimental session, even on days when other drugs were given. Behavioural tests were not run at week-ends, but the reserpine was injected every day once the series was started.

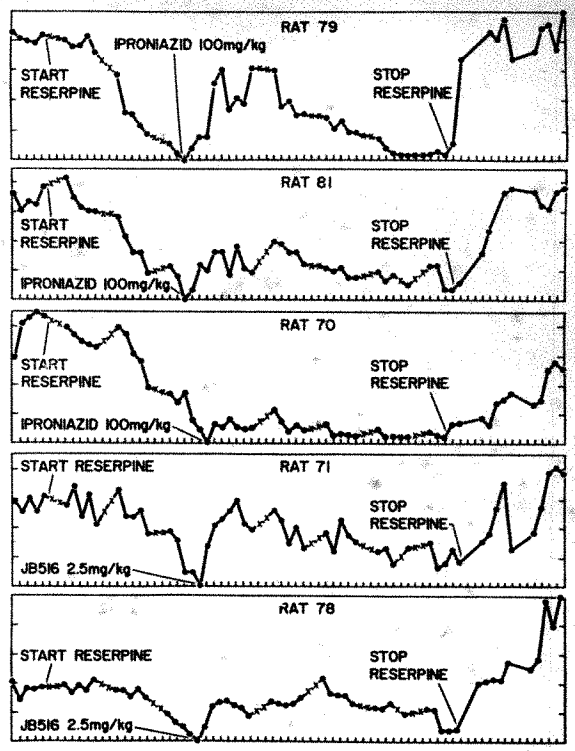

Fig. 1. Daily response output throughout the experiment for the five rats. Abscissa, daily 1-hr. test sessions: markers indicate successive days; ordinate, total number of lever responses; each marker denotes 400 responses. Reserpine was administered immediately after each test session on week-days and also on week-ends (indicated by crosses) when behavioural tests were not made. The first three reserpine injections were 0·5 mgm./kgm., and all succeeding ones, 0·2 mgm./kgm. A single dose of iproniazid or *JB* 516 was injected half an hour before the start of the test session indicated

After several reserpine injections with no apparent effect, the rates of response declined rapidly. When the rates were about 10 per cent or less of the pre-reserpine-levels, the monoamine oxidase inhibitors were administered. Three of the animals were injected with iproniazid phosphate (100 mgm./kgm. intraperitoneally) and two with β-phenyl*iso*propylhydrazine hydrochloride (2·5 mgm./kgm. intraperitoneally) half an hour before the start of the test period. Reserpine was injected as usual after this period, and daily for several weeks thereafter.

Fig. 1 gives the daily lever-pressing rates for the five animals throughout the course of the experiment. With the exception of rat 70 (which probably required a larger dose of iproniazid), substantial recovery from the reserpine inhibition may be observed on the second or third day after the dosing with the inhibitor; the reversal lasted about one month. Without the protection of an inhibitor, a reserpine series of this sort is usually lethal; the animals stop eating and seem to be less resistant to disease.

Also interesting was the observation that the monamine oxidase inhibitors actually increased the suppression of lever-pressing for many hours immediately after the dosing. In Fig. 1 it may be seen that on the day that the inhibitor was given, the response output of all animals approximated zero. Such absolute suppression of the lever-pressing rate within half an hour after an iproniazid or *JB* 516 injection has been observed invariably in more than twenty experiments. These doses of iproniazid and *JB* 516

have no obvious effects on the lever-pressing performance of rats not treated with reserpine.

These findings bear upon theories that attribute the behavioural effects of reserpine to the changes this drug brings about in the levels of endogenous brain monoamines; the serotonin and catechol amine in the brain are both depleted extensively and both have been taken to be implicated[1,3].

The present observation of a delayed reserpine reversal by the monoamine oxidase inhibitors follows the time-course of recovery of norepinephrine in the brain more closely than that of serotonin. Spector *et al.* have reported that the level of serotonin in the brain in reserpinized rabbits rose almost to normal within 2 hr. after an injection of *JB* 516, while the level of norepinephrine remained virtually unchanged[4]. During this time of recovered serotonin-levels in the present experiments, the inhibition of lever-pressing behaviour was not reversed, but actually was increased. The present observation that the peak of the recovery was delayed for a number of days corresponds with a similarly delayed increase in the norepinephrine-level in the brains of rabbits treated with monoamine oxidase inhibitors[4]. Also favouring an important role for the catechol amines are the findings that amphetamine, a close structural and pharmacological relative of the catechol amines, and cocaine, a known potentiator of catechol amine activity, both potently and rapidly reversed the behavioural inhibition produced by reserpine. Reversal of reserpine-induced depression of behaviour with cocaine has been observed by J. Seifter and one of us (L. S.) in experiments at the Wyeth Institute for Medical Research.

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Electrophoretic Mobilities of Normal and Regenerating Liver Cells

BY measuring the electrophoretic mobility of cells, Ambrose, James and Lowick[1] have demonstrated that the average charge density of neoplastic kidney and liver cells is almost double that of the homologous normal cells.

It was further shown[2,3] that the increase in the negative charge density of tumour cells is due to a gradual alteration of surface properties in direct relation to the degree of malignancy.

These observations gave rise to the question as to whether the increased charge density of neoplastic cells is specifically characteristic of malignancy, or could perhaps be considered as one of the manifestations of normal growth.

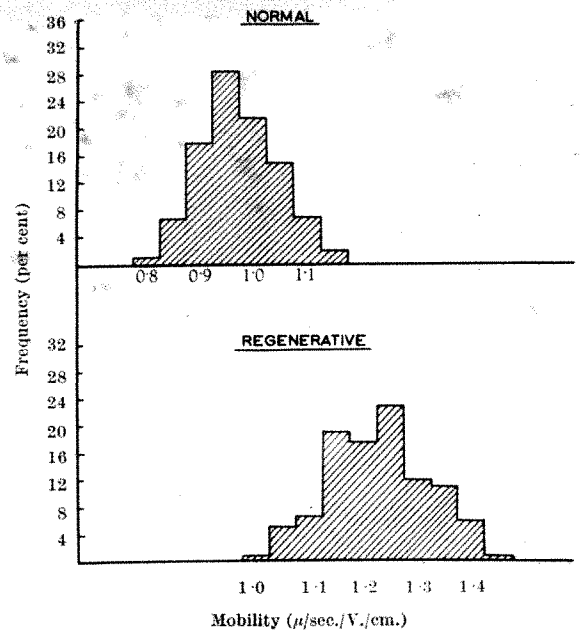

Fig. 1. Electrophoretic mobilities of single liver cells. Cells from normal liver show a mean mobility of 1·000 ± 0·015. Cell from regenerative liver 24 hr. after partial hepatectomy 1·257 ± 0·021 *S.E.*

In an attempt to shed light on this problem, the electrophoretic mobility of regenerating liver cells was compared with that of the homologous non-regenerating cells.

Cell suspensions of adult rat liver were prepared by perfusing the liver with 0·05 *M* ethylenediamine tetraacetic acid slightly homogenized in a loose-fitting Potter–Elvehjem glass homogenizer[4] and washed several times with phosphate-buffered saline[5]. This procedure yielded a rich suspension of liver cells. For electrophoretic measurements the cells were transferred to Sørensen's phosphate buffer *M*/15 (*p*H 7·4; ionic strength 0·174) and measured by the Northrop–Kunitz electrophoretic cell on a horizontal plane[6]. 100 cells, at least, were measured for each experiment. Erythrocytes served as internal control, and accordingly only animals in which the erythrocyte mobility was in the range of 1·21–1·27 μ/sec./V./cm. were used.

The measurements were carried out on coded samples so that the observer was unaware of the origin of the cells at the time of measurement.

Fig. 1 shows an increase by an average of 25 per cent in the mobility of the cells 24 hr. after partial hepatectomy, thus indicating the increased negative charge density of the regenerating liver cells.

When the changes in charge density of the cells during the regenerative process were followed up, an increase in mobility could already be observed at 6 hr. after the operation. The mobility was still high after 48 hr. However, in measurements taken after a considerable delay of 20 days, it was found that the cell mobility had returned to the normal level.

These experiments would indicate that the increased charge density of cells is also a manifestation of a normal growth process. It may be therefore that the growth associated with malignancy may be the cause of the increased charge density changes previously described[1,2] rather than a property specific to malignant cells.

A detailed account of this work will be published elsewhere.

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HÆMATOLOGY

Separation of Reticulocytes by means of Multi-Layer Centrifugation

RETICULOCYTES regarded as the youngest erythrocytes in the circulating blood have particular properties such as respiration[1,2], biosynthesis of hæm *in vitro*[3], electrophoretic mobility and osmotic resistance[4] different from those of mature erythrocytes. Separation of reticulocytes in a pure and physiological state seems necessary in studying their properties and functions[5].

We succeeded in separating reticulocytes by means of a multi-layer centrifugation with a gum acacia solution. The separating procedures are similar to those of leucocytes and bone marrow cells[6,7] reported previously. The technique depends on the difference in densities between reticulocytes and mature erythrocytes. Separating media with various degrees of specific gravity are prepared immediately before the experiment by diluting a stock solution with physiological saline solution. The stock solution is prepared as follows: about 30 ml. of distilled water is put into a flask, to which about 30–32 gm. of gum acacia powder is added and stirred with a glass rod. The stirring is continued while the flask is being put in a water-bath kept at 80–90° C. Then water is added slowly up to about 90 ml. After the powder is dissolved, it is centrifuged at 1,000*g* for 20 min. The supernate is diluted with distilled water to a density of 1·090 at 15° C. The density is measured by a hydrometer which covers the range 1·060–1·120 in steps of 0·001 unit. As this solution is hypotonic to blood cells, sodium chloride is added to keep the solution isotonic with blood cells—usually about 0·2 per cent. The *p*H of this solution is adjusted to 7·4 by adding a few drops of a saturated sodium hydroxide solution.

The stock solution can be stored for several weeks in a tightly closed container kept in a cold room. The proper dilution of the stock solution to secure desired densities for the separation of reticulocytes can be calculated from the following formula:

$$X = \frac{1 \cdot 090}{D - 1} \times A$$

where X is volume of physiological saline solution to be added, A is volume of stock solution, D is the density desired.

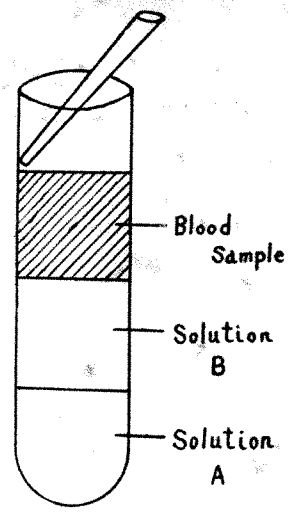

Fig. 1. Layered solutions before centrifugation

Usually two solutions A and B are used for separation; A with a specific gravity of 1·068–1·078 according to the preliminary test and B is 1·050 (15° C.). Each specific gravity desired should be determined by a preliminary test with blood cells, because there are individual and seasonal variations in density of reticulocyte.

Reticulocytosis is caused in adult rabbits weighing 2·5–3·0 kgm. by repeated bleeding or administration of phenylhydrazine; thus 10 ml. of blood per kgm. body-weight is withdrawn daily from the ear vein or by heart puncture until the reticulocyte count reaches about 30 per cent; or 0·3 ml. of a 2·5 per cent phenylhydrazine hydrochloride solution per kgm. body-weight is injected subcutaneously daily until the reticulocyte count reaches about 50 per cent. The blood of the rabbit with reticulocytosis is withdrawn from the ear vein in measured amounts of 3·8 per cent sodium citrate or neparin solution. The blood is washed with physiological saline solution and then centrifuged at 1,000*g* for 20 min. The supernate and buffy coat (a concentrated leucocyte and platelet layer) are pipetted off.

The sedimented red blood cells are suspended in a two- or three-fold volume of physiological saline

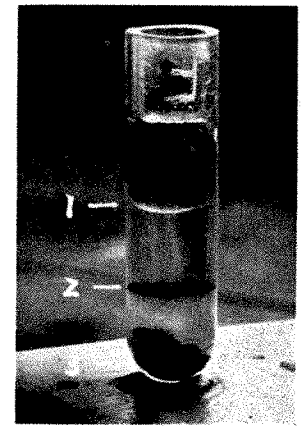

Fig. 2. Separated blood cells in a centrifuge tube. 1, Fibrin layer with leucocytes and platelets; 2, reticulocyte layer; 3, mature erythrocyte layer

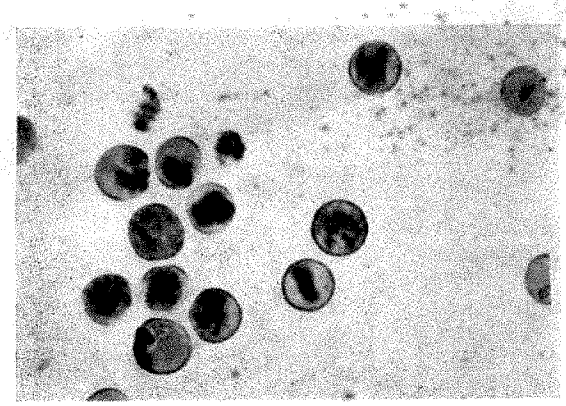

Fig. 3. Separated reticulocytes (brilliant cresyl blue staining). (× 800)

solution and used for a multi-layer centrifugation. All the procedures are carried out in a cold room kept at 2°–0° C.

Two ml. of solution *A* is poured into a centrifuge tube (13 mm. in inner diameter, 10 ml. in capacity) and 2 ml. of solution *B* is layered over the *A* carefully along the inner wall of the tube with a pipette. Then about 3 ml. of the blood sample is put on *B* (Fig. 1). The layered solutions are centrifuged at 4,000–5,500*g* for 15 min. A Marusan electric centrifuge (horizontal head) is employed: conical head centrifuges do not seem convenient for a multi-layer centrifugation. After centrifugation the following three layers are formed in a centrifuge tube (Fig. 2): from the top to the bottom, (1) fibrin lying with a few leucocytes and platelets; (2) reticulocyte (immature erythrocyte) layer; (3) mature erythrocyte layer. The reticulocytes float on the boundary of solutions *A* and *B* forming a stratum, so that they can be easily collected with a pipette. The reticulocytes thus prepared show a 95–100 per cent purity in separation (Fig. 3). Their functions and properties will be discussed in the *Japanese Journal of Physiology*.

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Human Embryo Hæmoglobin

ALTHOUGH evidence of the presence of a second fœtal hæmoglobin in young human fœtuses is accumulating[1–6], uncertainty still seems to prevail in some quarters as to the existence of this embryonic hæmoglobin[7]. The following report of a paper-electrophoretic study of the hæmoglobins of six 6–12-week-old and five 15–18-week-old human fœtuses may therefore be of some interest.

Hæmolysates containing about 10 per cent hæmoglobin were prepared from citrated cord blood following the technique of Singer *et al.* The spots were run on Whatman No. 1 filter paper for 20–21 hr. in barbital buffer at a *p*H of 8·6 and at approximately 0·1 ionic strength.

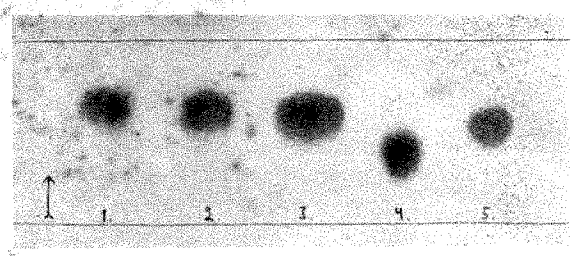

Fig. 1. Electrophoretic pattern of hæmoglobins. 1, 2 and 3, normal adult hæmoglobin; 4, hæmoglobin from 12-week-old fœtus; 5, normal full-term new-born infant. Arrow indicates direction of migration

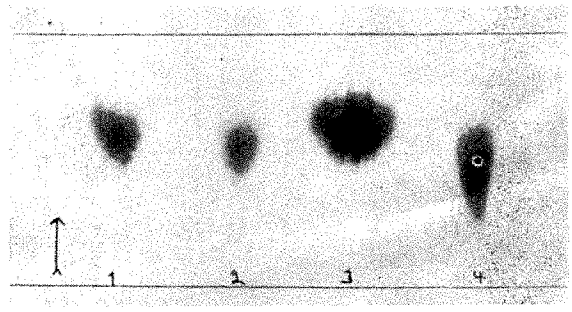

Fig. 2. Electrophoretic pattern of hæmoglobins. 1, Mixture of hæmoglobin from 12-week-old fœtus and full-term new-born infant; 2 and 4, hæmoglobin from 12-week-old fœtuses; 3, normal full-term new-born infant. Arrow indicates direction of migration

As can be seen from Table 1 and Figs. 1 and 2, the migration of the hæmoglobins in the group of 7–12-week-old fœtuses was definitely slower than the migration of the hæmoglobins in the group of 15–18-week-old fœtuses and of full-term infants and adult controls. In relation to the migration of normal adult hæmoglobin the mean ratio fœtal hæmoglobin : adult hæmoglobin was 0·86 in the group of small fœtuses and 0·98 in the group of 15–18-week-old fœtuses.

After migration a mixture of hæmoglobins from a 12-week-old fœtus and a full-term new-born infant showed signs of separation (Fig. 2).

It seems reasonable to assume that the hæmoglobin in the blood of the 7–12-week-old fœtuses described here is identical with the embryonic

Table 1. MIGRATION (CM.) OF HÆMOGLOBINS FROM SIX 7–12-WEEK-OLD AND FIVE 15–18-WEEK-OLD HUMAN FŒTUSES. WHATMAN NO. 1. VERONAL BUFFER *p*H 8·6, 20–21 HR., 4·5–6 M.AMP.

Age of fœtus, weeks	Migration (cm.) of: Fœtal hæmoglobin	Adult hæmoglobin	Fætal hæmoglobin/adult hæmoglobin	Mean
7 (6 cm.)	7·6	8	0·94	
8 (6 cm.)	7·4	8	0·92	
10 (8 cm.)	7·5	8·7	0·86	0·86
11 (10 cm.)	6·0	7·0	0·85	
12 (9 cm.)	4·5	5·0	0·9	
12 (9 cm.)	3·5	5·0	0·7	
15 (16 cm.)	8·5	8·7	0·97	
16 (16 cm.)	8·3	8·1	1·02	
18 (20 cm.)	8·0	8·5	0·94	0·98
18 (22 cm.)	7·8	8·0	0·98	
18 (21 cm.)	8·0	8·2	0·98	

hæmoglobin of a 10-week-old human fœtus which Halbrecht and Klibansky identified by means of paper electrophoresis. The "primitive type *P*" embryonic hæmoglobin described by Allison[2] and the early embryonic hæmoglobin distinguished through alkali denaturation by Drescher and Künzer[1] may well be identical with the hæmoglobin of the small fœtuses reported here.

The migration pattern of the hæmoglobins of the 15–18-week-old fœtuses differed significantly from the hæmoglobins of the 7–12-week-old group. The mobility of the hæmoglobins of the older group of fœtuses showed but small differences as compared with the hæmoglobin of normal full-term infants.

From the results of this investigation it was thus possible to distinguish a human embryonic hæmoglobin from a group of 7–12-week-old fœtuses, which, on paper electrophoresis under the conditions described, showed a mobility definitely slower than that of the hæmoglobin of normal full-term infants. The mobility of the hæmoglobins of the group of 15–18-week-old fœtuses did not differ significantly from that of normal full-term infants.

These findings support the view[4] that the hæmoglobin in the erythrocytes derived from the mesoblastic tissue during early embryonic life is of a different type from the hæmoglobin of hepatic and medullary origin. If this holds true, most of the hæmoglobin of mesoblastic type is replaced by hæmoglobin of hepatic origin in the course of 15–18 weeks of fœtal life.

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PATHOLOGY

Leucocytic Emigration from Inflamed Capillaries

THE precise manner in which margination and emigration of leucocytes occur in acute inflammation has not been elucidated despite numerous careful studies with the light microscope. Utilizing electron microscopy we have observed the emigration of leucocytes from capillaries in areas of acute inflammation in dog pancreas. Capillary endothelial cells react to injury by forming intra-lumenal finger-like projections of cytoplasm. These projections insinuate themselves around, and envelop, adjacent leucocytes, and, in this manner, draw the latter into the capillary wall (Fig. 1). This intramural localization of leucocytes is equivalent to 'margination' as seen by light microscopy and would appear to occur by a process similar to that of phagocytosis. The leucocytes are then extruded through the antiluminal border of the endothelial cell where they are separated from the extravascular space only by the basement membrane

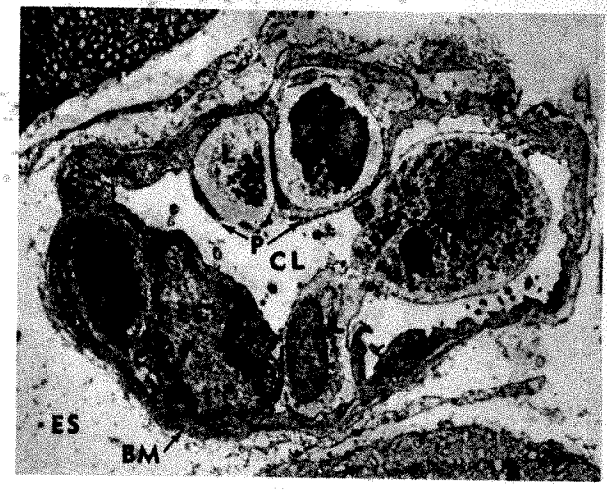

Fig. 1. Electron photomicrograph of an inflamed capillary in which leucocytes (*L*) are surrounded by endothelial cytoplasmic processes (*P*). Lumen of capillary (*CL*), endothelial cell (*EC*), basement membrane (*BM*), extravascular space (*ES*). (× c. 4,670)

of the endothelial cell. After separation of leucocyte and endothelial cell by as much as 300 Å., new basement membrane forms between them and is continuous with the old. Simultaneously old basement membrane adjacent to the leucocyte becomes smudged and frayed and gradually melts away, releasing the leucocyte into the extravascular space.

Only rarely are interruptions seen in the continuity of either endothelial cell or basement membrane during the passage of leucocytes through them. In most instances, both endothelial cell and basement membrane are continuous and are re-formed behind the leucocyte before either is breached ahead of it. That the process is highly selective is demonstrated by the fact that segmented leucocytes are involved predominantly. The nature of this selectivity was not determined in the present work; it may be related to humoral factors acting on either the leucocyte or the endothelium. Agents which affect the degree or extent of inflammatory exudation may act on the endothelial cell.

The exact processes of margination and emigration described here may not occur in all species and for all inflammatory stimuli. Preliminary observations suggest that species variations may exist. Under the conditions of the experiment described here, however, the endothelial cell appears to play a very active part in these processes. Full details of this work will be published in the *American Journal of Pathology*.

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Blood Corticotrophin in Cushing's Syndrome

PREVIOUS work on the level of blood corticotrophin in cases of Cushing's syndrome has been scanty and has not involved a full-scale bioassay of concentrated extracts used at sufficiently high dose-levels. Some of the early work on this subject was reviewed by Loraine[1] and semiquantitative values for four Cushing's patients have been given by Clayton[2].

From our experiments, values are given for the corticotrophin content of blood from two patients with Cushing's syndrome and from normal and hypertensive subjects.

Corticotrophin was extracted from large volumes of blood (500–1,000 ml.), collected between 10 and 11 a.m. The blood was run directly into glacial acetic acid to prevent possible enzymic destruction of the hormone[3]. In order to concentrate it for bioassay the corticotrophin was extracted by adsorption on oxycellulose followed by elution with 0·1 *N* hydrochloric acid by Astwood's method[4] as modified for blood by Sydnor and Sayers[5]. The latter obtained an 85 per cent recovery of corticotrophin added to hypophysectomized rat blood. In our experiments, the eluate was stirred with moist 'De-acidite *FF*' resin (carbonate form), sufficient being added to bring the *p*H to 2·7. The solution was then freeze-dried, stored dry over phosphorus pentoxide at 4° C. and was re-dissolved in 0·9 per cent saline, acidified with a trace of 0·01 *N* hydrochloric acid, for intravenous injection into rats.

The blood concentrates were assayed by their action in depleting adrenal ascorbic acid in hydrocortisone-treated rats[6–8]. Our assays involved the use of 30 rats and compared the effect of three dose-levels of the blood concentrates with three dose-levels (0·13, 0·40, 1·2 mU.) [1 milliunit (1 mU.) = 1/1,000 I.U.] of the 2nd International Standard for corticotrophin. The highest dose of the concentrate was equivalent to at least 50 ml. of blood. The accuracy was satisfactory for a bioassay method, average limits of error calculated at the 5 per cent level being 58–165 per cent. Results are given in Table 1.

Table 1. CORTICOTROPHIN CONTENT OF HUMAN BLOOD

Type of patient	Sex and age (yr.)	Volume of blood concentrated (ml.)	Potency of blood concentrate in rat assay	Limits of error expressed as percentage of the potency†	Blood corticotrophin mU.‡/100 ml. blood
Normal* I	1 *M* 30, 1 *F* 34, 1 *F* 37	1,080	0·77	43–131	0·71
Normal* II	1 *M* 35, 1 *M* 40	1,000	0·58	43–232	0·71
Hypertensive	*M* 51	1,000	0·59	55–183	0·72
Cushing's case 1	*F* 38	750	1·31	74–135	2·16
Cushing's case 2	*M* 44	450	0·81	74–136	1·80

* Blood was pooled from 3 and 2 individuals.
† Calculated at 5 per cent level.
‡ 1 mU. = 1/1,000 I.U.

In normal subjects, Sydnor *et al.*[9] and Paris *et al.*[10] believed from their experimental work that the corticotrophin content of blood was less than 0·5 mU./100 ml. Levels of 30–200 mU./100 ml. reported by Bornstein *et al.*[11] have been criticized by Loraine[1], who suggested that these levels would have been accompanied by clinical features of adrenocortical hyperfunction.

It seems unlikely that the high values for our two Cushing's patients are caused by hypertension (see Table 1). Clearly more cases should be studied in greater detail, with values before and after treatment correlated with the pathology of the adrenal and pituitary glands.

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RADIOBIOLOGY

A Sexual Difference in the Concentration of Iodine-131 by the Submaxillary Gland of Mice

A SEXUAL dimorphism in the submaxillary gland of mice has been described by Lacassagne[1]. In the male the secretory tubuli are more developed than in the female. This difference has since been reported as depending on endocrine glands[2–4].

Human saliva concentrates iodine-131 (ref. 5). Since this demonstration, experiments have been carried out on the iodine-concentrating capacity of salivary glands. Logothetopoulos and Myant[6] established this fact for the submaxillary gland of mice and it was shown that the degree of concentration is related to the strain of the animals[7]. Radioautographic studies[6] led to the conclusion that the secretory tubuli are the structures of the gland which concentrate iodine.

Table 1

Total iodine-131 per mgm. of submaxillary tissue / Total iodine-131 per mgm. of blood				
Males		Females		*P*
No. of animals	Mean ± *S.E.*	No. of animals	Mean ± *S.E.*	
61	5·25 ± 0·31	40	3·89 ± 0·32	< 0·01

In the present communication we report our findings on the sexual difference in the iodine-concentrating capacity of submaxillary glands of mice.

Sixty-one male and forty female *C3H* mice were injected intraperitoneally with 5 μc. of carrier-free solution of iodine-131. 1 hr. later the submaxillary gland was removed and blood collected under ether anæsthesia. The glands and blood were weighed and radioactivity measured in a well counter. The ratio:

$$\frac{\text{total } ^{131}\text{I per mgm. submaxillary tissue}}{\text{total } ^{131}\text{I per mgm. blood}}$$

was taken as a measure of the degree to which submaxillary tissue is able to concentrate iodine.

The results are given in Table 1.

These results show that there is a sexual difference in the capacity to concentrate iodine by the submaxillary gland of mice.

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Uptake of Magnesium-28 by the Skeleton of a Sheep

IN order to find the cause of hypomagnesæmia in adult ruminants, it is necessary to have a better understanding of the mechanism controlling magnesium-levels in blood and particularly the relationship between bone and blood magnesium. Bone from cows suffering from hypomagnesæmia showed no depletion of magnesium[1], and this has led to the theory that the lability of bone magnesium is much reduced in adult animals[2]. There are no figures in the literature, however, for either the amount or the rate of mobilization of skeletal magnesium in adult ruminants, but such data can be obtained from work on the uptake of radioactive magnesium by bone. Because of the short half-life of magnesium-28, only that part of the bone magnesium which is rapidly exchanged with the magnesium of plasma and other body fluids can be measured.

After six days on a constant diet of grass nuts containing 1·2 gm. of magnesium, a five-year-old Greyface wether, weighing about 65 kgm., was given 40–60 μc. carrier-free magnesium-28 as the chloride into the jugular vein. 10 hr. later, immediately after sampling the blood, the sheep was killed by exsanguination under nembutal anæsthesia, and duplicate samples of bone, free so far as possible from blood and bone marrow, were taken from various parts of the skeleton and their radioactivity determined the same day in a well-type scintillation counter.

The values obtained for the calcium–magnesium ratio and specific activity of the samples of selected bones are given in Table 1. The specific activities are expressed both as the percentage of dose × 10^2 per mgm. of total magnesium and as the percentage of the specific activity of the plasma, the latter being a measure of the proportion of bone magnesium which has exchanged with the magnesium of body fluids during the 10-hr. period.

A marked variation in specific activity from bone to bone was observed and was greater in regions of rapid bone metabolism than in compact bone. Thus

Table 1. RATIO OF CALCIUM TO MAGNESIUM IN THE SELECTED BONES AND THEIR UPTAKE OF MAGNESIUM-28 AT 10 HR. AFTER INTRAVENOUS ADMINISTRATION

Bone	Calcium/magnesium	Specific activity (percentage of dose) (× 10^2 per mgm. magnesium)	Specific activity (as percentages of specific activity of plasma)
Femur shaft	57	0·048	0·86
Femur epiphysis	52	0·130	2·3
Rib shaft	56	0·079	1·4
Rib sternal end	46	0·129	2·3
Lumbar vertebra	46	0·099	1·7

the sternal end of the rib and the epiphysis of the femur showed the greatest exchange and the femur shaft the lowest.

The over-all percentage of bone magnesium in equilibrium with the magnesium in the body fluids was low; the values for the samples of individual bones ranged from 0·86 to 2·3 per cent. The limiting factor may be the exchange-rate itself or the amount of bone magnesium which is available for exchange. It is interesting to note that the variation in specific activity of individual bones was in the same order as the degree of magnesium depletion in the corresponding bones from magnesium-depleted calves[3].

There are no analytical figures in the literature for the magnesium content of the skeleton of either adult cattle or sheep. Estimates can be made from the calcium content of the skeleton of dairy cows[4] and sheep, and the calcium–magnesium ratio in bone. The calculated values for cows range from 90 to 160 gm. depending on the size of the animal, and for sheep from 8 to 10 gm.; the figures for sheep are based on only three analyses. If the reserves of bone magnesium are assumed to be the same as the percentage of bone magnesium which has later reached equilibrium with the magnesium of body fluids, namely, 2 per cent, the skeleton of dairy cows contains 1·8–3 gm. of magnesium which can be released to satisfy physiological needs, that is, enough for 3–5 gallons of milk. In the case of sheep, the reserves (160–200 mgm.) are equivalent to the endogenous fæcal loss for 1 day[5]. The lactating animal may be more efficient in mobilizing bone magnesium than the non-lactating animal, since the resorption of bone mineral to provide the calcium necessary for lactation will also release magnesium[6]. This effect, however, will be small because of the wide ratio of calcium to magnesium in bone and the fact that the release of calcium from bone is small, for example, less than 20 gm. a day for dairy cows[6].

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BIOLOGY

Effect of Chelating Agents on Plasmodium Formation by the True Slime Mould, *Didymium nigripes*

SPORES of *Didymium nigripes*, a true slime mould, germinate to liberate myxamœbæ which multiply by binary fission. After a period of exponential growth, the uninucleate myxamœbæ fuse to form macroscopic, multinucleate veins of rhythmically flowing protoplasm called plasmodia. Following an indefinite period of growth, the plasmodia differentiate into spore-containing fruiting bodies. Kerr and Sussman[1] grew *D. nigripes* in monoxenic culture with *Aerobacter aerogenes* on a dilute glucose–peptone–yeast extract agar medium buffered with phosphate at *p*H 6·2 (hereafter called GPY/5). All stages of the life-cycle were regularly reproduced in less than 7 days. When 0·25 per cent (w/v) brucine was added to the GPY/5, plasmodia did not appear. Instead, the myxamœbæ remained indefinitely as such and could be sub-cultured as amœbæ. The myxamœbæ quickly formed plasmodia when harvested from the GPY/5-brucine plates and washed by differential centrifugation.

The morphogenesis of uninucleate myxamœbæ to multinucleate plasmodia is one of the most interesting, but least understood, stages in the life-cycle of the true slime moulds. According to Cadman[2] and Ross[3], plasmodium formation involves the pair-wise fusion of myxamœbæ as gametes to form zygotes. Presumably the zygotes develop into plasmodia by growth, nuclear division, and fusion with other zygotes. Since an understanding of this morphogenesis is an essential prerequisite to studies on the genetic life-cycle, and to studies of heterokaryosis and nuclear-cytoplasmic interrelationships in the plasmodium, an elucidation of its mechanics has been undertaken. The mechanism by which brucine inhibits plasmodium formation was studied in the hope that it would yield information on the normal process of plasmodium formation.

One possible action of brucine might be to stimulate the bacterial associate to produce a metabolite which in turn would inhibit plasmodium formation. This possibility was tested by growing myxamœbæ on GPY/5-brucine with a variety of bacterial associates, including *Escherichia coli*, *Sarcina lutea*, *Pseudomonas fluorescens* and *Aerobacter aerogenes*. Plasmodia did not appear in any instance. It therefore seemed probable that brucine was acting directly on the myxamœbæ rather than via the bacterial associate.

Several lines of evidence indicated that brucine might be inhibiting plasmodium formation by chelating with ions in the medium. First, although the medium used was saturated by 0·1 per cent (w/v) brucine, the inhibitory action of brucine became more and more complete as its concentration was raised to 0·25 per cent. This might be expected if brucine were acting as a chelating agent, but not if it were acting as a metabolic inhibitor. Second, brucine inhibits the formation of plasmodia rather than plasmodia themselves, for if plasmodia are sub-cultured on GPY/5-brucine, they grow and fruit normally. Third, the density of myxamœbæ profoundly influences the number of plasmodia which they form. Even in the absence of brucine, plasmodium formation was delayed when the myxamœbæ quickly reached a high density. Plasmodia appeared in greatest number when the myxamœbæ exhausted their bacterial food supply while still at a relatively low density. Brucine-inhibition was complete only when the myxamœbæ covered the entire plate at high density before exhausting their food supply; when myxamœbæ were plated clonally on GPY/5-brucine, occasional plasmodia appeared.

As a result of these observations, experiments were devised to test the hypothesis that multivalent cations are essential to plasmodium formation. The results are reported in Table 1. Chelating agents were added to GPY/5 media which were spread with spores of *D. nigripes* and 0·3 ml. of a broth culture of *A. aerogenes*. In each case the *p*H was adjusted to 6·0–6·5. The plates were incubated at 22° C. for 4 days and then scored for growth of myxamœbæ and appearance of plasmodia. Tetrasodium ethylenediamine tetraacetic acid at 10^{-3} *M* completely prevented the formation of plasmodia, even when the spores gave rise to clones. Either 10^{-3} *M* Mn^{++} or 10^{-3} *M* Fe^{++} reversed the inhibition of ethylenediamine tetraacetic acid to permit numbers of plasmodia to form. None of the other ions tested was effective. Other chelating agents, including sodium citrate, were also effective in inhibiting plasmodium formation.

Table 1. THE GROWTH OF MYXAMŒBÆ AND APPEARANCE OF PLASMODIA ON GPY/5 MEDIA TO WHICH VARIOUS AGENTS HAD BEEN ADDED

Addition	Amœbæ	Plasmodia
Control	+++	+++
0·25 per cent (w/v) brucine	+++	0
0·1 *M* Sodium citrate	++	0
10^{-3} *M* Ethylenediamine tetraacetate acid	++	0
5×10^{-4} *M* Ethylenediamine tetraacetic acid	+++	+
10^{-3} *M* Ethylenediamine tetraacetic acid		
+ 10^{-3} *M* calcium chloride	++	0
+ 10^{-3} *M* strontium chloride	++	0
+ 10^{-3} *M* magnesium chloride	++	0
+ 10^{-3} *M* manganese chloride	++	++
+ 10^{-3} *M* ferrous chloride	++	++

The experimental results thus confirm the hypothesis that multivalent cations are necessary for plasmodium formation. A likely mode of action of brucine is as a chelating agent, removing these ions from the medium.

The development of a technique which will measure plasmodium formation in a quantitative manner is in progress. These experiments will be reported elsewhere.

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Effect of Extracts from Fucoids in promoting Settlement of Epiphytic Polyzoa

IN a previous communication[1] it was suggested that the simple ciliated larvæ of some species of sedentary organisms might respond to qualitative differences in bacterial films formed on surfaces immersed in the sea, as was suggested by Wilson to explain the behaviour of the larvæ of *Ophelia bicornis* Savigny[2].

Table 1. SETTLEMENT OF *Alcyonidium polyoum* ON TREATED INERT SURFACES

Type of surface	No. settled in experiment (1)	(2)	(3)	Total No. of settled larvæ
Unfilmed surface	5	3	3	11
Surface filmed by standing in sea water for 24 hr.	1	4*	0	5
Surface similarly filmed and treated with extract of *Fucus serratus* in distilled water	90	46	26†	162

* Treated with distilled water for 2 hr. after filming.
† Extract of *Fucus* made up in sea water.

Table 2. RATIO OF NUMBER OF LARVÆ OF *Alcyonidium polyoum* SETTLED ON FILMS TREATED WITH ALGAL EXTRACTS (n_A) IN COMPARISON WITH SETTLEMENT ON FILMS TREATED WITH *F. serratus* (n_F)

Algal extract of :	Ratio n_A/n_F	
Fucus serratus	1·00	Probably effective
Fucus vesiculosus	1·04	
Ascophyllum nodosum	1·72	
Pelvetia canaliculata	0·63	
Fucus spiralis	0·09	Not effective
Laminaria digitata	0·25	
Ulva lactuca	0·04	
Gigartina stellata	0·00	
Control	0·22	

Some recent experiments with the larvæ of the polyzoan *Alcyonidium polyoum* (Hassall) have confirmed this. This species normally occurs on the fronds of *Fucus serratus* L., and its larvæ settle preferentially on fronds of this and related fucoids when offered a choice of different algal fronds[3]. When these larvæ were placed in a glass vessel and offered small rectangular pieces of inert material for settlement, as described in a previous communication[1], they tended to avoid filmed surfaces, as did the larvæ of *Bugula flabellata*, though they did not settle very readily on unfilmed surfaces. However, when the filmed surfaces were treated beforehand with an extract of *Fucus serratus* they become very attractive to the larvæ, as can be seen from Table 1. Extracts of other algæ were tested in the same way, but only certain species were regularly effective in promoting settlement. It can be seen from Table 2 that those species which promoted settlement all belonged to the Fucaceae. Of the most attractive sources, *Fucus serratus* L., *Fucus vesiculosus* L. and *Ascophyllum nodosum* (L.) le Jol, only *F. serratus* normally bears colonies of *Alcyonidium*. Perhaps the other two fucoids occur too high up the shore, or do not liberate the active principle on to the surface of the thallus. Similar results have also been obtained using the larvæ of the closely related polyzoan *Flustrellidra hispida* (Fabricius).

The settlement of these larvæ seems not to be due to any physical property of the film, such as its thickness, since, in the absence of *Fucus* extract, filmed surfaces are not attractive. However, when unfilmed surfaces were briefly treated with the extracts they did not attract the larvæ strongly; only filmed panels could be made artificially favourable for settlement.

The bacterial film is therefore necessary to promote good settlement, but it must be treated with the extract. The simplest hypothesis is that the active principle is transferred to the film, and, as it diffuses out, it attracts the larvæ. Other mechanisms which may lead to larval recognition are possible, however; for example, the existing bacterial film may modify substances present in the *Fucus* extract, or the bacterial flora of the film itself may be altered in the presence of an extract of *Fucus*. The mechanism by which the larvæ of *Alcyonidium polyoum* and *Flustrellidra hispida* recognize the treated film is now being investigated, while similar phenomena are being sought in the settlement behaviour of other marine larvæ.

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Sex Hormones as a Possible Factor influencing the Level of Parasitization in Frogs

LARGE numbers of frogs (*Rana temporaria*) have been examined for helminth parasites during the period 1956–60. On analysing the results of these investigations, it was found that the level of parasitization in male frogs during and immediately before the breeding season was considerably higher than that in females. This difference between the levels of parasitization in the two sexes was particularly marked in the case of the trematodes, *Polystoma integerrimum* and *Gorgoderina vitelliloba*, the nematode, *Rhabdias bufonis*, and the acanthocephalan, *Acanthocephalus ranae*. After the breeding season, the difference became less marked. This is evident from Table 1, which is based on the results obtained by examining approximately 500 frogs from a single locality, over a period of four years.

Table 1. LEVELS OF PARASITIZATION OF MALE AND FEMALE FROGS DURING AND OUTSIDE THE BREEDING SEASON

Species of parasite	Percentage of frogs parasitized during January and February		Percentage of frogs parasitized during April and May	
	Males	Females	Males	Females
Trematodes				
Polystoma integerrimum	14·0	8·1	16·1	17·0
Gorgoderina vitelliloba	10·2	5·3	12·8	7·6
Dolichosaccus rastellus	8·9	10·2	5·3	6·2
Haplometra cylindracea	49·6	41·8	53·0	44·4
Nematodes				
Rhabdias bufonis	52·3	29·4	47·8	37·4
Oswaldocruzia filiformis	71·6	82·3	76·9	74·2
Cosmocerca ornata	86·3	94·1	88·4	92·3
Acanthocephala				
Acanthocephalus ranae	13·4	8·0	22·5	24·0

Similar, although less conclusive, results have been obtained by Markov[1] and Mazurmovich[2].

The difference in parasitization-levels of male and female frogs, well marked in the breeding season and much less well marked at a time of the year when the gonads have suffered regression, may be explained by assuming that the female sex hormones depress the level of parasitization in some way or other. In order to test this particular hypothesis we took fifty male frogs from a population known to be heavily parasitized with helminths, and injected half of them with œstradiol benzoate (B.P.) in 20 per cent ethyl oleate and 80 per cent arachis oil. The other half were regarded as controls. The experimental series were given 0·5 mgm. of œstradiol benzoate in 0·1 mgm. doses over a period of 12 days. At the end of three weeks both the experimental and control frogs were killed and examined for helminths.

Table 2. COMPARISON OF PARASITIZATION-LEVELS IN MALE FROGS TREATED WITH ŒSTRADIOL AND UNTREATED FROGS

Species of parasite	Percentage of control frogs parasitized	Percentage of experimental frogs parasitized
Trematodes		
Polystoma integerrimum	16	4
Gorgoderina vitelliloba	24	12
Dolichosaccus rastellus	12	0
Haplometra cylindracea	56	40
Nematodes		
Rhabdias bufonis	64	32
Oswaldocruzia filiformis	80	72
Cosmocerca ornata	90	72
Acanthocephala		
Acanthocephalus ranae	20	8

The results of this examination are given in Table 2.

The results of these preliminary experiments suggest that the presence of the female hormone, œstradiol, in the tissues and fluids of the host does lead to a depression of the level of parasitization by helminths. We propose to investigate this phenomenon in more detail.

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Mobility of Barnacles

IF a young barnacle is removed from a surface the remains of the antennal suckers, marking the point at which the individual cemented itself as a cypris larva, may sometimes be found near the centre of its base. It has generally been assumed that this point of basal attachment is fixed. The position selected by the barnacle, when a larva, would then always be included within the outline of its base, though not necessarily at the centre, for if growth were not radially symmetrical the original point of attachment might become eccentric.

Recent experiments have been carried out in which the growth of operculate barnacles has been followed after they have settled on transparent plates. These observations show quite clearly that such animals possess a limited mobility when subjected to lateral pressure. If one side of a young colony is cleared of settlement and kept bare, the individuals forming the free edge of the colony will be pushed outwards by the growth of the rest. This pressure, exerted over a period of several months, can displace the outermost individuals a few centimetres from their original position. Fig. 1 shows how a young individual can be moved through several times its own diameter during the first six months of life. Evidently the cement layer between the hypodermis and the solid surface must slowly be sheared as it allows the shell and membranous base to glide along. The advancing edge of the base can form new adhesions to the substratum in the same way that it does during the expansion of the base in normal growth. Rotation of the barnacle in response to currents probably occurs also in the same manner[1]. Mobility has been observed both on smooth and on uneven surfaces.

Balanus balanoides, in common with other barnacles, has very strong powers of adhesion, so that when a number of individuals of about equal size

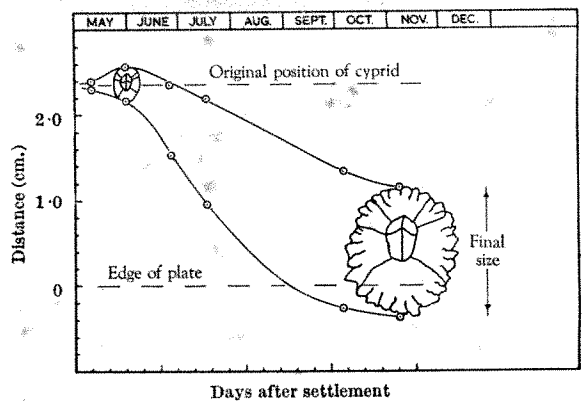

Fig. 1. Illustration of the movement of an individual *Balanus balanoides* (L.) which had settled at a distance of 2·4 cm. from the edge of a flat plate and was subjected to lateral pressure from other individuals growing above it (not shown). The ordinate gives the distance from the edge of the plate of the carinal and rostral ends of the base of the barnacle, the distance separating the lines representing its basal diameter. The abscissa gives the time which elapsed after settlement. By September the individual illustrated had begun to be forced over the edge of the plate

come in contact their bases remain attached to the solid surface and their sides become pressed together. Continued growth is then possible only upwards, unless the peripheral individuals can be slid outwards, when limited expansion of the whole colony may occur under its own two-dimensional pressure.

When the individuals which come into contact are not of the same age or do not belong to the same species, the result may be quite different. One specimen, usually the older, remains firmly attached, while the other is gradually displaced upwards on to the advancing shell plates of the former. This process can be readily observed when later settlements of *Elminius modestus* insinuate themselves among fast-growing spat of *Balanus balanoides*. The former are so completely squeezed out that they may come to project above the general level and can be detached by a gentle blow. If such individuals survive, their elevated position has some advantages, allowing more rapid growth and earlier maturity[2], and tending in the end to cause the underlying individuals to become silted up and smothered.

The ability to adhere strongly to a surface, but at the same time to retain sufficient mobility to move a short distance or to readjust themselves to alterations in the shape of the substratum, has two obvious advantages. It allows barnacles to grow on such surfaces as the shells of other animals, where there are slow relative movements or a gradual expansion of the whole area, without the danger of losing their adhesion. It also allows them, provided that the original settlement was sufficiently heavy, to expand into nearby bare spaces on a solid surface which were not, for some reason, initially colonized.

Most barnacles, within their normal geographical range, produce a superabundance of planktonic larvæ, which settle in greater numbers than is necessary for survival. Consequently the factor which chiefly limits the size of populations is shortage of settling space. Each species must therefore, so far as possible, occupy all the surface suitable to it and exclude competing organisms. It is in this respect that the faculty of limited mobility is of such importance. Without it a colony of barnacles would be able to occupy only a small area around each of the positions initially selected by the cyprids, and

competing organisms would be quite free to settle afterwards in any of the spaces left unoccupied. Without such mobility young individuals growing among larger ones would be easily lifted off or crushed as the older ones crowded them in; this indeed may sometimes happen[3]. The limited degree of sliding and adjustment possessed by barnacles therefore confers an advantage both to established populations, which are able to expand over any available space, and also to invading populations of new spat, which may in consequence be able to form a second tier of individuals using their competitors as an alternative, though mobile, substratum. The outcome of such a struggle between species depends not only on settlement pattern, population density and relative growth-rates, but also on the forces operating between the growing edge of the shell of each species and the substratum with which they are both in contact.

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Mechanism of Change in Permeability in Living Membranes

AN important feature of many excitable cells is that their permeability to ions and even to large molecules such as aldolase depends on the potential difference across the cellular membrane[1]. Thus, in nerve fibres a depolarization leads to a transitory increase in sodium permeability (P_{Na}), often followed by a slower development of an increase in potassium permeability (P_K). More recent studies of skeletal[2,3] and cardiac (Carmeliet, E., and Weidmann, S., personal communication) muscle have demonstrated an opposite relation between P_K and membrane potential that has been designated 'anomalous rectification'. The purpose of this communication is to point out the possibility that the mechanism of these changes in permeability may be related to that recently proposed on the basis of monomolecular film studies of drugs known to affect the ionic permeability of natural membranes[4-6]. This mechanism is based on recently demonstrated physico-chemical principles and is susceptible to experimental test.

Agents such as local anæsthetics, designated as 'stabilizers', decrease the permeability of living membranes or depress their ability to undergo the rapid increase in permeability during excitation[1,6]. They interact with monolayers of lipoidal molecules (for example, stearic acid) and thereby add their own bulk to the films; thus, molecular packing is increased, as reflected by a rise in surface pressure[5-9]. Conversely, compounds called 'labilizers' or 'unstabilizers', such as certain veratrum alkaloids, increase membrane permeability[1,6]. These gradually remove the lipoidal molecules from the monomolecular films and hence reduce packing and surface pressure[4,5]. It has been proposed from such observations and others that the degree of packing of membrane molecules surrounding a site of ion passage (for example, an intermolecular space) is related inversely to (*a*) the ease of ion transport, and especially (*b*) to the ability of ion transfer to increase during excitation[1,5,6]. The concept of changes in surface pressure through effects in the region adjacent to the locus of ion penetration focuses attention on membrane organization, which must be mesomorphic, that is, intermediate to a liquid and a solid[10]. Previous research has suggested this type of structure[6]; our recent work also suggests this, for the antagonistic effects of stabilizers and labilizers became apparent in the monolayers when the films are compressed to a condition intermediate to that of a liquid and solid[5].

The work on drugs has led to emphasis on electrostatic and van der Waals interactions between the membrane and extrinsic molecules as the basis for changes in packing and in permeability. The possibility of such changes with membrane potential arises if the natural membranes contain lipophilic (hydrophobic) cations and anions at low concentration. Guastalla *et al.*[11] have already shown that relatively weak electrical gradients (V./cm.) can govern the accumulation of such ions at an oil–water interface, the speed of the process depending on the intensity of the applied field. Natural membranes, with a thickness of the order of 100 Å., have across them a 'resting potential' of about 100 mV. and hence an electric field, E, of 100,000 V./cm.; the inner boundary is normally negative to the exterior[6].

Because of their nature, the lipophilic ions would not leave the membrane readily; therefore they would be distributed by the field as shown diagrammatically in Fig. 1*A*. The sketch on the left indicates only the ions capable of interacting with membrane molecules in the regions of sodium transfer, that on the right only those able to affect potassium transport. A_1 represents a small anion, perhaps with several charges, C a large cation with fewer charges, and A_2 an anion comparable in bulk and in number of charges to C. One more assumption is inherent in the model, namely, that only the outermost interface, M, possesses the mesomorphic state required for the permeability changes. The deeper region of the membrane is regarded as essentially fluid, thereby serving as a reservoir of lipophilic ions without contributing directly to the permeability changes. Experimental evidence for a superficial layer as the basis of permeability change in living membranes has recently been presented by Shanes and Berman[12], who also direct attention to other indications for this in the literature. The concentrations of the ions on the inner boundary of the interface regulate their degree of interaction with M.

Fig. 1*B* indicates an intermediate stage in the redistribution of the hydrophobic ions during a sudden depolarization of the membrane. A_1, by virtue of size and charge, responds most rapidly to the alteration in E. As it moves out of M, P_{Na} increases. If the depolarization is sustained, as shown in the lowermost part of Fig. 1, C becomes more uniformly distributed and so enters M and reduces P_{Na} again. Such a secondary decrease in P_{Na} is well known and has been designated 'inactivation'. Finally, as A_2 leaves M, P_K increases. If, in addition to or instead of A_2, cations were available comparable to C but more effective and able to enter the regions of potassium transport, then instead of the more familiar increase in P_K (and membrane conductance) with depolarization, that is, delayed rectification, a decrease would be obtained, that is, anomalous

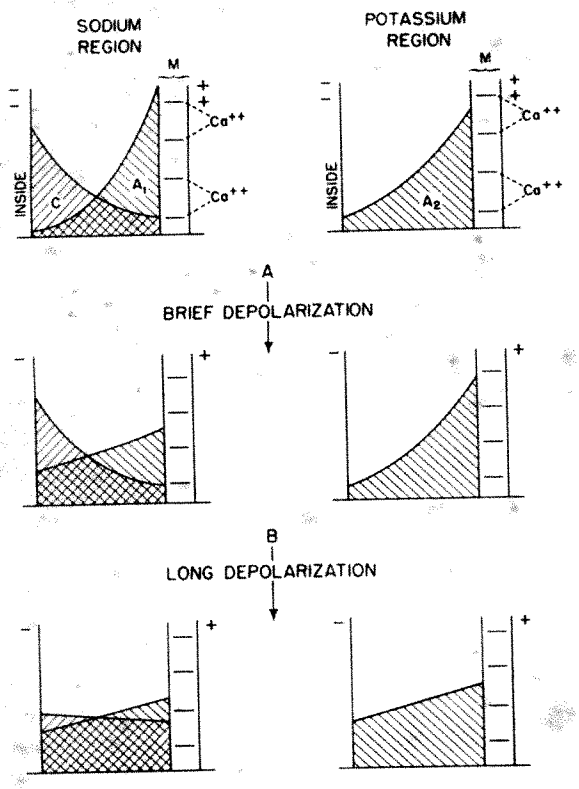

Fig. 1. Hypothetical representation of the distribution of lipophilic cations and anions in a resting, normally polarized excitable membrane (A) and during two successive periods of a moderate depolarization. M is an outer mesomorphic region susceptible to change in permeability by interaction with drugs or with the lipophilic anions (A_1, removal of which increases P_{Na}, and A_2, removal of which increases P_K) and cations (C, entry of which causes inactivation, that is, a secondary decrease in P_{Na}). The negative sites in M are molecular groups that contribute to cation selectivity; they are shown as partly occupied by calcium in the normally polarized cell

rectification. From this point of view, then, anomalous rectification is similar to the inactivation process for sodium, but apparently more effective inasmuch as permeability to potassium is lowered below the resting level. However, this difference in the inactivation processes might be merely a reflexion of a deficit in A_2, a deficit which makes P_K at rest comparable to P_{Na} after A_1 has been partly removed. S. Weidmann's observation (personal communication) that potassium depolarization produces relatively little increase in the membrane conductance of Purkinje fibres appears in keeping with this.

It would be premature to contend that all changes in permeability can be ascribed to one principle. For example, it is possible that at least part of the increase in permeabilities during depolarization is a consequence of removal of calcium ions from superficial sites concerned with ion passage[13]. Such removal could increase permeability by allowing the monovalent ions to penetrate at these points; in addition, it is possible that calcium removal exposes adjacent negative groups of neighbouring molecules in the membrane, which are thereby driven apart to admit sodium and potassium ions and perhaps large molecules as well. In keeping with these proposals, lowering of pH also accomplishes a reduction in ion permeability[6]. Note, however, another possible role for calcium (and hydrogen) ions in Fig. 1. By neutralizing negative groups of the membrane molecules in M, calcium could reduce the repulsion of anions and so enhance the entry of A_1 and A_2 into M, thereby lowering the permeability to sodium and potassium; concurrently, the attraction for cations would be reduced, thereby decreasing the entry of C into M and hence suppressing inactivation. This provides an electrostatic basis for the similarity between calcium deprivation and depolarization in respect of their effects on permeabilities and on inactivation[14,15].

It is necessary to set up working models employing the principles that have been outlined to determine to what extent the kinetics of changes in permeability in living systems can be duplicated. A possible test of the validity of the proposed hypothesis would be to determine whether the effects of various lipophilic ions, for example, tetraethylammonium and tetrabutylammonium, which have been striking in some excitable cells[16,17], give evidence of being modified in a predictable manner by alterations in membrane potential.

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Colchi-Autotetraploidy in *Adiantum capillus-veneris*

FERNS are well known for possessing polyploid complexes, but we do not know of any instance where Howard and Manton's[1] method has been used for analysis of their genome relations and elucidation of their nature of polyploidy. The primary reason for this appears to be the difficulties involved in raising autotetraploids in ferns. So far the standard practice has been to raise such strains by apospory[2]. Manton[3] alone made a meiotic analysis of the autopolyploid series in *Osmunda regalis* L. following this method and found reasonably high degree of multivalents.

The aposporous method of raising autopolyploids has certain inherent limitations in that it is laborious, time-consuming and above all it is uncertain. On the other hand, colchicine treatment is the most sure method available at present for inducing polyploidy. However, so far there has been a solitary attempt by Panigrahi[4], who applied colchicine to the young embryos of *Cyclosorus repandulus* (v.A.v.R.) Ching

at the three-leaved stage, but could only obtain a sectorial chimera as evidenced by root tip smears while no fronds were borne on it. We have treated with colchicine the rhizomes of a few locally available ferns. Besides easy manipulation, the rhizome treatment gives quick results and eliminates the long time that is usually required for the sporophytes to reach maturity in case of spore, sporeling and embryo treatments. Of the three methods tried (immersion in aqueous solution of colchicine, lanolin paste and injections) we find the immersion in 0·5 per cent solution for nearly 48 hr. to be uniformly successful. The rhizomes were not defoliated because otherwise the first leaves produced would be sterile and also the rhizomes usually die after treatment when defoliated. The present account deals with the results on *Adiantum capillus-veneris* L. Here the new fronds start appearing within about three weeks after treatment. A morphological comparison with the controls treated similarly with distilled water revealed that autotetraploids, though smaller in size, show the usual *gigas* characters (thickness of rachis and lamina, stomatal size).

During meiosis the controls show invariably 30 bivalents (Fig. 1). The autotetraploids possess quadrivalents and bivalents. An analysis of ten exceptionally clear cells reveals that the number of quadrivalents ranges from 13 to 10 and the bivalents from 34 to 40. The average associations are $12_{IV} + 36_{II}$ (Fig. 2). The quadrivalents are in the form of rings or chains and possess almost completely terminalized chiasmata at diakinesis. The high degree of terminalization may also augment the normal disjunction during anaphases. In one case two bivalents showed early disjunction. Meiosis is perfectly normal and apparently normal spores result. In *Osmunda regalis*[3] the percentage of quadrivalents per cell is nearly 66, while in the present case it is about 40, and trivalents are absent. The difference may be due to the smaller size of the chromosomes in the latter.

As indicated above, the spores are well filled and apparently normal. Sixty-four spores result in each sporangium. Interesting enough is the presence among them of about 3–5 per cent spores with bilateral symmetry, while the rule for the species and the genus is tetrahedral. Perhaps this may be due to the colchicine action. It is pertinent to mention here that Mehra and Loyal[5] have observed another aberration, namely, branched rhizoids, being caused by colchicine action in the sporelings of *Goniopteris prolifera* Roxb. The change in symmetry of the spores is not due to the polyploid condition, because no such aberration has been found in any of the polyploid ferns discovered so far in Nature.

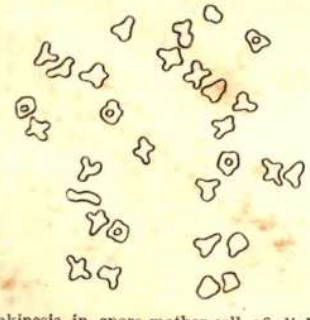

Fig. 1. Diakinesis in spore-mother-cell of diplold *Adiantum capillus-veneris*, $n = 30$. (× 1,000)

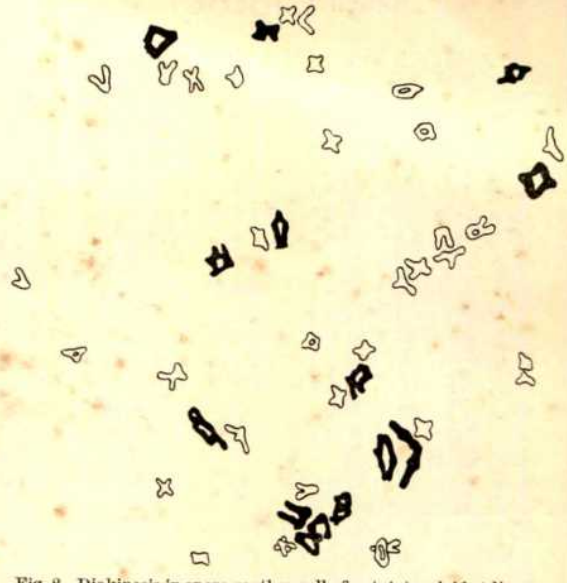

Fig. 2. Diakinesis in spore-mother-cell of autotetraploid *Adiantum capillus-veneris*, showing $13_{IV} + 34_{II}$. (× 600)

The present findings reveal that the rhizome treatment has obvious advantages over the uncertain method of apospory. Here in the meristem there is a single apical cell, the products of which give rise to the leaf and root primordia. Hence once the apical cell is rendered polyploid, all the subsequent fronds will naturally be autopolyploids, some of which will be fertile. The resulting spores should normally yield diploid gametophytes which can be used for crossing with natural tetraploids.

The occurrence of perfectly normal disjunction and well-filled and apparently normal spores by the autotetraploid in *Adiantum capillus-veneris* is rather important. The reason for this may lie in the fact that the present species is diploid throughout its range, and that in the genus there already exist potentialities for polyploidy up to the hexaploid[6] (apogamous) level. Furthermore, the heterozygous nature of this horticultural fern is an additional point in favour. These are the two important points that are usually taken into consideration before embarking on a programme of induced autopolyploidy.

Apart from assessing the role of autopolyploidy in the evolution of ferns, the autopolyploids will also be useful in producing autotriploids from which trisomic lines for genetic studies may be raised. Their use in biosystematic studies of the fern polyploid complexes is of course unquestioned. The details of this work will appear elsewhere.

We are indebted to Prof. P. N. Mehra for advice, and to Dr. T. N. Khoshoo for criticism.

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MICROBIOLOGY

Alleged Transformation of Yeast

CRUDE preparations of deoxyribonucleic acid from one yeast strain, called the donor, sometimes appear to confer fermentation properties of the cell on a second strain, the acceptor, when added to the growth medium[1-3]. For example, when a yeast which did not ferment sucrose was grown in wort containing a preparation of deoxyribonucleic acid derived from a sucrose-fermenting strain, the transfer of part of the culture to a bijou bottle containing sucrose dissolved in yeast water (3 per cent 'Difco' yeast extract in water) resulted in fermentation. Single-cell isolates obtained from the treated yeast, which had been serially subcultured through the same medium, also fermented sucrose, and on crossing with the original acceptor strain gave Mendelian segregation of sucrose-fermenting power. These observations were explained[1-3] by assuming that nuclear transformations akin to that already observed in various bacterial species[4-9] had been induced in the acceptor yeast by the deoxyribonucleic acid from the donor. In view of the potential importance of such transformation from both the technological and scientific points of view an attempt has been made to investigate this phenomenon further.

The yeast strains used were those originally employed by Oppenoorth[2]. The acceptor strains included (1) *R7*, a yeast which was originally isolated by Winge and Roberts as a descendant of crossings between strains of *Saccharomyces cerevisiae*, *Saccharomyces chevalieri* and *Saccharomyces italicus*, and (2) *S. chevalieri K83S58*. Both acceptor yeasts fermented galactose and glucose but neither fermented raffinose or sucrose. The donor strain was *S. chevalieri W332*, which fermented both raffinose and sucrose.

Preparations of deoxyribonucleic acid were obtained from 48-hr. cultures of the donor yeast grown in shake culture at 25° C. in either wort or a medium consisting of yeast extract (Difco, 0·3 per cent), malt extract (0·3 per cent), peptone (0·5 per cent) and glucose (1·0 per cent) in water. The extraction procedure for deoxyribonucleic acid and the method of dissolving the product in wort were as described by Oppenoorth[2]. As will emerge, a critical finding was that the sterilization procedure used for the solution of deoxyribonucleic acid affected the result. The solution was sterilized either by (*a*) filtration through a glass filter (porosity *S*) or (*b*) filtration through a Seitz filter containing a Ford 'Sterimat' pad (grade *SB*). A solution (3·0 ml.) of ethanolic hydrogen chloride, prepared by diluting concentrated hydrochloric acid (8·0 ml.) to 100 ml. with ethanol, was added to aliquot portions (1·0 ml.) of the solution of deoxyribonucleic acid before and after sterilization. After standing for 15 min. the resulting precipitate was removed by centrifugation, washed with ethanolic hydrogen chloride and dissolved in water for estimation of deoxyribonucleic acid content by the method of Seibert[10]. It was afterwards found that sterilization by method (*a*) had no significant effect on the concentration of deoxyribonucleic acid, but sterilization by method (*b*) completely removed the deoxyribonucleic acid from solution in wort.

The effects of the solutions obtained by methods (*a*) and (*b*) on the acceptor strains were then investigated. In a typical case a series of McCartney bottles containing wort (4·0 ml.) or the test solution (4·0 ml.) was inoculated from a 1-day culture of yeast *R7* grown in wort. The yeast was incubated with shaking at 25° C. for 4 days. After growth the wort was removed by centrifugation and the residual yeast suspended in water (0·2 ml.). Aliquot portions (0·04 ml.) of the suspensions were then transferred in duplicate to bijou bottles, individually containing sucrose (2 per cent) dissolved in yeast water, while the remaining yeast was washed four times with water. The latter yeast was suspended finally in water (0·12 ml.) and duplicate portions (0·04 ml.) were transferred to sucrose medium as before. At the same time a portion of the washed yeast suspension was serially diluted with water to give cell concentrations of approximately 1×10^8, 5×10^5 and 1×10^3 cells/ml. and portions (0·02 ml.) of these suspensions were inoculated on to a solid medium prepared by the incorporation of agar (Davis 'Nutrient', 2 per cent) into the synthetic medium of Harris and Thompson[11] and using sucrose (0·5 per cent) as the source of carbon instead of glucose. The donor yeast grew satisfactorily on this medium while the acceptor yeasts failed to grow although they were viable as shown by growth when glucose was the carbon source. The bottles and plates were incubated at 25° C. and examined at intervals over a period of 30 days. The ability of the yeast to grow on the synthetic medium containing sucrose as sole carbon source was also investigated by means of the hæmocytometer slide-culture technique of Gilliland[12], which more accurately reflects the ability of cells to grow than the conventional plating techniques. In this instance, a portion of the washed yeast was suspended in the synthetic medium containing gelatin (6 per cent) and incubated on the slide at 18° C. for 6 hr. The slides were then examined microscopically for micro-colonies arising from sucrose-fermenting strains. The results (Table 1) show that: (1) the ability of the acceptor yeast to ferment sucrose was lost by thorough washing; (2) the presence of deoxyribonucleic acid in the growth medium was not necessary for a positive fermentation result to be observed; and (3) the ability of the yeast to ferment sucrose was not reflected in its ability to grow on solid medium with sucrose as sole carbon source.

Table 1. SUCROSE FERMENTATION BY ACCEPTOR YEASTS TREATED IN DIFFERENT WAYS

Growth medium	Treatment of yeast	Fermentation result*	
		Yeast *R7*	Yeast *K 85S58*
Wort	washed	none	none
Wort	unwashed	none	none
Wort/deoxyribonucleic acid Seitz filtered	washed	none	none
Wort/deoxyribonucleic acid Seitz filtered	unwashed	+ (after 2 days)	+ (after 2 days)
Wort/deoxyribonucleic acid glass filtered	washed	none	none
Wort/deoxyribonucleic acid glass filtered	unwashed	+ (after 2 days)	+ (after 2 days)

* No growth was observed on sucrose plates or sucrose–gelatin slides

A possible explanation of the results was that invertase was present in the deoxyribonucleic acid preparations used. To investigate this possibility, portions (0·01 ml.) of the deoxyribonucleic acid/wort solution were added to bijou bottles containing sucrose or raffinose (2·0 per cent) dissolved in yeast water. After incubating for 24 hr. at 25° C. the sugars present were examined by chromatography using a mixture of ethyl acetate, pyridine and water (10 : 4 : 3, v/v) as developing solvent and the dip

reagent of Harris and MacWilliam[13] for detecting the sugars. It was thus found that considerable hydrolysis of sucrose and raffinose to monosaccharides had in fact occurred. Clearly, the deoxyribonucleic acid preparation was contaminated with invertase in sufficient quantity to yield monosaccharides responsible for the positive fermentation tests observed in the earlier work. Moreover, the enzyme passed through the Seitz filters used and gave rise to the positive fermentation tests even in the absence of deoxyribonucleic acid. It is therefore apparent that such fermentation tests are insufficient in themselves to indicate transformation. The further evidence for transformation presented earlier, namely, the isolation of single cells capable of fermenting sucrose or raffinose from subcultures originally not possessing this faculty, is not conclusive. In this connexion, the presence of hydrolytic enzymes in the test medium will allow growth to occur on the monosaccharides produced when the yeast is sub-cultured through a series of bijou bottles containing the test polysaccharide. In these circumstances cells capable of fermenting the polysaccharide might arise by mutation and subsequent selection even though controls not containing the deoxyribonucleic acid–enzyme mixture as used by Oppenoorth[2] fail to produce mutants of this type. It appears therefore that the evidence presented for transformation of yeasts in the manner suggested is capable of alternative explanation, and that further investigation is required to substantiate the earlier claims.

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VIROLOGY

Plaque Formation by an Orphan Virus of Fowls

WHEN Sharpless *et al.*[1] and Fontes *et al.*[2] reported the adaptation of fowl lymphomatosis virus (*RPL*.12) to chicken embryo tissue culture, and later when plaque assay methods were described for this virus[3–5], there was promise of an *in vitro* system for the study of viral oncogenesis. However, the suspicion that this virus may not in fact be the causal agent of fowl lymphomatosis was aroused when it was found that the inoculation of high-titre tissue culture material into chickens of a stock known to be susceptible to the *ES*4 strain of fowl lymphomatosis virus was not followed by the formation of tumours even after six months. Moreover, when these birds were challenged with *ES*4 virus, they were found to be completely susceptible (Carr, J. G., Macpherson, I. A., and Stoker, M. G. P., unpublished results). It was also shown that a high dilution of pooled normal sera from the *ES*4 susceptible flock neutralized plaque formation by the virus in tissue culture. A possible explanation of these results is that the virus we were studying was a fowl orphan virus present in poultry stocks. Since then confirmation has been received in personal communications from B. R. Burmester, G. R. Sharpless and R. J. Huebner, respectively, giving results of extensive investigations in the United States. These show that the virus is enzootic in many flocks.

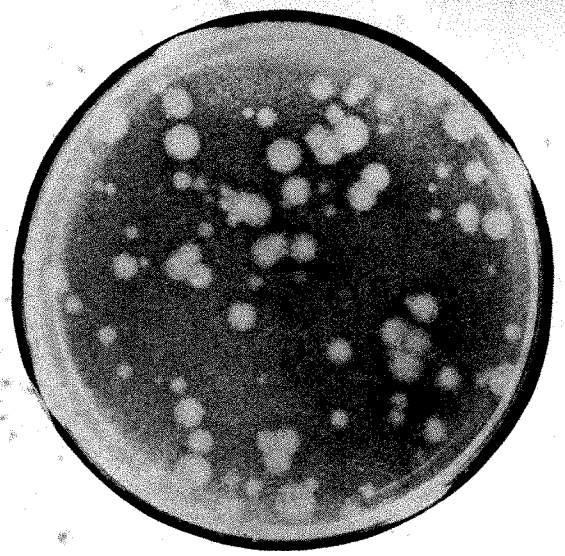

Fig. 1

Despite its apparent lack of relationship to fowl lymphomatosis this ubiquitous and hardy virus may be of considerable interest in its own right. The purpose of this communication is to describe an improved method of plaque assay which is more sensitive and gives considerably better resolution than the techniques previously reported. It has the additional advantage that it can be adapted for rough assays of both virus and neutralizing antibody.

The method was based on that described by Cooper[6]. Base layers of 4 ml. containing 10 per cent calf serum, 10 per cent tryptose phosphate broth (Difco) and 0·9 per cent agar (Difco) in Eagle's medium were prepared in 60-mm. Petri dishes. When the base layers had set they were overlayed with 2·5 ml. of the same medium containing 0·1 ml. of virus dilution and 3×10^7 freshly trypsinized liver cells from 17-day-old chick embryos. On the fourth day of incubation 2·5 ml. of 0·01 per cent neutral red in agar medium was added and plaques (Fig. 1) counted daily until a maximum count was obtained 3–4 days later.

Table 1. RELATIVE SENSITIVITIES OF PLAQUE TECHNIQUES FOR A FOWL ORPHAN VIRUS

Method	Relative sensitivity
Agar suspension technique as described in the text with :	
(1) Chick embryo liver	100
(2) Chick embryo kidney	100
(3) Whole chick embryo	4
(4) Young adult fowl liver	65
Monolayers of chick embryo liver (ref. 4)	13

The relative sensitivity of this method compared with other systems is given in Table 1. Although chick embryo kidney cells were found to be as sensitive as liver cells, the latter were preferred since higher yields could be obtained. For rough assays 0·1 ml. of virus dilution or virus/antibody mixture was added to 0·9 ml. of agar medium held at 44° C. and 0·02 ml. of this agar dilution was allowed to set on a base layer. A 60-mm. Petri dish accommodates 6–8 spots. When set, the spots were overlayed with liver cells in agar and then treated as described above. Since discrete plaques can be distinguished in these spots a direct measure of infectivity is obtained.

It will be seen from Fig. 1 that there was a continuous gradation of plaque size (0·5 mm.–5 mm. diameter). When cloned virus from large and small plaques was plated, the same wide distribution of plaque size was obtained from each clone. Incubation of virus and cells in fluid suspension for 2 hr. before plating did not lead to greater uniformity of plaque size. Buthala also found several sizes of plaques when this virus was plated on monolayers of chicken embryo kidney. The explanation of this effect is not known.

B. R. Burmester, G. R. Sharpless and A. K. Fontes[7] have found that this virus is in some ways similar to the adenoviruses of man and have suggested that it be called *GAL* (gallus, adenolike).

I wish to express my thanks to Prof. M. G. P. Stoker for his helpful advice and criticism.

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Effect of Ultrasonic Vibration on the Hæmagglutinating Activity of Some Para-influenza Viruses

THE effect of sound vibration on influenza virus has been described previously[1,2]. Lief and Henle[3] showed that sonic treatment of influenza virus neither increased the hæmagglutinin titre nor changed the ratio of the hæmagglutinin titres obtained with chicken and guinea pig erythrocytes. The results briefly reported here deal with the effect of ultrasonic vibration on the hæmagglutinating activity of some para-influenza viruses.

Different para-influenza viruses were cultivated in cultures of calf or monkey kidney cells. Culture fluids containing large amounts of infectious virus were centrifuged at 2,500 r.p.m. for 30 min. The supernatants were subjected to ultrasonic vibration at about 20 kc./sec. for 10 min. in an *MSE* Mullard ultrasonic disintegrator. The hæmagglutinin tests were generally performed at 4° C. employing guinea pig and chicken erythrocytes.

Table 1. GUINEA PIG HÆMAGGLUTININ TITRES OF UNTREATED AND ULTRASONIC-TREATED VIRUSES

	Incubation	Para-influenza-1 Sendai	Para-influenza-2 *CA*	Para-influenza-3 *Umeå**	*SA S* 1†
Untreated	4° C.	8	2	16	16
Treated	4° C.	128	16	128	256
Untreated	37° C.	128	8	128	64
Treated	37° C.	256	16	256	256

* A Swedish bovine strain.
† A Swedish strain of the myxovirus *SA*, described by Schultz and Habel (ref. 4).

The results presented in Table 1 show that if the hæmagglutinin tests were performed at 4° C., the guinea pig hæmagglutinin titres increased 8–16 times after ultrasonic treatment of virus. If, however, the hæmagglutinin tests were performed at 37° C., the guinea pig hæmagglutinin titres were higher and did not increase to the same extent after treatment.

The rise in guinea pig hæmagglutinin after ultrasonic treatment was not accompanied by an increase of chicken hæmagglutinin (Table 2). Similar observations have been made with influenza virus treated with ether[3]. To ascertain whether the effect of ultrasonic vibration was due to a release of non-infectious and less-sedimentable hæmagglutinin, untreated and treated virus samples were centrifuged at 25,000 r.p.m. for 1 hr. in a Spinco preparative centrifuge. The supernatants and sediments were titrated for hæmagglutinin and infectivity. The results of this experiment are recorded in Table 3, which shows that the level of hæmagglutinin was 16 times greater in the supernatant of the treated virus than in that of the untreated virus. Furthermore, the ratio guinea pig hæmagglutinin/TCD_{50} was about 100 times greater in the supernatant than in the sediment of ultrasonic-treated virus.

Table 2. HÆMAGGLUTINATING ACTIVITY OF UNTREATED AND ULTRASONIC-TREATED VIRUS

Virus	Untreated		Treated	
	GPHA	CHA	GPHA	CHA
Sendai	8	128	128	128
CA	2	2	16	2
Umeå	16	<2	128	<2
S 1	16	128	256	186

GPHA, Guinea pig hæmagglutinin; CHA, chicken hæmagglutinin.

Table 3. GUINEA PIG HÆMAGGLUTININ TITRES OF PARA-INFLUENZA VIRUS CENTRIFUGED AT 25,000 R.P.M. FOR 1 HR.

Titre/ml.	Untreated		Ultrasonic treated	
	Supernatant	Sediment	Supernatant	Sediment
GPHA	8 (8)*	32 (256)	128 (128)	256 (256)
log TCD_{50}	5·9	7·9	5·7	8·1

* After ultrasonic treatment.

The effect of ultrasonic vibration on the hæmagglutinating activity of para-influenza viruses may be due to a disaggregation of a non-infectious hæmagglutinin. Further investigations dealing with this hypothesis will be published later.

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FORTHCOMING EVENTS

Monday, January 2

PLASTICS INSTITUTE (in the Lecture Theatre of the Institution of Electrical Engineers, Savoy Place, London, W.C.2), at 2.30 p.m.—Mr. H. A. Thomas: "Plastics and Textiles" (Young People's Lecture).

SOCIETY OF CHEMICAL INDUSTRY, LONDON SECTION (14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Mr. H. F. Corsan: "Financial Management in the Chemical Industry".

Wednesday, January 4

BRITISH OCCUPATIONAL HYGIENE SOCIETY (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 10 a.m.—Meeting on "Health Physics".

SOCIETY OF CHEMICAL INDUSTRY, CORROSION GROUP—CATHODIC PROTECTION PANEL (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Discussion of "Galvanic Anodes". Opening Speakers. Dr. G. E. Gardam, Mr. P. V. Palmer and Mr. K. P. Scott.

BRITISH INSTITUTION OF RADIO ENGINEERS, RADAR GROUP (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6.30 p.m.—Mr. W. E. Brunt: "Automatic Techniques in Civil Air Line Communications Systems".

Thursday, January 5

INSTITUTION OF MECHANICAL ENGINEERS, INDUSTRIAL ADMINISTRATION AND ENGINEERING PRODUCTION GROUP (at 1 Birdcage Walk, Westminster, London, S.W.1), at 10.30 a.m.—Informal Discussion on "The Reliability of Mechanical Engineering Parts of Data Processing Systems".

ROYAL AERONAUTICAL SOCIETY (at 4 Hamilton Place, London, W.1), at 3 p.m.—Mr. R. J. Lees: "Gyroscope and Pendulum—the Modern Travel Agents" (Young People's Lecture).

ROYAL INSTITUTION OF NAVAL ARCHITECTS (at 10 Upper Belgrave Street, London, S.W.1), at 4.45 p.m.—Mr. A. Hunter, O.B.E.: Third Amos Ayre Lecture.

INSTITUTION OF ELECTRICAL ENGINEERS (at Savoy Place, London, W.C.2), at 5.30 p.m.—Dr. J. S. Forrest: "The Application of Electronics to the Electricity Supply Industry" (Third Hunter Memorial Lecture).

INSTITUTE OF METALS, LONDON LOCAL SECTION (at 17 Belgrave Square, London, S.W.1), at 6.30 p.m.—Dr. J. E. Hughes: "Metallurgy in Electronics".

ROYAL PHOTOGRAPHIC SOCIETY OF GREAT BRITAIN, MEDICAL GROUP (at 16 Princes Gate, London, S.W.7), at 7 p.m.—Mr. Charles Engel and Mr. John Brace: "Closed Circuit Television in Medical Diagnosis, Research and Teaching".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

ASSISTANT LECTURER in PSYCHOLOGY IN THE DEPARTMENT OF PHILOSOPHY—The Registrar, University College, Singleton Park, Swansea (January 14).

LECTURER IN PHYSICS (EXPERIMENTAL); a LECTURER IN THEORETICAL PHYSICS; and ASSISTANT LECTURERS IN PHYSICS—The Registrar, The University, Manchester 13 (January 14).

RESEARCH ASSISTANT (with some knowledge of metallurgical techniques), for work in the metal physics group under the direction of Dr. P. B. Hirsch—The Secretary to the Department of Physics, Cavendish Laboratory, The University, Free School Lane, Cambridge (January 15).

LECTURER IN VETERINARY HISTOLOGY AND EMBRYOLOGY—The Secretary of University Court, The University, Glasgow (January 18).

CHAIR OF MECHANICS—The Registry, The Old Schools, The University, Cambridge (January 21).

SCIENTIFIC OFFICER or SENIOR SCIENTIFIC OFFICER (with a good honours degree, preferably with postgraduate experience), to work on biochemical processes in seeds and seedlings—The Secretary, National Vegetable Research Station, Wellesbourne, Warwick (January 21).

LECTURER or ASSISTANT LECTURER IN STATISTICS—The Registrar, The University, Leeds 2 (January 24).

SENIOR LECTURER or LECTURER IN MATHEMATICS IN THE FACULTY OF ENGINEERING, University College of the West Indies, Trinidad—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (January 25).

LECTURER IN THE DEPARTMENT OF FOOD TECHNOLOGY at the University of New South Wales—The Agent-General for New South Wales, 56 Strand, London, W.C.2, and The Appointments Section, The University of New South Wales, Box 1, Post Office, Kensington, New South Wales, Australia, marking envelope "University Appointment" (Australia and London, January 27).

LECTURERS or ASSISTANT LECTURERS IN SOCIAL ANTHROPOLOGY, GEOLOGY, MATHEMATICS and PHYSICS at the University College of Rhodesia and Nyasaland—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (January 30).

SENIOR LECTURER (preferably with research interest in the application of mathematics to some engineering subject) IN ENGINEERING MATHEMATICS—The Secretary, The Queen's University, Belfast, Northern Ireland (January 30).

CHAIR OF PHARMACOLOGY in the University of the Witwatersrand, Johannesburg, South Africa—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (South Africa and London, January 31).

PLANT BREEDERS (2) (with a degree in agriculture or science or an equivalent) within the University of Sydney, to carry out wheat breeding at the North-West Wheat Research Institute, Narrabri—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, January 31).

SENIOR LECTURER IN ANIMAL PRODUCTION (MORTLOCK FELLOW) IN THE DEPARTMENT OF AGRONOMY at the Waite Agricultural Research Institute, University of Adelaide, Adelaide, South Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, January 31).

UNIVERSITY LECTURER (with special qualifications in applied thermodynamics, and preferably an interest in heat transfer apparatus and some industrial or research experience) IN MECHANICAL ENGINEERING—The Secretary, The University, Aberdeen (January 31).

LECTURER IN HYDRAULICS AND HYDROLOGY IN THE DEPARTMENT OF CIVIL ENGINEERING—The Registrar, King's College (University of Durham), Newcastle upon Tyne 1 (February 4).

AGRONOMIST or PLANT PHYSIOLOGIST (honours graduate in science or agricultural science with relevant postgraduate research experience, and preferably prior experience with tobacco) at the Tobacco Research Institute, C.S.I.R.O., Mareeba, North Queensland, to investigate factors affecting the nitrogen status of the tobacco plant, together with various problems in tobacco agronomy arising in North Queensland—Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2, quoting Appointment No. 815/29 (February 11).

CHAIR OF GEOLOGY tenable in the Newcastle Division of the University of Durham—The Registrar, University Office, 46 North Bailey, Durham (February 11).

LECTURER (with special qualifications or experience in inorganic or physical chemistry) IN CHEMISTRY at the University of Canterbury, Christchurch, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand and London, February 17).

CHAIR OF APPLIED MECHANICS tenable in the Newcastle Division of the University of Durham—The Registrar, University Office, 46 North Bailey, Durham (February 18).

ASSISTANT EXPERIMENTAL OFFICER (with a degree in science or diploma in horticulture or agriculture), to assist in field experimental work—The Secretary, National Vegetable Research Station, Wellesbourne, Warwick.

ASSISTANT LECTURER (graduate in chemistry, and preferably with experience in the food industry), for duties which will include the teaching of chemistry and food quality control—The Principal, National College of Food Technology, St. George's Avenue, Weybridge, Surrey.

BIOCHEMIST (graduate in chemistry, biochemistry or physiology) IN THE PATHOLOGY DEPARTMENT, for work connected with biochemical investigations on patients—The Group Secretary, or Consultant Pathologist, Camberwell Hospitals Management Committee, Dulwich Hospital, East Dulwich Grove, London, S.E.22.

LECTURER IN CHEMICAL ENGINEERING—Head, Department of Chemistry and Chemical Engineering, University of Saskatchewan, Saskatoon, Saskatchewan, Canada.

RESEARCH ASSISTANT (preferably with an honours degree in physical and inorganic chemistry) IN THE DEPARTMENT OF MINERALOGY AND PETROLOGY, for a programme of research concerning fundamental solid-state problems in the field of cement chemistry—Dr. J. D. C. McConnell, Department of Mineralogy and Petrology, Downing Place, Cambridge.

SENIOR LECTURER IN INORGANIC CHEMISTRY; a LECTURER IN INORGANIC CHEMISTRY; and a LECTURER IN CHEMICAL ENGINEERING—The Registrar, Bradford Institute of Technology, Bradford 7.

SENIOR TECHNICIAN or TECHNICIAN (with instrument or physics workshop experience) IN THE RADIOTHERAPY DEPARTMENT, for duties which include Physics Workshop, Isotope Laboratory, Radium and Mould Room work—The Group Secretary, Romford H.M.C., Oldchurch Hospital, Oldchurch Road, Romford, Essex, quoting Ref. 17/39.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Association of Scientific Workers. Science and Education: a Policy Statement by the Association of Scientific Workers. Pp. 16. (London: Association of Scientific Workers, 1960.) 1s. [279

Fourth Report from the Select Committee on Estimates, together with part of the Minutes of Evidence taken before Sub-Committee D, and an Appendix, Session 1959–60—Colonial Office. Pp. xxxvii+280. (London: H.M. Stationery Office, 1960.) 14s. net. [310

Ministry of Aviation. Reports on Plastics in the Tropics. No. 12: Polyvinyl Chloride. Pp. 56. (London: H.M. Stationery Office, 1960.) 6s. net. [310

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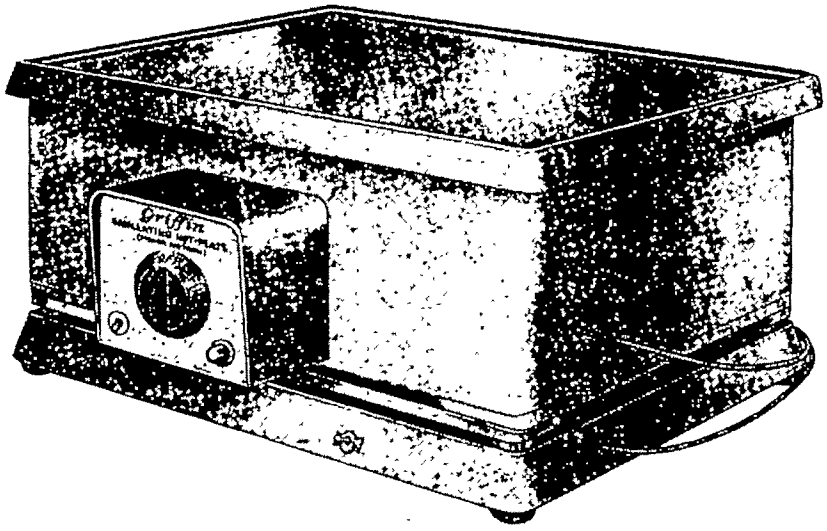

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APPOINTMENTS VACANT

UNIVERSITY OF WALES
UNIVERSITY COLLEGE OF SWANSEA
DEPARTMENT OF ENGINEERING

Owing to the large expansion of the Departmental facilities for both teaching and research, a number of appointments will be made to the Staff both immediately and from October 1, 1961 Applications are invited from graduates in Engineering, Physics, Metallurgy or Applied Mathematics for the following posts:

CIVIL ENGINEERING
Professor B. G Neal

Lecturer or Assistant Lecturer with interests in any branch of Civil Engineering

CIVIL OR MECHANICAL ENGINEERING

Lecturer or Assistant Lecturer with special interests in Strength of Materials and related fields.

MECHANICAL ENGINEERING
Professor R. H. Macmillan

Two Lecturers or Assistant Lecturers, one with particular interests in the fields of Heat Transfer and Thermodynamics, the other preferably having experience in the Design of Machines, but applicants with other interests will be considered.

Research Demonstrator to undertake a limited amount of teaching and pursue supervised research preferably in Heat Transfer, Hydrodynamic power transmission, Fatigue or creep.

ELECTRICAL ENGINEERING
Professor W. Fishwick

Lecturer or Assistant Lecturer with special interests in Control Engineering, Electrical Apparatus or related fields.

Lecturer or Assistant Lecturer with interests in any branch of Electrical Engineering, including Theoretical Electro-technics.

Qualifications for, and further details of, these posts are as follows: Lecturer. Applicants should hold a good honours degree and have not less than three years postgraduate experience in research or industrial design Excellent facilities exist for research. Assistant Lecturer Applicants should hold a good honours degree and have at least one year's industrial or postgraduate experience. Research is strongly encouraged and the assistant may register for a Ph.D. degree. Research Demonstrator. Applicants should have obtained a good honours degree and have had at least one year's industrial or postgraduate experience. The appointment will be tenable for three years, during which time the holder will be expected to work for the Ph.D degree, submitting a thesis at the end of the period.

Salaries are on the following scales, to which are added F.S S U. benefits and family allowances Lecturer, £1,050 by £50 to £1,400 by £75 to £1,850 per annum; Assistant Lecturer, £800 by £50 to £950 per annum, Research Demonstrator, £700 per annum.

Further particulars can be obtained from the Registrar, University College, Singleton Park, Swansea, by whom applications (two copies), must be received not later than Saturday, January 21, 1961.

UNIVERSITY COLLEGE OF RHODESIA AND NYASALAND

Applications are invited for Lectureships or Assistant Lectureships in GEOLOGY, MATHEMATICS, PHYSICS. Salary scales Assistant Lecturer, £1,200 by £50 to £1,350 per annum Lecturer, Grade II, £1,350 by £50 to £1,600 per annum; Grade I, £1,600 by £50 to £1,900 per annum. Passages to Salisbury for appointee wife, and dependent children on appointment, with allowance for transport of effects. Superannuation and medical aid schemes. Unfurnished accommodation at rent of 15 per cent of salary Assistance given for triennial visits overseas

Detailed applications (six copies), naming three referees, by January 30, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C 1, from whom further particulars may be obtained

PLANT MANAGER DESIGNATE

A vacancy exists for an Assistant Plant Manager for an overseas processing unit. It would be intended that the successful applicant would work under the present Manager for a short period before succeeding him The appointment calls for a qualified mechanical or chemical engineer with experience of the independent management of extraction or refining plant. A knowledge of solvent processes would be an advantage but not essential.

Applicants should be not more than 45, preferably with overseas experience and probably earning at least £3,000 per annum at present

Write, Box DE/41, c/o 95 Bishopsgate, E C 2.

AUSTRALIA
UNIVERSITY OF NEW SOUTH WALES
VACANCIES FOR STAFF IN SCHOOL OF BIOLOGICAL SCIENCES

The School of Biological Sciences of the University of New South Wales is under the headship of the professor of Biochemistry (Professor B. J. Ralph) and consists of four departments These are the Department of Biochemistry (Professor B J. Ralph), Department of Microbiology (Professor to be appointed), Department of Botany (Dr. Mary Hindmarsh) and Department of Zoology (Dr Elsie M. Stephenson). The undergraduate work of the School is concerned with the preparation of students, at pass and honours levels, in biochemistry, microbiology, botany, zoology and entomology in the Faculty of Science, and biochemistry, microbiology and entomology in the Applied Biology course. In 1962 and later years the relevant Departments will be responsible for medical biochemistry and medical microbiology in the courses in medicine and medical science. Specialized subjects are also provided for courses in the Faculty of Applied Science All departments of the School are active in research and prepare students for Masters' degrees and for the Doctorate of Philosophy.

Lecturers in the Departments of Botany and Zoology are expected to assist generally with elementary teaching, but are otherwise encouraged to specialize within their own particular discipline The Departments of Biochemistry and Microbiology are particularly concerned with the application of these sciences, and formal postgraduate courses in industrial biochemistry and microbiology are being developed. As the School handles a considerable number of part-time and full-time students, some evening lecturing is inevitable, but this is limited in extent. Applicants with experience and/or research interests in any of the divisions of botany or zoology, or in medical biochemistry or medical microbiology are particularly sought.

The following vacancies exist Senior Lecturers, Lecturers All Departments. Teaching Fellows Botany, zoology and biochemistry. Senior Tutors Biochemistry, botany and microbiology. Tutor/Demonstrators Botany and zoology

Applicants should possess at least the following academic qualifications. Senior Lecturer, a higher degree or equivalent qualifications Lecturer, a degree with honours or equivalent qualifications. For these positions postgraduate experience is desirable: Teaching Fellow Applicants must possess a degree with honours Teaching Fellows are required to register for a higher degree Senior Tutor: a degree with teaching experience. Tutor: a degree Tutors and Senior Tutors will have opportunity to study for a Master's degree on a part-time basis

Further details may be obtained from the Head of the School of Biological Sciences.

Subject to satisfactory medical examination Lecturers and Senior Lecturers will be eligible to join the superannuation scheme. Teaching fellows and tutors, and normally senior tutors are subject to annual re-appointment (limit for teaching fellows normally three years' service)

Salary ranges Senior Lecturer, £A 2,579 to £A.3,029 per annum Lecturer, £A 1,759 to £A 2,464 per annum. Senior Tutor, £A.1,759 to £A 2,074 per annum. Teaching Fellow and Tutor. £A 1,129 to £A 1,349 per annum.

Passages to Sydney for appointees and their families. Commencing salary according to qualifications and experience

Four copies of applications, including the names of two referees, should be lodged with the Agent-General for New South Wales, 56 Strand, London W C 2, England, and a copy forwarded to the Appointments Section, the University of New South Wales, Box 1, Post Office, Kensington, New South Wales, Australia, by airmail to arrive before February 10, 1961. Applicants resident outside the United Kingdom and Eire need only submit one copy of their application to the London address.

UNIVERSITY OF MANCHESTER
IMPERIAL CHEMICAL INDUSTRIES FELLOWSHIPS

Applications are invited for the above Research Fellowships, founded by Imperial Chemical Industries Ltd, tenable in the University and available for research in various branches of Chemistry, Chemical Engineering, Engineering, Technology, Physics and allied subjects The value of the Fellowships will be within the range of £800 to £1,100 per annum according to qualifications and experience

Regulations governing the award of the Fellowships may be obtained from the Registrar, the University, Manchester 13, to whom applications should be sent not later than February 14, 1961.

SENIOR RESEARCH OFFICER
ELECTROLYTIC ZINC COMPANY OF AUSTRALASIA LIMITED

Applications are invited for a position as a Senior Research Officer in the Company's Research Department at Risdon, near Hobart, Tasmania. Applicants should possess a university degree in chemistry or chemical engineering; they should have obtained honours or higher degrees, and should have had some years' experience in research. The Research Department is concerned with development projects and is responsible for the solution of problems which arise in connection with the Company's various activities, which include the production of zinc, ammonium sulphate, superphosphate, sulphuric acid, etc The duties are essentially similar to those in the Research Department of any large chemical industry. Applicants should preferably be in the age range 28 to 35 years. The commencing salary offered for the position will depend on the qualifications and experience of the successful applicant, but will be at the rate of not less than £A.2,100 per annum. In addition, a bonus based on the rate of dividends declared by the Company is paid half-yearly; for 1959 the bonus was approximately 15 per cent of salary. The appointee will be eligible to participate in the Company's Staff Provident Fund and in the Medical, Hospital and Dental Schemes run by the Company. The Company will pay fares for a successful applicant and his family (if any) to travel to Australia by sea. An unfurnished house or flat can be made available on a rental basis for a married applicant

Applications should include details of education and experience and must include details of subjects studied at the University and the standard of passes obtained Applications should include the names of at least three referees and should be addressed to The General Superintendent, Electrolytic Zinc Company of Australasia Limited, G P O Box 377-D, Hobart, Tasmania, Australia.

COMMONWEALTH MYCOLOGICAL INSTITUTE

Applications are invited for the post of Abstractor. Candidates should have sound knowledge of German and Dutch and ability to abstract in English from these languages. Scandinavian and/or Spanish and Portuguese languages an added qualification Knowledge of microbiology and/or botany an advantage Salary according to qualifications and experience in the range £640 to £1,325 per annum

Apply in writing, the Director, Ferry Lane, Kew

D S I R ROAD RESEARCH LABORATORY, Harmondsworth, Middlesex, requires Scientific Officers or Senior Scientific Officers for research (1) Physicists on rheology of solid-liquid systems and of viscous and visco-elastic fluids to provide basic information for design of bituminous and concrete road mixtures. (Ref. A.521/OA); (2) Chemists on problems of surface chemistry and other physico-chemical aspects of behaviour of bituminous road materials also on problems arising from presence of organic matter in soils (Ref F.857/OA); (3) Civil and Mechanical Engineers on (a) mechanical mixing and laying of bituminous road surfacing materials, (b) problems of design and construction of earthworks for roads (practical experience of site work an advantage), (c) stabilised soil and cement-bound base materials (Ref E 473/OA) Varied and interesting work both in laboratory and field, providing contacts with other scientists and engineers in U.K. and abroad Facilities for qualifying for A.M I.C.E for posts (3) above Qualifications, first- or second-class honours degree or equivalent for Scientific Officers. For Senior Scientific Officers at least three years' postgraduate experience. Salary (men) Scientific Officer, £730 to £1,205. Senior Scientific Officer, £1,330 to £1,640 Prospects of promotion in mid-thirties to Principal Scientific Officer, £1,700 to £2,375 —Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S W 1 (quote appropriate reference) Closing date January 31, 1961.

ROYAL VETERINARY COLLEGE (University of London). Research Assistant required in the Department of Animal Husbandry and Veterinary Hygiene for studies in poultry husbandry. The appointment will be for two years in the first instance under a grant from the Agricultural Research Council. Candidates must possess a suitable veterinary qualification or a degree in agriculture or natural science. Salary according to age, qualifications and experience Superannuation under F.S.S.U.—Application forms and further particulars, obtainable from the Secretary, Royal Veterinary College, Royal College Street, London, N.W.1, should be returned not later than January 14, 1961.

AUSTRALIA
UNIVERSITY OF NEW SOUTH WALES
PROFESSOR OF GEOLOGY

The University invites applications for appointment to the position of Professor of Geology in the School of Mining Engineering and Applied Geology. Salary will be £A 4,279 per annum. The School is a composite one and includes departments of Mining Engineering, Geology and Geophysics, Fuel Technology and Mineral Beneficiation. The Department of Geology conducts courses leading to the degree of Bachelor of Science in Applied Geology and also in pure Geology. The main emphasis in the School is on applied geological research and it is essential that applicants should have high academic qualifications in geology with substantial interest, experience and research record in some aspects of applied geology. The Head of the School is Professor D. W. Phillips who is also the Pro-Vice Chancellor. The Professor appointed will be expected to assist him with the administration of the School so that some familiarity with the disciplines of the other departments in the School would be desirable. Applicants interested in this position may obtain further details relating to the staff and activities of the School from the Dean of the Faculty of Technology, Professor Myers. Subject to the consent of the Council of the University, Professors may engage in a limited amount of higher consultative work. The successful applicant will be eligible, subject to satisfactory medical examination, to join the superannuation scheme which provides a maximum pension of £A.2,184 per annum. First-class ship fares to Sydney of appointee and his family will be paid Professors are eligible for six months' study leave on full salary after three years of service, or twelve months after six years of service. The University reserves the right to fill the Chair by invitation With the approval of the University and its bankers, married men may be assisted by loans to purchase a home.

Four copies of application (including the names of three referees and a recent photograph of the applicant) should be lodged with the Agent-General for New South Wales, 56-57 Strand, London, W.C.2, England, and a copy forwarded to the Appointments Section, the University of New South Wales, P.O Box 1, Kensington, N.S.W, Australia, to reach there before February 3, 1961. Applicants outside the United Kingdom need only submit one copy of their application to the London address

GOVERNMENT OF THE FEDERATION OF RHODESIA AND NYASALAND
VACANCY: ENTOMOLOGIST
DEPARTMENT OF TSETSE AND TRYPANOSOMIASIS CONTROL AND RECLAMATION
MINISTRY OF AGRICULTURE

Applications are invited for the post of Entomologist in the Tsetse and Trypanosomiasis Control and Reclamation Branch of the Ministry of Agriculture, based in the tsetse areas of Southern Rhodesia. Duties will be mainly on field investigations, preparatory to tsetse control projects, and in their direction. Applicants must have a university degree, preferably honours in a biological subject, zoology, entomology (need not have specialized, but previous relevant experience is an advantage), botany Commencing salary will be between £735 per annum and £1,365 per annum, depending on qualifications and relevant post-qualification experience, in a scale rising to £1,732 10s. per annum. A field allowance of £7 10s. per mensem is payable at present for officers living under field conditions. Passages are provided for recruits and their families to the Federation, and conditions include security, good pensions, generous sick leave, vacation and occasional leave, medical aid, grants towards holiday travel, low income tax.

Application forms and further details from Secretary (R), Rhodesia House, 429 Strand, W.C 2. Closing date January 7, 1961.

UNIVERSITY OF MANCHESTER
TURNER AND NEWALL RESEARCH FELLOWSHIPS

Applications are invited for the above Research Fellowships, founded by Messrs. Turner and Newall Ltd., tenable in the University and available for research in engineering, inorganic chemistry, physics and allied subjects The value of the Fellowships will be within the range of £800 to £1,100 per annum according to qualifications and experience.

Regulations governing the award of the Fellowships may be obtained from the Registrar, the University, Manchester 13, to whom applications should be sent not later than February 14, 1961

WELSH COLLEGE OF ADVANCED TECHNOLOGY
CATHAYS PARK, CARDIFF
DEPARTMENT OF APPLIED PHYSICS

Applications are invited for the posts of (a) Lecturer or Assistant Lecturer (Grade B) in Electronics. (b) Assistant Lecturer (Grade B) in Physics. Applicants should have a good honours degree in physics or electrical engineering, and be able to teach (a) Electronics and/or Telecommunications, (b) Physics and/or Applied Physics, to students taking Dip Tech. Courses, and have had industrial and/or research experience. Teaching experience at University or Technical College level would be an advanage. Successful candidates would be expected to pursue some research and every assistance and encouragement will be given to this end. The Department's research activities are largely confined to Solid State Physics and application from those particularly interested in some aspect of Solid State Physics or Applied Physics would be particularly welcome. Salary (a) Lecturer, £1,370 by £35 to £1,550 per annum (b) Assistant Lecturer (Grade B), with good honours degree, £865 by £27 10s. to £1,315 per annum starting salary according to qualifications.

Further particulars and application forms can be obtained from the Registrar at the College, to whom they should be returned by January 14, 1961.

ROBERT E. PRESSWOOD,
Clerk to the Governing Body.

City Hall,
Cardiff.

AUSTRALIA
UNIVERSITY OF NEW SOUTH WALES
SENIOR LECTURER IN PHYSIOLOGY
FACULTY OF MEDICINE

The University invites applications for appointment to the position of Lecturer in the School of Physiology within the Faculty of Medicine. Salary: £A 2,579 range £A.3,029 per annum. Commencing salary according to qualifications and experience Applicants must have research and teaching experience in the fields of cardiovascular physiology and respiratory physiology. The successful applicant will participate in the new teaching programme of the School and establishment of the cardiopulmonary research laboratory. The appointee will be expected to enter on duty in this position about June, 1961. First-class ship fares to Sydney of the appointee and his family will be paid. Appointee will be eligible, subject to satisfactory medical report, to contribute to the State Superannuation Fund.

Four copies of applications (including the names of two referees) should be lodged with the Agent-General for New South Wales, 56 Strand, London, W.C.2, and a copy forwarded by airmail in an envelope marked "University Appointment" to the Bursar, the University of New South Wales, Box 1, Post Office, Kensington, New South Wales, Australia, before January 31, 1961. Applicants resident outside the United Kingdom and Eire need only submit one copy of their application to the London address.

AGRICULTURAL RESEARCH COUNCIL

Assistant Experimental Officer required, to be responsible for preparative work in a research programme concerned with biochemical and developmental genetics General experience of biological laboratory methods and a special experience of biochemistry, genetics embryology or histology, an advantage. Salary within scale £490 to £945 according to age. Candidates should have a School Leaving Certificate with passes in three subjects at higher level, including two science subjects; a Higher National Certificate, or equivalent. Superannuation.

Apply, with names of three referees to, the Secretary, Poultry Research Centre, King's Buildings, West Mains Road, Edinburgh, 9, within two weeks.

ESSEX COLLEGE
ASSUMPTION UNIVERSITY OF WINDSOR
WINDSOR, ONTARIO, CANADA

The Department of Physics offers Graduate Assistantships to candidates wishing to proceed to an M Sc in physics Stipend up to $2,000 for eight months, depending on qualifications and duties in the department. There is a possibility of additional income during the summer months At present research is proceeding in beta-ray spectroscopy, optical pumping, molecular collision problems, and electromagnetic interactions in shock waves

Inquiries should be addressed to the Chairman, Department of Physics, Assumption University of Windsor.

AUSTRALIA
UNIVERSITY OF NEW SOUTH WALES
LECTURER IN FOOD TECHNOLOGY

The University invites applications for appointment to the position of Lecturer in the Department of Food Technology. Salary: £A.1,759 range £A 2,464 per annum. Commencing salary according to qualifications and experience. Applicants should possess a degree with honours in biochemistry or microbiology, or equivalent qualifications, and some previous experience in the food industry is desirable but not essential. The successful applicant will lecture to undergraduate and postgraduate students in food technology and undertake research in some aspects of biochemistry or microbiology, as applied to food science or food technology. First-class ship fares to Sydney of appointee and his family will be paid. Successful applicant will be eligible to contribute to the State Superannuation Fund.

Four copies of applications, including the names of two referees, should be lodged with the Agent-General for New South Wales, 56 Strand, London, W.C 2, and a copy forwarded by airmail in an envelope marked "University Appointment" to the Appointments Section, the University of New South Wales, Box 1, Post Office, Kensington, New South Wales, Australia, before January 27, 1961. Candidates outside the United Kingdom and Ireland need only submit one copy of their applications to the London address

AUSTRALIA
UNIVERSITY OF NEW SOUTH WALES
FACULTY OF ENGINEERING
TEACHING FELLOWS

Vacancies for teaching fellows exist in the Schools of Mechanical, Electrical and Civil Engineering. Applicants must possess a degree with honours, and will be expected to enrol for a higher degree and undertake a limited amount of teaching duties. Engagement is on an annual basis to a maximum of three years Salary: £A 1,129 range £A.1,349 per annum. Commencing salary for all positions will be according to qualifications and experience

Further details regarding these positions may be obtained from the Head of the appropriate school. Ship fares to Sydney of appointees and their families will be paid. Four copies of applications (including the names of two referees), should be lodged with the Agent-General for New South Wales, 56-57 Strand, London, W C.2, and a copy forwarded by airmail to the Appointments Section, the University of New South Wales, Box 1, Post Office, Kensington, New South Wales, Australia, before January 27, 1961.

UNIVERSITY OF ST. ANDREWS

Applications are invited for a Senior Lectureship or a Lectureship in Electrical Engineering in the Department of Electrical Engineering, Queen's College, Dundee, to commence not later than October 1, 1961. It is intended to appoint the most suitable candidate irrespective of his particular interest Salary scales: Senior Lectureship, £1,925 by £75 to £2,425; Lectureship, £1,050 by £50 to £1,400 by £75 to £1,850 (efficiency bar £1,400). F.S.S.U; family allowance, grant towards furniture removal expenses.

Applications (six copies), containing the names of three referees, to the undernoted, from whom further particulars may be obtained, not later than January 21, 1961.

PATRICK CUMMING,
Joint Clerk to the University Court

Queen's College,
Dundee.

UNIVERSITY COLLEGE OF THE WEST INDIES

Applications are invited for (a) Senior Lectureship and (b) Lectureship in Geology. The Senior Lecturer will be for the time being, the Head of the Department of Geology which is about to be established and which will prepare students for degrees of University of London as from October, 1961. Salary scales (under review) (a) £1,500 by £75 to £2,250 per annum. (b) £1,150 by £50 to £1,450 by £75 to £1,900 per annum. Point of entry determined by qualifications and experience. Child allowance. F.S.S U Unfurnished accommodation at rental not in excess of 10 per cent of basic salary Up to five full passages on appointment, termination and study leave (once every three years). Duties to be assumed by April 1, 1961, or as soon as possible thereafter. The Head of Department will be eligible for entertainment allowance at the rate of £200 per annum.

Detailed applications (six copies), naming three referees, by January 27, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained

AUSTRALIA

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION

RESEARCH PHYSICIST

The Organization's Division of Metrology, National Standards Laboratory, Sydney, N.S.W., invites applications for the position of Research Physicist in the Interferometry Section from honours graduates, majoring in physics with some years' postgraduate research experience, preferably to Ph.D. level.

The Section, which has a well-equipped vacuum coating laboratory as well as equipment for studying surfaces and thin films by multiple-beam interferometry, is engaged on research and development in interferometry, particularly the measurement of length and associated quantities such as flatness, surface structure and optical phase change at reflection. The appointee is required for research in interference spectroscopy and light source development involving the production study and use of various spectral radiations from isotopic light sources as primary and secondary wavelength standards in metrology.

SALARY: Dependent on qualifications and experience within the ranges: £A 1,510 to £A.2,265 per annum or £A.2,395 to £A.2,720 per annum.

Promotion within C.S.I.R.O. is by merit and may ultimately go beyond the upper limit of the scale within which the original appointment is made.

Fares paid. Further information on conditions etc., supplied on application to.

Mr. E. J. Drake, Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2,

to whom applications (quoting Appointment No. 750/222) should be addressed by February 11, 1961.

UNIVERSITY OF EDINBURGH

Applications are invited for I.C.I. Research Fellowships in Biochemistry, Chemistry, Engineering, Pharmacology, Physics or Chemical Technology (Chemical Engineering), normally tenable for a period of three years. Some appointments will date from October 1, 1961 (or earlier in the case of selected candidates who may be available before that date). The initial salary will depend upon qualifications and experience, but will normally be within the range £800 to £1,100 per annum, together with F.S.S.U. benefits and family allowance. In the case of an overseas applicant, the University is also prepared to consider the provision of an allowance towards defraying the cost of travel to and from Great Britain. Forms of application and further particulars may be obtained from the undersigned.

Applications (two copies), should be submitted not later than February 16, 1961.

CHARLES H. STEWART,
Secretary to the University.

UNIVERSITY OF MELBOURNE

SENIOR LECTURESHIP IN CLINICAL BIOCHEMISTRY

Applications are invited for the above-mentioned position. The Senior Lecturer's duties will be chiefly with medical students and it is essential that he should be familiar with modern methods in clinical biochemistry. It is also desirable that he should hold a medical qualification. The salary range is £A.2,480 per annum to £A.2,950 per annum or, if medically qualified, £A 2,600 per annum to £A 3 250 per annum. Commencing salary will be fixed according to qualifications. Superannuation similar to F S S.U. in Great Britain will be provided.

Conditions of appointment may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W C.1. Applications close in Australia and London on February 4, 1961.

UNIVERSITY OF OXFORD

DEPARTMENT OF BIOCHEMISTRY

It is proposed to appoint a Departmental Demonstrator in Biochemistry as soon as possible. The salary will be up to £1,000 per annum (or up to £1,150 in the case of medically qualified candidates). The person appointed will be required to become a member of the Federated Superannuation System for Universities not later than two years after the date of his appointment, and an allowance of £50 per annum for each dependent child is payable.

Three copies of application, including a statement of age, qualifications and experience and giving the names of two referees, should be sent to the Administrator, Department of Biochemistry, South Parks Road, Oxford, not later than March 4, 1961.

FEDERAL GOVERNMENT OF NIGERIA

SCIENTIFIC OFFICER

(MINERAL DRESSER)

The Geological Survey Division of the Federal Ministry of Mines and Power have vacancies for Scientific Officers (Mineral Dressers) to undertake research on mineral dressing, particularly in connection with the recovery of minerals from alluvial concentrates in the Plateau tinfields.

Candidates should hold a good honours degree in mineral dressing or mining engineering, preferably with some experience in industry. Candidates should preferably not be over 35 years of age.

Contract appointment for one tour of 15 to 18 months in the first instance with prospect of extension. Salary according to qualification and experience £1,434 to £2,196 per annum (including inducement addition) plus gratuity of £100 to £150 on satisfactory completion of service. Outfit allowance of £60 payable for salaries not exceeding £1,740. Free passages for officer and wife. Liberal home leave on full pay. Quarters and income tax at low local rates. Children's allowances while separated.

Write for application forms and further particulars, stating briefly age, qualifications and experience, to the Appointments Secretary, Federal Public Service Commission, Nigeria House, 9 Northumberland Avenue, London, W C 2, quoting J.2/8.

IMPERIAL CANCER RESEARCH FUND

(DIVISION OF BIOCHEMISTRY)

Technical Officer (age 22 or over). Applicants should possess at least Higher National Certificate in Chemistry or equivalent qualifications, and have had experience in synthetic organic chemistry and/or micro-analysis and/or spectroscopy. Salary: £920 by £35 by £40 to £1,260 plus £20 London weighting. Junior Technical Officer (age 18 or over). Applicants should have G.C.E. A-level passes in chemistry and physics or equivalent. Training will be given in methods of micro-analysis and spectroscopy. Salary: £410 by £35 by £40 to £860 plus £10 London weighting.

Applications should be addressed to: Scientific Administrator, Imperial Cancer Research Fund, Lincoln's Inn Fields, London, W.C 2

UNIVERSITY OF LIVERPOOL

Applications are invited for Imperial Chemical Industries Research Fellowships in Physics, Chemistry, Biochemistry, Engineering, Metallurgy and Pharmacology or any related subjects. Appointments will date from October 1, 1961. The salary will depend upon qualifications and experience but will normally be within the range £700 to £1,000 per annum, together with F.S.S.U. benefits and family allowances.

Applications, three copies, stating age, details of qualifications and experience, publications, and research work in progress and completed, together with the names of two referees, should be received not later than February 11, 1961, by the Registrar from whom further particulars may be obtained. (Candidates overseas who find it more convenient to do so may send one copy only by airmail.) Ref. CV/N.

FEDERAL GOVERNMENT OF NIGERIA

SCIENTIFIC OFFICER

(GEOPHYSICIST)

The Geological Survey Division of the Federal Ministry of Mines and Power have vacancies for Scientific Officers (Geophysicist) to conduct geophysical surveys using a.c., and d.c. resistivity apparatus, d.c potential equipment, vertical forces magnetic variometer, shallow seismic gear, and equipment for logging resistivities and temperature gradients in boreholes.

Candidates must hold a good honours degree in geophysics, physics or engineering. Alternatively a good honours degree in geology, with physics or applied mathematics as subsidiary subjects. Experience in applied geophysics and some knowledge of electrical circuitry and an ability to maintain apparatus will be added advantages. Candidates should preferably not be over 35 years of age.

Contract: appointment for one tour of 15 to 18 months in the first instance with prospect of extension. Salary according to qualifications and experience £1,434 to £2,196 per annum (including inducement addition) plus gratuity of £100 to £150 on satisfactory completion of service. Outfit allowance of £60 payable for salaries not exceeding £1,740. Free passages for officer and wife. Liberal home leave on full pay. Quarters and income tax at low local rates. Children's allowances while separated.

Write for application forms and further particulars, stating briefly age, qualifications and experience, to the Appointments Secretary, Federal Public Service Commission, Nigeria House, 9 Northumberland Avenue, London, W.C.2, quoting J.3/8.

WEST AFRICAN COCOA RESEARCH INSTITUTE

GHANA

SENIOR BOTANIST

To take charge of the Botany Division comprising plant breeding and plant physiology sections. Candidates must have a first- or second-class honours degree in botany or equivalent qualification, with at least 15 years' research experience and a good record of published work. Proven ability to plan and supervise research programmes and experience with tree crops, preferably in the tropics, is also desirable. Appointment on contract/gratuity terms for two tours each of 15 to 18 months in the first instance. Salary in scale £2,460 to £2,940. Gratuity £12 10s. for each month of satisfactory service. Quarters with heavy furniture provided at moderate rental. Free return passages once in each tour for officer, wife and up to three children under 18 years of age. Generous leave. Education allowances.

Apply, stating name in full and giving brief particulars of qualifications and experience, to Director of Recruitment, Colonial Office, S.W.1, quoting BCD.197/200/028/C1.

JUNIOR TECHNICIAN FOR BIOCHEMICAL work required at once at Twyford Laboratories Ltd., Twyford Abbey Road, London, N.W 10. Training given in general laboratory and workshop practice, leading to assisting in research projects. Best of conditions and prospects. G.C.E. advanced level in two science subjects or equivalent required.—Apply to Secretary at above address.